THE NEUROPSYCHOLOGICAL AND PSYCHOSOCIAL DEVELOPMENT OF CHILDREN AND ADOLESCENTS WITH LIPOID PROTEINOSIS

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Dedication

This thesis is dedicated to my late father and mother, Dawie and Elsabe Steenberg, in thanks for their loving encouragement throughout my life and the example they had set as hard-working and passionate academics.

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Declaration

I declare that this thesis hereby submitted by me for the degree Philosophiae Doctor (Child Psychology) at the University of the Free State is my own independent work and has not previously been submitted by me at any other university or faculty. I furthermore cede copyright of the thesis in favour of the University of the Free State.

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Erika Steenberg

31 January 2014

Abstract

Lipoid proteinosis (LiP) is a rare hereditary disease, which often results in bilateral, symmetrical and circumscribed calcifications in the mesial temporal region (especially the amygdala). While studies on the neuropsychological and neuropsychiatric difficulties of adults with LiP have been published, a lack of research focusing exclusively on the neuropsychological and psychosocial development of children and adolescents with LiP was identified. A heterogeneous group of five children and adolescents with LiP, ranging in age from 4 to 17 years, and who represented the entire known population of children and adolescents with LiP in South Africa, was assessed with standardized neuropsychological measures and behaviour checklists. Two control participants were matched to each LiP participant according to IQ, home language, right- or left-handedness, sex, race and geographic environment (urban/rural). Each child or adolescent with LiP was compared separately with the control participants matched to them, as well as with the norm groups on which the various instruments were standardized. Variable results were obtained, but in general the children and adolescents with LiP performed significantly worse (practical significance) compared with controls on measures of memory, facial emotion recognition and executive function. Three of the LiP participants also adapted less well socially than their control participants did. All the LiP participants presented with behaviour problems, although the severity and types of behaviour problems varied. Two of the participants in this study presented with amygdala lesions that may have influenced their scores on neuropsychological measures and the ratings of their behaviour, but this possibility can be substantiated only by further research that includes the imaging of controls. The study provides a baseline assessment for future longitudinal and developmental research on LiP; therefore, the study can be regarded as a pilot study.

Key words: lipoid proteinosis, hereditary disorder, neuropsychological development, psychosocial development, age-related trends, neuropsychology, child, adolescent, South Africa

Opsomming

Lipoïedproteïnose (LiP) is 'n seldsame oorerflike siekte wat dikwels tot bilaterale, simmetriese en omskrewe verkalkings in die mesal-temporale brein area (veral die amigdala) lei. Die neuropsigologiese en neuropsigiatriese probleme van volwassenes met LiP is al voorheen ondersoek, maar 'n gebrek aan navorsing wat uitsluitlike op die neuropsigologiese en psigososiale ontwikkeling van kinders en adolessente met LiP fokus, is geïdentifiseer. 'n Heterogene groep van vyf kinders en adolessente met LiP, wie se ouderdomme van 4 tot 17 jaar gewissel het en wat die hele bevolking van kinders en adolessente met LiP in Suid-Afrika verteenwoordig het, is met gestandaardiseerde neuropsigologiese instrumente en gedragsvraelyste geassesseer. Twee kontrole-deelnemers is vir elke LiP-deelnemer volgens IK, huistaal, handvoorkeur, geslag, ras en geografiese omgewing (stad/platteland) afgepaar. Elke kind of adolessent met LiP is vergelyk met hulle spesifieke kontrole-deelnemers sowel as met die normgroep waarop die meetinstrumente gestandaardiseer is. Wisselende resultate is verkry, maar in die algemeen het die kinders en adolessente met LiP betekenisvol (praktiese beduidendheid) swakker as die kontrole-deelnemers op metings van geheue, herkenning van emosionele gesigsuitdrukking en uitvoerende funksies presteer. Drie van die LiP-deelnemers het ook sosiaal minder goed as hulle kontrole-deelnemers aangepas. Al die kinders en adolessente met LiP het gedragsprobleme getoon, alhoewel die intensiteit en tipes van gedragsprobleme gewissel het. Twee van die LiP-deelnemers het bilaterale verkalking van die amigdala getoon wat hulle resultate op neuropsigologiese instrumente en gedragsvraelyste kon beïnvloed het. Hierdie moontlikheid kan slegs bevestig word deur verdere navorsing te onderneem wat die beelding van die kontrolegroep sowel as die LiP-deelnemers insluit. Die studie verskaf 'n basislyn vir toekomstige longitudinale en ontwikkelingstudies; dus kan die studie as 'n loodsstudie gesien word.

Sleutelwoorde: lipoïedproteïnose, oorerflike afwyking, neuropsigologiese funksionering, psigososiale ontwikkeling, ouderdomverwante tendense, neuropsigologie, kind, adolessent, Suid-Afrika

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Chapter 1

Introduction

Lipoid proteinosis (LiP), also known as *Hyalinosis cutis et mucosae* or Urbach-Wiethe disease (UWD), is a rare hereditary disorder first described by Urbach and Wiethe (1929). This disorder is characterised by deposits of hyaline-like storage material in every organ, especially in the mucous membranes such as the mouth, pharynx, larynx and skin (Hamada, 2002). The most classic symptoms and signs of LiP are hoarseness, excessive and extensive scarring of the skin, a widespread warty hyperkeratosis, beaded eyelid papules, and thickening of vocal chords (Hamada et al., 2003). Radiological findings indicate that individuals with LiP often have bilateral calcifications in the anteromesial temporal region of the brain (Srinivasan, Ramprabananth, Srividya, & Ushanandhini, 2009; Yakout, Elwany, Abdel-Kreem, & Seif, 1985). The calcifications are hypothesised to be associated with a wide range of neurological, neuropsychiatric and neuropsychological symptoms (Thornton et al., 2008).

As the disorder is more prevalent in South Africa compared to other countries (Ramsay & Jenkins, 2003; Van Hougenhouck-Tulleken et al., 2004) a number of South African case studies of LiP have been published (Emsley & Paster, 1985; Gordon, Gordon, & Botha, 1969; Heyl, 1963). These case studies mainly focused on the physical symptoms of individuals with LiP and did not employ a control group when cognitive testing was done. In 2006, Thornton (2006) completed an extensive study on the neuropsychology and neuropsychiatry of LiP, concentrating on the South African community of individuals with the disorder. In line with wider literature on LiP, Thornton (2006) found that adults with LiP in the South African community often had epilepsy, cognitive deficits and psychiatric problems. Although the incidence of LiP in the Northern Cape community in South Africa is high, Thornton (2006) could find only a few children and adolescents under the age of 18 years with the disorder. The LiP participants under the age of 18 years in Thornton's (2006) study were interviewed and assessed via neuropsychological instruments, but their results were not included among the data that were analysed statistically. The researcher of this study was involved in the data-gathering phase of Thornton's (2006) study and had the opportunity to interview a 12-year-old child with LiP and his mother. The psychiatric interview indicated that this child had several psychiatric diagnoses. This led to an interest

in the effect of LiP on the functioning of children and adolescents with the disorder. Previously, Steenkamp (1997) explored the emotional and psychosocial adjustment of a few adolescents and adults with LiP. However, Steenkamp's (1997) research did not extend to the neuropsychological aspects of the disorder, and children were not included in the study.

Noticing a lack of research on the neuropsychological and psychosocial functioning of children and adolescents with LiP, the researcher identified an unexplored area of research in the field. The researcher was encouraged to complete a study that focused specifically on children and adolescents with LiP. Such research was viewed as an important initial step in understanding the progression of cognitive and psychosocial difficulties in LiP and the development of individuals with the disorder.

Problem Statement

Several cases of children and adolescents with LiP in South Africa and worldwide have been reported since the disorder was first described. Examples of such reports include case studies by Acar, Yildiz, Yuksel, Ustun and Unlu (2012), Kaya, Tursen, Kokturk, Ikizoglu, and Dusmez (2003), Omrani et al. (2012), and Van Rooy, Swart, and Pietrzak (1991). Generally, these studies have been limited to the physical symptoms, genetic aspects and treatment of the disorder. The onset of the physical symptoms of LiP is often described to be early in life and even at birth. Central nervous system (CNS) symptoms and signs, such as calcification of the amygdala and epilepsy, have also been described in children and adolescents with LiP (Baykal, Topkarci, Yazganoglu, Azizlerli, & Bykan, 2007; Brajac, Kaštelan, Gruber, & Periš, 2004). However, much less is known about the onset and progression of CNS signs and symptoms compared to the physical signs and symptoms of the illness.

Generally, temporal lobe pathology and temporal lobe lesions in children and adolescents are associated with several neuropsychiatric and neuropsychological difficulties such as depression, memory deficits, psychosis and epilepsy (Caetano et al., 2007; De Haan, Mishkin, Baldeweg, & Vargha-Khadem, 2006; Fogarasi & Arzimanoglou, 2011). Early amygdala damage and pathology are also linked with deficits in social cognition and atypical social development (Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004b; Fine, Lumsden, & Blair, 2001; Munson et al., 2006). Taking into account

the general literature on temporal lobe lesions in children and adolescents, it seems possible that temporal lobe lesions (and specifically bilateral amygdala lesions) associated with paediatric LiP may have a negative effect on the neuropsychological and psychosocial development of children and adolescents with the disorder.

Sparse reports of the cognitive and psychosocial functioning of children and adolescents with LiP suggest that they may have similar cognitive, neuropsychiatric and psychosocial difficulties than adults with the disorder (Emsley & Paster, 1985; Steenkamp, 1997; Thornton, 2006). However, it has been suggested that bilateral temporal lobe lesions are associated with the duration of the disease (Appenzeller et al., 2006; Baykal et al., 2007; Rahalkar, Kelkar, Gharpuray, & Patwardhan, 2001). Therefore, the age of onset and progression of signs and symptoms may determine which cognitive and psychosocial difficulties are present and to what extent. Owing to ongoing development during childhood and adolescence, the neuropsychological and psychosocial difficulties of children and adolescents with LiP may differ from those of adults with the disorder.

General literature on children and adolescents with skin disorders and hoarseness indicate that the visibility of their skin lesions and the noticeability of their hoarse voices often have a negative effect on their social interaction and adjustment (Connor et al., 2008; Lewis-Jones, 2006; Walker & Lewis-Jones, 2006). Therefore, it is likely that children and adolescents with LiP, who very often have had skin lesions and hoarseness since infancy, may struggle with psychosocial adjustment. This has been confirmed by a study reporting psychosocial difficulties in adolescents with LiP (Steenkamp, 1997). However, literature on the prevalence, onset and progression of calcifications of the amygdala and the neuropsychological and psychosocial functioning of children and adolescents with LiP is limited (Emsley & Paster, 1985; Savage, Crockett, & McCabe, 1988; Steenkamp, 1997; Thornton, 2006). Consequently, the cognitive and psychosocial difficulties of children and adolescents with LiP and the progress of the illness throughout childhood and adolescence are still poorly understood. Therefore, it was deemed necessary to expand the knowledge base regarding the neuropsychological and psychosocial functioning of children and adolescents with LiP.

Aims of the Study

The primary aim of this study is to increase knowledge and understanding of the neuropsychological and psychosocial functioning of children and adolescents with LiP. The study aims to describe the neuropsychological and psychosocial functioning of children and adolescents with LiP and to compare their functioning with typically normal developing peers.

The secondary aim of the study is to explore whether any developmental or age-related trends are apparent in the neuropsychological and psychosocial functioning of children and adolescents with LiP across age and to what extent such developmental age-related trends may differ between children and adolescents with the disorder and typically normal developing peers.

Exposition of Chapters

Because LiP is a rare genetic disorder, Chapter 2 concentrates on a description of the prevalence, genetics, pathophysiology, signs and symptoms of the illness. This chapter also concentrates on what is known about the neuropsychological and psychosocial functioning of adults with LiP, as more research is available with regard to their difficulties. Children and adolescents with LiP may have the same neuropsychological, neuropsychiatric and psychosocial difficulties as adults with the disorder. Therefore, this chapter will provide a background of what is known about the illness.

Chapter 3 provides a literature review of the presentation and progression of symptoms and signs of LiP, specifically during childhood and adolescence, in order to illustrate the potential effect it may have on the development of individuals with this disorder. This is followed by a description of the research on the neuropsychological and psychosocial functioning of children and adolescents with LiP. As this information is limited, the effects of early temporal lobe or amygdala damage on the neuropsychological functioning (memory, social perception and executive function) of children and adolescents with other conditions, as well as the effect of disfigurement and hoarseness on psychosocial development, are discussed.

Chapter 4 deals with the aims and hypotheses, study design, participants, data collection procedures, measures, ethical considerations and statistical analysis of data, while the results of the research are reported in Chapter 5. In Chapter 6, the results obtained on the neuropsychological measures and behaviour checklists are discussed. Chapter 7 contains the main conclusions, limitations and recommendations for future research.

Chapter 2

Prevalence, Genetics, Pathophysiology, Signs and Symptoms of LiP

Lipoid proteinosis (LiP) is a rare autosomal recessive disorder, also known as Urbach-Wiethe Disease (UWD) or *hyalinosis cutis et mucosae* (Feiler-Ofry et al., 1979; Gordon et al., 1969; Horev et al., 2005). LiP is one of more than 40 neurocutaneous disorders that typically affect the nervous system (both the CNS and ANS) and the skin, although several other organs may also be affected (Rook, 1976; Sanat & Flores-Sanat, 2006). As deposits of hyaline-like material are stored and have been found in various organs of the body, LiP can also be described as a systemic illness (Caccamo, Jaen, Telenta, Varela, & Tiscornia, 1994; Caplan, 1967; Feiler-Ofry et al., 1979; Newton, Rosenberg, Lampert, & O'Brien, 1971), but the effect of deposits of hyaline-like substances in the mucous membranes and skin is generally more apparent clinically (Cordoro, Osleber, & DeLeo, 2013).

The signs and symptoms of the disorder include mucocutaneous symptoms, such as skin vulnerability, plaque-like infiltrates, deposition of hyaline material in the larynx leading to hoarseness, and extracutaneous symptoms, such as bilateral calcifications in the medial temporal areas of the brain (Vago, Hausser, Hennies, Enk, & Jappe, 2007). The severity of the signs and symptoms of the disorder varies between individuals (Nasiri, Sarrafi-rad, Kavand, & Saeedi, 2008; Salih et al., 2011; Van Hougenhouck-Tulleken et al., 2004). Despite it being well described that signs and symptoms are often present at birth or in early infancy (Nanda et al., 2001; Salih et al., 2011; Scott & Findlay, 1960), LiP amongst adults has been researched significantly more than it has been among children and adolescents. This necessitates an initial outline of what is known about LiP in adulthood in order to provide a context for a discussion of the condition in children and adolescents.

Thus, this chapter aims to provide an overview and description of LiP in general. The prevalence, genetics and pathophysiology of the condition will be reviewed first, followed by the most prominent signs and symptoms of LiP. Finally, the neuropsychological, psychiatric and psychosocial difficulties most commonly associated with LiP will be highlighted.

The Prevalence of LiP in Adults

Between 350 and 400 cases of LiP have been reported worldwide (Aroni, Lazaris, Papadimitriou, Paraskevakou, & Davaris, 1998; Thornton et al., 2008). The reported incidence of LiP in South Africa (Van Hougenhouck-Tulleken et al., 2004), Sweden (Aroni et al., 1998) and Turkey (Dogramaci, Murat, Celik, & Bayaroullari, 2012) is higher when compared to other parts of the world. The number of reported cases in Turkey has reached 84 (Dogramaci et al., 2012). Xu, Wang, Zhang, Han, & Zhang (2010) also suggest that LiP might not be as rare in China as was assumed previously. The authors (Xu et al., 2010) report 22 Chinese individuals from 19 families who visited a Chinese clinic since 2006. Rook (1976) cautions that the apparent rarity of LiP in some countries could be due to a lack of familiarity with its signs and symptoms. Nevertheless, it is reported that approximately one third of the known cases of LiP in the world (i.e. approximately 100 cases) have been reported in South Africa, with most of these in the Northern Cape region (Van Hougenhouck-Tulleken et al., 2004). Van Hougenhouck-Tulleken et al. (2004) estimate a LiP incidence of one in every 324 people in the Northern Cape community, based on the LiP carrier rate among 100 asymptomatic Namaqualand people. Thus, while the world prevalence of LiP appears to be relatively low, the prevalence in South Africa, particularly in the Northern Cape region, seems to be relatively high.

Genetics and LiP

To understand the genetics of LiP, the concepts of mutation and inheritance as they relate to LiP need to be reviewed.

Mutation

All South African individuals with LiP seem to be homozygous for the mutation Q276X in exon 7 (Ramsay & Jenkins, 2003; Van Hougenhouck-Tulleken et al., 2004). According to Van Hougenhouck-Tulleken et al. (2004), this confirms the view that all LiP individuals in South Africa are descended from a single founder family. The mutation Q276X most likely achieved its high frequency in Namaqualand through rapid population expansion from a relatively small population and through a high degree of initial inbreeding (Van Rooy et al., 1991). Owing to the identification of the gene, LiP can be

diagnosed more effectively now by using an anti-extracellular matrix protein 1 antibody, and it makes carrier screening feasible (Chan, Liu, Hamada, Sethuraman, & McGrath, 2007; Hamada, 2002).

Inheritance Pattern

LiP follows an autosomal recessive inheritance pattern (Hamada et al., 2002; Horev et al., 2005) and is equally prevalent in both sexes (Aroni et al., 1998). In recessive inheritance, the disorder is apparent in offspring when both parents are carriers, when one parent is affected and the other is a carrier or when both parents are affected (Phelps, 2004). Thus, the probability of inheritance is 25% when both parents are carriers, 50% when one parent is affected and the other is a carrier, or 100% when both parents are affected. Therefore, symptomatic children can be born to asymptomatic parents (carriers), but when both parents are symptomatic, all their children will have the illness. Affected individuals (carriers or symptomatic individuals) with unaffected partners (neither symptomatic nor a carrier) have only unaffected children (Phelps, 2004). The autosomal recessive inheritance pattern of LiP implies that more than one member of a family and extended family may be affected (Al-Natour, 2008; Kurtoglu, Atabek, Adal, & Pirgon, 2007; Wang et al., 2006). Despite the fact that family members can have the same condition (LiP), the severity of symptoms and signs often varies from one family member to another (Ehsani, Ghiasi, & Robati, 2006; Nasiri et al., 2008; Poyrazoğlu, Günöz, & Darendeliler, 2008; Stephan et al., 2013).

Pathophysiology of LiP

The details of the different hypotheses (Newsome, 2004; Sboukis, Kobayasi, and Karamerist, 2003; Sercu et al., 2008; Uchida, Hayashi, Inaoki, Miyamoto, and Fujimoto, 2007) with regard to the pathogenesis of LiP will not be discussed here. A basic understanding of the pathophysiology of LiP is that the mutated ECM1 gene gives rise to loss of protein-protein interactions, thereby causing skin and other abnormalities such as hoarseness (Hamada et al., 2002; Staut & Naidich, 1998). Hyaline material is deposited in the dermis and mucous basement membrane around blood vessels and adnexal epithelia followed by infiltration of the surrounding connective tissue (Muda et al., 1995; Ringpfeil, 2005). This results in symptoms such as thickening of the skin, recurrent parotitis, infiltration of the larynx (Rallis et al., 2006; Savage et al., 1988), and anomalies in the

respiratory and upper digestive tract (Ramsay & Jenkins, 2003; Van Hougenhouck-Tulleken et al., 2004).

According to Salih et al. (2011), the ECM1 gene has several transcripts, each of which may be differentially active in various tissues, including various parts of the brain. ECM1 interacts with other proteins (Salih et al., 2011), including MMP-9 (matrix metalloproteinase) that was suggested to have an important role in temporal lobe synaptic physiology (Wilczynski et al., 2008). Therefore, ECM1 mutations might affect brain function, compromise homeostasis or impair repair mechanisms in the temporal lobes of individuals with LiP (Ching, Zhang, Chew & Quan, 2007; Fujimoto et al., 2006). Hamada (2002) hypothesised that, because Exon 7 of ECM1 also contains a calcium-binding domain, an absence of this motif in LiP might help explain the intracranial calcification present in some LiP individuals. This abnormality may result in thickening of the capillary walls and other small vessels, predominantly in the capillaries of the hippocampus, which later progresses to perivascular calcium deposition (Appenzeller et al., 2006; Kleinert, Cervus-Navarro, Kleinert, Walter, & Steiner, 1987). Small areas of perivascular infarctions and demyelination, in addition to calcification, have been noted in the adjacent brain area (Teive et al., 2004; Yakout et al., 1985). This ultimately leads to distortion of the medial temporal lobe structure (Claeys et al., 2007). The signs and symptoms of LiP will now be described in more detail.

Signs and Symptoms of LiP

Hoarseness and Skin Signs

Skin signs and hoarseness are the two most prominent mucocutaneous signs of LiP (Hamada et al., 2002; Vago et al., 2007; Van Hougenhouck-Tulleken et al., 2004). Although variable in the onset, progression and intensity of hoarseness is evident (Amichai, Grunwald, Zvulunov, Avinoach, & Halevy, 1996; Hofer, 1974), it develops in almost all people with LiP (Van Hougenhouck-Tulleken et al., 2004). In most cases, these symptoms are the first clinical manifestations of LiP and are often present at birth or in early infancy (Grosfeld, Spaas, & Auping, 1964; Hofer, 1974).

Skin lesions and scarring are evident in LiP, as the skin is markedly vulnerable (Hamada et al., 2002). Van Hougenhouck-Tulleken et al. (2004) found that scarring was

particularly evident on the face and usually started in childhood. Yellowish-whitish, beaded papules on the eyelid margins were found to be a classic sign of LiP (Blodi, Whinery, & Hendricks, 1960; Vago et al., 2007). Scarring alopecia and delayed hair and nail growth are also mucocutaneous signs of LiP (Vago et al., 2007).

Skin lesions may increase in severity and extent as the person grows older (Feiler-Ofry et al., 1979; Hofer, 1974; Nagasaka, Tanaka, Ito, Tanaka, & Shimizu, 2000). The formation of lesions occurs in two overlapping stages (Hamada et al., 2003). The first stage, lasting for several years and often continuing into the late teens, is characterised by blistering, erosions and pustulation (Van Hougenhouck-Tulleken et al., 2004). Healed eruptions result in depressed acneiform scarring with altered pigmentation (Kaya et al., 2003). During the second stage, the skin becomes thickened and yellowish due to the hyaline deposits, and waxy papules and plaques develop predominantly on the face, scrotum and axillae (Hamada et al., 2003). It has been suggested that frequent exposure to the sun might lead to a more severely scarred and aged appearance (Sander et al., 2006; Van Hougenhouck-Tulleken et al., 2004). Therefore, individuals living in semi-arid areas, such as the Northern Cape, may have a more severely scarred and aged skin appearance compared to individuals living in a different geographical area. Because of their visibility and cosmetic consequences, the skin signs and symptoms may have a negative effect on the psychosocial functioning of individuals with LiP. Furthermore, hoarseness may have a negative effect on the individual's communication with others and subsequent psychosocial development.

Extracutaneous Signs and Symptoms of LiP

Other organs and systems (beside the skin and CNS) that are affected by LiP include the endocrine system (recurrent parotitis), the respiratory and digestive systems (Al-Ekrish & Al-Sadhan, 2012; Caccamo et al., 1994; Parimalam, Sampath, & Manoharan, 2009), and the eyes (Abtahi et al., 2012; Bahadir et al., 2006; Sainani, Muralidhar, Parthiban, & Vijayalakshmi, 2011). Van Hougenhouck-Tulleken et al. (2004) found that symptoms in the upper respiratory tract (difficulty in breathing, worsening of respiratory difficulties triggered by infections of the upper respiratory tract) were the most significant features causing morbidity in people with LiP. Xerostomia, dysphagia, speech impediments, immobile hardened tongue, tongue ulcerations, vesicular glossitis, transient lip and tongue

swelling and difficulty opening the mouth have been reported frequently in LiP due to the infiltration of the upper aero digestive system (Vago et al., 2007). The eyesight, colour vision and eye sensitivity of individuals with LiP can also be affected due to hyaline deposits in the conjunctiva, cornea, trabecula, iris and retina or other rare ocular manifestations (Abtahi et al., 2012; Maize, Maize, & Metcalf, 2009; Sellami et al., 2006). According to Bahadir et al. (2006), focal degeneration of the macula has been found in a third of examined LiP patients reported in the literature.

Apart from the extracutaneous symptoms and signs associated with the deposition of hyaline material, LiP also brings about certain congenital abnormalities (Chan et al., 2003; Vago et al., 2007). Dental surgery is sometimes necessary due to aplasia and additional teeth (Marta et al., 2008).

The description of the extracutaneous and congenital signs and symptoms of LiP indicates the extensive nature of the disorder, involving several organs and systems of the body.

Central nervous System Signs and Symptoms

Epilepsy. The most prevalent neurological complication in LiP is reported being epilepsy (Baykal et al., 2007; Newsome, 2004). Both partial and secondary generalised seizures, including absence seizures, can occur in people with LiP during adulthood or in childhood (Hofer, 1973; Johnson & Hepler, 1989; Messina et al., 2012; Newton et al., 1971). The worldwide incidence of seizures in LiP is unknown (Claeys et al., 2007), but Thornton (2006) notes a 27% reported incidence of epilepsy among people suffering from LiP in the Northern Cape (South Africa) and a 71% confirmed incidence in a non-Northern Cape (South African) LiP group.

The presence of calcified foci in close proximity to the temporal cortex appears to be of aetiological significance with regard to epilepsy in LiP (Hurlemann et al., 2010; Newton et al., 1971), possibly suggesting the association between the lesion severity and the onset of epilepsy. However, Chan et al. (2007) indicated that epilepsy in LiP not necessarily always correlates with the presence or absence of brain calcification. Furthermore, infrequent epileptic discharges in the temporal-occipital brain regions of a brother and sister with LiP were observed via EEG, whereas they denied having seizures (Al-Natour,

2008). The literature suggests that seizures are prevalent in a substantial proportion of individuals with LiP, but the association between seizures and temporal lobe calcification in these individuals is not completely clear.

Intracranial manifestations. The true incidence of brain calcification in LiP is difficult to estimate, as not all affected individuals undergo brain imaging (Chan et al., 2007). Nonetheless, it has been reported that 50% to 75% of individuals with LiP over the age of 10 years, have bilateral amygdala calcifications (Aroni et al., 1998; Hamada et al., 2002; Hofer, 1973).

The dominant brain pathology in individuals with LiP is bilateral calcification of the amygdala and parahippocampal gyrus (Appenzeller et al., 2006; Doğru et al., 2008; Friedman, Mathews, & Swanepoel, 1984; Gonçalves, De Melo, Matos, Barra, & Figueroa, 2010; Leonard, Tyan, & Sheldon, 1981; Özbek, Akyar, & Turgay, 1994; Siebert, Markowitsch, & Bartel, 2003). Lesions or other abnormalities can also be found in isolation, or additional to the amygdala lesions, in any area of the brain such as the head of the caudate, *globus pallidus* (Newton et al., 1971), basal nuclei (Anderson, Costantion, & Stratford, 2004), striatum (Goncalves et al., 2010), lentiform nucleus, pineal gland, left semi oval centre (Siebert et al., 2003), uncal region (Quirici & Da Rocha, 2013), posterior cranial fossa area (Kachewar & Kulkarni, 2012) and parietal cortex (Doğru et al., 2008; Şenol et al., 2007; Siebert et al., 2003). Complete degeneration of all portions of the amygdala is often present (Francis, 1975; Hurlemann et al., 2010), while bilateral decreased perfusion is sometimes evident (Siebert et al., 2003).

Amygdala lesions were suggested to be progressive (Hurlemann et al., 2010; Siebert et al., 2003; Terburg et al., 2012). Siebert et al. (2003) found that amygdala calcifications in LiP tend to expand into the uncinate and parahippocampal gyri over time. Repeated scanning of two adult twin sisters with LiP indicated that their amygdala lesions initially primarily affected the basolateral sub region alone, but after a period of approximately three years, their lesions progressed to incorporate the whole amygdala region (Hurlemann et al., 2010). Terburg et al. (2012) found that the three younger women in a group of five had calcified brain tissue localised in the basolateral amygdala, but the lesions in the two oldest research participants appeared to extend into the borders of the right superficial or corticoid amygdala.

Intracranial calcification in LiP seems to be associated with neurological, neuropsychiatric and neuropsychological sequelae (Claeys et al., 2007; Thornton et al., 2008; Wiest, Lehner-Baumgartner, & Baumgartner, 2006). Neurological sequelae include seizures (Ito et al., 2000; Omrani et al., 2012), ataxia (Kleinert et al., 1987), migraine (Arkadir et al., 2013; Claeys et al., 2007; Messina et al., 2012) and dystonia (Teive et al., 2004). In addition, Messina et al. (2012) reported the case of an adult woman with LiP who presented with a left lenticular nucleus haemorrhage, resulting in right hemiparesis and consequently motor slowing. After excluding any other causes, the authors concluded that the haemorrhage was most likely the consequence of alterations of the brain blood vessels due to the impact of the ACM1 (protein) mutation in LiP. It was not known how many individuals with LiP might have presented with similar (hemiparesis) symptoms (Messina et al., 2012). Although neurological and neuropsychological sequelae in LiP are mostly associated with intracranial calcifications, this is not always the case (Maruani et al., 2007). Adults with LiP may have neuropsychiatric or neurological symptoms (such as seizures) in the absence of intracranial calcifications (Chan et al., 2007; Maruani et al., 2007). Furthermore, neurological and neuropsychiatric symptoms are not always evident in individuals with intracranial calcifications (Aziz, Mandour, El-Ghazzawi, Belal, & Talaat, 1980; Friedman et al., 1984; Yakout et al., 1985). Therefore, the association between neurological and neuropsychiatric sequelae in LiP and intracranial calcification is not always clear.

Other yet unidentified brain mechanisms or less visible brain changes may explain the final manifestation of neuropsychiatric pathology in LiP (Hurlemann et al., 2009; Maruani et al., 2007). One such mechanism may be a decrease in serotonergic neurotransmission (a decrease in 5-HT receptor binding potential), frequently linked to anxiety and mood symptoms (Albert & Lemonde, 2004; Owens & Nemeroff, 1998; Senkowski, Linden, Zubrägel, Bär, & Gallinat, 2003) and altered memory and executive processes (Enge, Fleischhauer, Lesch, Reif, & Strobel, 2011; Harrell & Allan, 2003) in individuals not suffering from LiP. Neuropsychiatric and neurological symptoms may be associated with brain changes that are not observed easily on CT or MRI (Maruani et al., 2007). Maruani et al. (2007) examined a patient with LiP who presented with ataxia, dizziness, psychomotor retardation and amnesia. By means of brain scintigraphy in their patient with LiP, the authors (Maruani et al., 2007) observed bilateral hypoperfusion of the frontal areas, the anterior and internal right temporal lobe, including the amygdala, and of the left

thalamic core. *Brain scintigraphy* is an imaging procedure in which a radioisotope is administered intravenously, and its distribution is then monitored with a gamma camera to form two-dimensional images (Brain scintigraphy, 2008).

Boes et al. (2011) and Morgan (personal communication, 28 July 2009) have suggested other structural brain differences in LiP. Morgan (personal communication, 28 July 2009) explained that the results of an unpublished MRI study of a group of females with LiP showed highly selective bilateral amygdala calcification as well as generalised volume decreases in gray and white matter. The orbitofrontal cortex was most affected. It was postulated that the orbitofrontal volume decreases were due to early loss of the amygdala, as the orbitofrontal cortex develops from the amygdala (Mega, Cummings, Salloway, & Malloy, 1997) and depends on the amygdala for in- and output (Bachevalier & Loveland, 2006; Mega et al., 1997). Boes et al. (2011) also observed (MRI) morphometric abnormalities in two patients with longstanding focal bilateral amygdala lesions caused by LiP. Both individuals in the study by Boes et al. (2011) showed significant proportional increases in the volume of gray matter of the ventromedial prefrontal cortex (VMPFC) and anterior cingulate cortex (ACC), while cortical thickness was increased in the VMPFC and ACC and decreased in the ventral visual stream. There were no morphometric changes in the dorsolateral prefrontal cortex or dorsal visual stream cortices. The findings are contradictory, as one study indicated decreased gray matter volume, especially in the orbitofrontal area (Morgan, personal communication, 28 July 2009), whereas the study by Boes et al. (2011) indicated increased gray matter volume in other brain areas. Nevertheless, the findings from both studies (Boes et al., 2011) indicate that cortical regions connected to the amygdala undergo structural changes with longstanding amygdala damage.

Overall, available information seems to suggest that the principal brain degeneration in LiP lies within the amygdala, but individuals with LiP may also have more widespread brain damage. There is increasing evidence of variables associated with structural and neurochemical changes in the brains of individuals with LiP (Hurlemann et al., 2009).

Neuropsychological Deficits in Adults with LiP

Despite the presence of bilateral circumscribed calcifications in LiP, the literature on the neuropsychology of LiP is limited, due to the rarity of the condition. Most researchers

were restricted to using single case studies or including small groups in their studies of the neuropsychological functioning of individuals with LiP (Adolphs, Cahill, Schul, & Babinsky, 1997; Hurlemann et al., 2007; Markowitsch, Calabrese, & Wurker, 1994). In these studies, the same individuals with LiP were often tested over several years. An example thereof is the extensive range of published research papers based on experimental and neuropsychological research involving the woman identified as "SM" (Gupta, Duff, & Tranel, 2011; Paul, Corsella, Tranel, & Adolphs, 2010; Tranel & Hyman, 1990). Most individuals with LiP who participated in neuropsychological or neuroscience research presented with bilateral amygdala lesions as identified by CT and MRI (Bach, Hurlemann, & Dolan, 2013; Tranel & Hyman, 1990; Van Honk, Eisenegger, Terburg, Stein & Morgan, 2013). The main aim of much of the published research on LiP appears to have been to gain a better understanding of the effects of amygdala lesions on social cognition and emotional memory (Adolphs, Baron-Cohen, & Tranel, 2002; Calder et al., 1996; Gosselin, Peretz, Johnsen, & Adolphs, 2007; Markowitsch et al., 1994). Bihippocampal lesions, associated with memory impairment, have also been described (Emsley & Paster, 1985; Ghika-Schmid et al., 1997) – the results thereof will be elaborated on in the section on memory functioning in persons with LiP. Research on LiP also included descriptions of neuropsychological assessment results that were more extensive (Hurlemann et al., 2007; Siebert et al., 2003; Tranel & Hyman, 1990), and included a study on the neuropsychological functioning of a large group of individuals with LiP (Thornton et al., 2008). Consequently, more information became available with regard to a range of neuropsychological functions such as attention and executive functioning in individuals with LiP.

Recent studies provided more information with regard to changes in the neuropsychological functioning of individuals with LiP over time during adulthood (Feinstein, Adolphs, Damasio, & Tranel, 2011; Hurlemann et al., 2010). One such study indicated no deterioration of neuropsychological functioning, despite progression of amygdala lesions noted on MRI in two adult monozygotic twins with LiP (Hurlemann et al., 2010). Similarly, Feinstein et al. (2011) remarked that SM (the woman with LiP first described by Tranel & Hyman in 1990) displayed stable neuropsychological functioning and behaviour over a period of two decades, despite additional lesions appearing in the putamen to the end of this period. These studies included only one and two individuals with LiP respectively, and the results may therefore not represent the nature of the

progression of neuropsychological deficits in all individuals with LiP. Memory, social cognition, attention, and executive functioning in adults with LiP will now be discussed in more detail.

Memory and Learning

The view that there are different memory systems and that a distinction can be made between declarative and non-declarative memory is now accepted widely (Lum, Kidd, Davis, & Conti-Ramsden, 2010; Markowitsch, 2008; Squire, 2004). Declarative memory supports the capacity to recollect facts and events and can be contrasted with non-declarative memory abilities such as motor learning, habits, simple forms of conditioning and priming (Squire & Zola, 1996).

The neural correlates of memory and learning. Although Brand and Markowitsch (2006) postulated that the neural correlate of declarative memory was not a single brain structure, it was suggested that the structures of the medial temporal lobe memory system (hippocampal region and the adjacent entorhinal, perirhinal and parahippocampal gyrus and amygdala) are specifically important for declarative memory (Corkin, 2002; Markowitsch, 2000; Piguet & Corkin, 2005; Squire, 1992; Squire, Stark, & Clark, 2004). It was suggested that the medial temporal lobe structures are anatomically and functionally diverse and that declarative memory functions depend on the dynamic interaction among specific medial temporal lobe structures, as well as on interactions with widely distributed cerebral regions (Tulving & Markowitsch, 1998). There is ongoing research into the distinct roles of the various medial temporal lobe structures and pathways in memory processes (Suzuki & Amaral, 2004). Some research findings were suggested to provide anatomical evidence that the hippocampus, perirhinal and parahippocampal areas and the amygdala seem to play distinct roles in memory processes (Phelps et al., 1998; Vargha-Kadem et al., 1997; Zola-Morgan, Squire, Amaral, & Suzuki, 1989).

Two interconnected but separable limbic circuits were proposed to be important for encoding and consolidating information, namely the Papez circuit and the amygdaloid or basolateral limbic circuit (Brand & Markowitsch, 2006). Owing to its important role in processing the emotional significance of emotional stimuli, it was proposed that the amygdala is involved in emotional memory and contingency learning, viewed as a form of implicit memory (LeDoux, 1996; Sah, Faber, De Armentia, & Power, 2003). Neural

projections from the amygdala were suggested to target several other memory systems (including the declarative and non-declarative memory system) in the brain, enhancing memory for emotionally relevant or arousing stimuli (Brand & Markowitsch, 2006; Kensinger & Corkin, 2004).

Research results suggest that bilateral damage to medial temporal lobe structures in adults leads to impairment of declarative memory (Corkin, 1984; Levy et al., 2003; Neylan, 2000; Squire, Schmolk, & Stark, 2001). Bilateral amygdala lesions are possibly associated with specific deficits in emotional memory (Adolphs, Tranel, & Buchanan, 2005; Cahill, Babinsky, Markowitsch, & McGaugh, 1995). Based on the literature, it seems plausible that temporal lobe lesions caused by LiP may be associated with deficits in learning, working memory, declarative memory, emotional memory, and some forms of non-declarative memory.

Declarative memory deficits in LiP. Variable memory deficits have often been identified in individuals with LiP (Ghika-Schmid et al., 1997; Quirici & Da Rocha, 2013; Thornton et al., 2008) and some studies also indicated intact declarative memory functions (Brand, Grabenhorst, Starcke, Vandekerckhove, & Markowitsch, 2007; Hurlemann et al., 2007). There does not seem to be any specific pattern of memory deficits, such as mostly verbal versus mostly visual memory deficits, in adults with LiP (Siebert et al., 2003; Thornton et al., 2008). The research results of a study by Thornton et al. (2008) indicate a general tendency for deficits in both verbal and visual memory, as well as verbal learning. Thornton et al. (2008) reported deficient verbal learning, verbal recognition memory, immediate and delayed verbal memory, as well as delayed visual memory in individuals with LiP.

The variable memory functioning in individuals with LiP may be the consequence of variable brain pathology (Siebert et al., 2003). For instance, a group of individuals with LiP and memory deficits (Siebert et al., 2003) presented mostly with clearly visible complete degeneration in all portions of the amygdaloid complex bilaterally, but with variable additional brain pathology. Three individuals appeared to have decreased bilateral perfusion in the temporal lobes tending to expand into the uncinate and parahippocampal gyri. Other calcifications were also found in some of the participants, such as small bilateral calcifications in the lateral parietal cortex and bilateral calcification in the

lentiform nucleus, and in one individual, the right basal ganglia were affected (Siebert et al., 2003). However, no specific correlations between the types and severity of the brain lesions and types of memory deficits have been identified in the study by Siebert et al. (2003) or in any other study. The exception is that variable temporal lobe lesions seem to be present in all individuals with LiP who had memory deficits and for whom individual imaging data were described, such as reported by Emsley and Paster (1985) and Tranel and Hyman (1990).

Overall, the literature suggests that variable deficits in declarative memory (immediate and delayed verbal memory, visual memory, verbal learning, and recall of affective words) have been reported in individuals with LiP. An association between bilateral circumscribed temporal lobe lesions and memory deficits in LiP seems very likely, given indications in the literature on the neurological substrate underlying memory functions in general as well as in the literature on memory functioning in adults with LiP.

Emotional memory deficits in LiP. Studies of individuals with LiP and bilateral amygdala calcification indicate that memory for verbal and visual emotional material and memory for biographical information were often deficient when compared to controls (Adolphs et al., 1997; Babinsky et al., 1993; Cahill et al., 1995; Markowitsch et al., 1994). The small number of individuals with LiP included in some studies did not allow generalisable conclusions with regard to the effect of amygdala damage on emotional memory (Adolphs et al., 1997), but a study of a group of ten individuals with LiP (Siebert et al., 2003) confirmed the deficits in emotional memory. Siebert et al. (2003) found that memory for emotionally arousing material was highly impaired in this group of individuals with LiP. Individuals with LiP remembered negative and positive emotional pictures much more poorly when compared to controls, while valence judgments of negative, positive, and neutral pictures were similar between individuals with LiP and controls. These results are consistent with research results indicating that arousal, but not valence of emotional stimuli, seems to be the primary factor in encoding and remembering (Kensinger & Corkin, 2004). Brand et al. (2007) also reported poor performance ($p < 0.05$) in individuals with LiP on a measure of delayed free recall of memory for affective words. Deficits in emotional memory among individuals with LiP may be explained by the role of the amygdala in enhancing memory for emotionally meaningful stimuli, and therefore, their performance in this task may have been affected negatively by amygdala damage.

Recent studies by Bach, Talmi, Hurlemann, Patin, and Dolan (2011) and Tsuchiya, Moradi, Felsen, Yamazaki, and Adolphs (2009) show that, although conscious recollection of emotional material in adults with LiP is affected by amygdala damage, automatic or low-level processing and subsequent recall of aversive words occurred normally in the presence of amygdala damage. This conclusion was based on a study of two individuals with bilateral amygdala lesions, showing that they retained facilitated recall of aversive words during the attentional blink (Bach et al., 2011). The attentional blink refers to a paradigm where two masked targets (T1 and T2) are presented within approximately 500 ms of each other (Shapiro, Arnell, & Raymond, 1997, p. 291). People are often unable to report the second target (T2) correctly, even though they reported the first target (T1) accurately. Researchers (Isaak, Shapiro, & Martin, 1999; Shapiro, Raymond & Arnell, 1994) hypothesised that allocating attention to T1 and allocating attention to the presentation of interference stimuli following T2 leaves less attention for T2, rendering T2 vulnerable to decay. In the study by Bach et al. (2011) emotionally arousing words were presented within a trial consisting of rapid serial visual presentations, leading to prioritising of the emotionally relevant items (aversive words) by LiP persons with amygdala damage as well as controls. This result may indicate that automatic processing and subsequent recall of emotionally relevant material relies on brain areas other than the amygdala, but the amygdala may be necessary for conscious recall of emotional material (Bach et al., 2011). Bach et al. (2011, p. 1306) also explain their results in terms of the age of lesion onset: An intact amygdala may be necessary for prioritised processing of relevant stimuli in adulthood, but when amygdala lesions occur early in life, such as in LiP, adaptive mechanisms may compensate for this deficit. In cases where no difficulty in conscious processing of emotional faces has been found (such as in an adult with herpetic encephalitis), the opposite theory may be relevant: If amygdala damage occurs later (adulthood), one has already acquired the learned response to emotional material and can therefore adapt after the damage (Hamann et al., 1996). Once again, conclusions with regard to automatic recall of emotional material are based on two studies involving three individuals with LiP and may not apply to all individuals with LiP.

The above discussion indicates variable results with regard to emotional memory in LiP, possibly showing that recall of emotionally significant material in individuals with LiP and amygdala damage depends on the nature and level of processing involved (sub-conscious versus conscious processing), the type and location of the lesion, and when the

damage occurred during the person's development.

Social Cognition

Recognition of facial emotion. Emotional expressions can be seen as aspects of emotional reaction and social communication (Adolphs, 2002b). Emotional signals can occur in any sensory modality. For instance, facial expression recognition refers to the process of interpreting facial expressions as one of a range of visual emotional signals that have been studied extensively (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Adolphs & Spezio, 2006; Calder et al., 1996; Kipps, Duggins, McCusker, & Calder, 2007).

The amygdala and recognition of facial emotion. Several brain structures have been suggested to be involved in the process of recognising the emotion expressed by a human face, including the occipitotemporal cortices, amygdala, orbitofrontal cortex, basal ganglia and right parietal cortices (Adams, Gordon, Baird, Ambady, & Kleck, 2003; Adolphs, 2006; Adolphs & Spezio, 2006). It has been postulated that the amygdala is involved primarily in processing stimuli related to threat or danger (Adolphs, Russell, & Tranel, 1999; Adolphs & Tranel, 2000) and that the amygdala triggers resources to help deal with ambiguity in the environment (Anderson & Phelps, 2000; Whalen et al., 1998). Therefore, the amygdala has been associated specifically with the ability to recognise fear (Adolphs, Tranel, Damasio & Damasio, 1995; Anderson & Phelps, 2000; Calder, Lawrence & Young, 2001, Schmolck & Squire, 2001), but some studies implicate the amygdala in the recognition of all negative facial expressions (Adolphs, Russell, et al., 1999; Adolphs, Tranel, et al., 1999) and also positive emotions (Garavan, Pendergrass, Ross, Stein, & Risinger, 2001; Hamann, Ely, Hoffman, & Kilts, 2002). These results may be compatible with the hypothesis that the amygdala is involved in processing biologically relevant stimuli, independent of their valence (Fitzgerald, Angstadt, Jelsone, Nathan, & Phan, 2006; Winston, Strange, O'Doherty, & Dolan, 2002). Thus, the amygdala is probably involved in moderating the encoding of negative and positive arousing visual stimuli, including all facial expressions of emotion. Therefore, it would be plausible that individuals with LiP and amygdala damage can have deficits in facial emotion recognition.

Recognition of facial emotion in persons with LiP. Several studies indicate that some individuals with LiP have considerable deficits in facial emotion recognition (Adolphs et al., 2002; Adolphs et al., 1995; Adolphs, Tranel, et al., 1999; Brand et al.,

2007; Hurlemann et al., 2007). Some studies indicate that the recognition of fearful facial expressions specifically, as opposed to intact ability to recognise other facial expressions, was affected (Adolphs et al., 1995; Adolphs, Tranel et al, 1999; Calder et al, 1996). A study of an individual with LiP and bilateral hippocampal damage, where the amygdala was intact, indicates that the individual had normal facial expression recognition, but was impaired with regard to the auditory perception of fear (Ghika-Scmid et al, 1997). This indicates that when the amygdala is not damaged in LiP, facial emotion recognition may be intact, but the recognition of fear in other modalities may be affected negatively.

Although most studies indicate deficits in the recognition of fearful facial expressions, Terburg et al. (2012) indicates that the recognition of fearful facial expression may be enhanced in some individuals with LiP. They found hypervigilant responses to unconsciously presented fearful faces in a group of five adults with LiP and basolateral amygdala damage. Terburg et al. (2012) concluded that the basolateral amygdala may have an inhibitory function with regard to the threat vigilance system of the brain and that amygdala damage may therefore cause hypervigilant responses to fearful facial expressions. Furthermore, individuals with LiP and basolateral amygdala damage also exhibited enhanced performance on dynamic facial fear recognition (Terburg et al., 2012). The authors explain this phenomenon by arguing that failure of the bilateral amygdala to inhibit basal fear responses (autonomic responses) may cause hypervigilance to emotionally meaningful areas of faces. Terburg et al. (2012) suggested this to be especially true for enhanced fixation on the eyes by individuals with LiP and basolateral amygdala damage. (Terburg et al., 2012). This prolonged fixation on the eyes might then lead to facilitation of fear recognition (Terburg et al., 2012).

Overall, it is evident that results with regard to recognition of fearful faces in individuals with LiP and amygdala damage vary and seem to be contradictory. Not all studies on people with LiP have necessarily provided correlating brain scans. The differences in results may be due to types of lesion (for example basolateral amygdala as opposed to calcification of the entire amygdala and extra-amygdala structures) and types of measure used (static versus dynamic faces). The differences in results (such as enhanced fear recognition versus deficits in fear recognition) may also be based on responses to unconsciously fearful faces versus consciously presented fearful faces. Nevertheless, these findings with regard to different perceptions of fear suggest compatibility with theories

indicating multiple emotion systems (Kipps et al., 2007; Watson, Wiese, Vaidya, & Tellegen, 1999).

In contrast to findings of specific difficulty with or enhanced fear processing in individuals with LiP (Adolphs, Tranel et al., 1995; Calder et al, 1996), other studies indicate impaired processing of all negative expressions in some individuals with LiP (Adolphs, Tranel et al., 1999), and in some studies even positive emotions (Siebert et al., 2003; Thornton et al., 2008). Siebert et al. (2003) and Thornton et al. (2008) found that adults affected by LiP were significantly less likely to recognise fear and all other basic facial expressions (anger, disgust, surprise, sadness, happiness and neutrality) when compared to a control group. These results support the hypothesis that the amygdala appears to be necessary for moderating the encoding of not only arousing negative, but also arousing positive visual stimuli (Yang et al., 2002). However, Thornton et al. (2008) did not include neuroimaging in their study: therefore, it cannot necessarily be concluded that their deficits in facial emotion recognition were correlated with circumscribed amygdala damage.

Brand et al. (2007) made use of a battery of measures concentrating on different aspects of facial emotion recognition (discrimination and naming). Two individuals reported by Brand et al. (2007) did not have any difficulty in facial affect discrimination or facial affect naming. A third individual presented with poor performance in facial affect naming, but intact performance on a measure of facial affect discrimination. This indicates that individuals with LiP may achieve variable results on measures of facial emotion recognition, and they may achieve variable results on instruments measuring different aspects of facial emotion recognition (such as naming versus discrimination).

Other factors that can possibly explain variable results with regard to facial emotion recognition among individuals with LiP include the age of onset of the lesion, the type and extent of damage (Schmolck & Squire, 2001; Terburg et al., 2012), and intelligence or level of education (Thornton, 2006). Thornton (2006) suggests that intelligence and education probably play a mediating role in the ability to identify facial expressions, as individuals with LiP and a higher level of education performed better in facial emotion recognition tasks when compared to individuals without LiP who were less educated. However, Thornton et al. (2008) found that gender, the presence or absence of seizures and

substance abuse did not significantly influence the ability to identify facial expressions in adults with LiP.

The conclusion is that individuals with LiP may have variable difficulties in facial emotion recognition tasks, while facial emotion recognition may by intact in some individuals with LiP. The same individuals with LiP and amygdala lesions may also achieve different results on an instrument measuring one aspect of facial emotion recognition compared to an instrument measuring a different aspect of facial emotion recognition.

Theory of mind (ToM)

The neural network underlying ToM. ToM is defined as the ability to represent the full range of mental states (beliefs, desires, intentions, imagination, emotions), to reflect on the contents of the minds of self and others, and to understand and predict behaviour in terms of these states (Baron-Cohen, 2001b; Bellerose, Beauchamp, & Lassonde, 2012). ToM is a complex ability, and it is most likely that a neural network or circuit rather than a specific brain structure underlies its functioning (Amodio & Frith, 2006; Saxe, Moran, Scholz, & Gabriele, 2006). It has been suggested that the amygdala structures and their connecting complex of neural systems were at the core of the capacity to interpret the mental states of others (Brothers, 1995). However, recent research led to the conclusion that the neural circuit underlying ToM in adults probably consists of the medial prefrontal cortex, amygdala, the superior temporal sulcus, bilateral temporoparietal junctions, anterior insular cortex and para- and anterior cingulate cortex (Amodia & Frith, 2006; Lamm & Singer, 2010; Pfeifer, Lieberman & Dapretto, 2007; Saxe et al., 2006).

The current literature on ToM suggests that the core circuit related to ToM (amygdala, medial temporal lobe, prefrontal cortex, cingulate cortex) may be necessary for all ToM tasks, but specific brain areas may facilitate different ToM tasks (Bellerose et al., 2012). According to the componential understanding of ToM (Saxe, Carey, & Kanwisher, 2004; Saxe & Powell, 2006; Smith, Hermelin, & Tsimpli, 2003), two distinct neural circuits subserve two distinct ToM abilities. The amygdala was suggested to play an important role in the earlier developing ToM system, consisting of the ability to decode others' mental states from observable cues (Sabbagh, 2004; Tager-Flusberg & Sullivan, 2000). The ability to reason about others' mental states (inferential reasoning) may rely on the left

medial frontal regions (Sabbagh, 2004; Tager-Flusberg & Sullivan, 2000). Findings of at least two studies suggest that the early and late developing components of ToM rely on distinct cognitive and neural mechanisms, and that these mechanisms remain distinct into adulthood (Saxe et al., 2004; Saxe & Powell, 2006). This view of ToM suggests that the amygdala plays a role with regard to an earlier developing ToM system, and it follows that amygdala damage in LiP (if occurring early on) may affect these ToM abilities (such as the recognition of mental states and social emotions).

ToM in persons with LiP. Adolphs et al. (2002) observed that adults with amygdala damage (including one adult with LiP who had bilateral amygdala damage) found it more difficult than controls to recognise *social emotions,* but not other complex mental states that are not normally considered emotions. *Social emotions* refer to complex affective states that only make sense in an explicit social context, such as arrogance, guilt, admiration and flirtatiousness (Lamm & Singer, 2010, p. 579). *Mental states that normally are not considered emotions* include interest, thoughtfulness and boredom (Adolphs et al., 2002). The ability to decode social emotions may be viewed as a component of the early developing system of ToM and has been suggested to rely on an intact amygdala (Sabbagh, 2004; Tager-Flusberg & Sullivan, 2000). Brand et al. (2007) also reported that while the recognition of social emotions was intact in two adults with LiP, a third adult with LiP with amygdala damage performed poorly on social emotion recognition. The results of these studies (Adolphs et al., 2002; Brand et al., 2007) suggest that certain aspects of ToM development (such as decoding of complex emotions) may be affected by amygdala lesions in LiP. However, some individuals with LiP who have amygdala damage may not have any difficulty in tasks measuring this ability. The research on which these conclusions are based included only a few individuals with LiP; therefore, it is not necessarily generalisable to all adults with LiP.

Amygdala pathology, among other abnormalities, has been identified in individuals with autism (Baron-Cohen, 2001a; Dziobek, Bahnemann, Convit, & Heekeren, 2010; Munson et al., 2006); therefore, it is plausible that individuals with LiP could have such symptoms (Paul et al., 2010). Two adults with LiP who likely had partial amygdala lesions since early adolescence **(**one was scanned for the first time at age 14 and the other was scanned at age 23 and had complete bilateral amygdala damage**)**, obtained typical scores on the Empathising Quotient (EQ) self-rating questionnaire, indicating an intact

drive to understand the mental states of others. Overall, adults with LiP obtained variable results on measures of ToM, and individuals with LiP may be impaired in specific aspects of ToM.

Attention

The role of the amygdala in attention. Studies provide evidence that interaction between the frontal, temporal and parietal lobes, the limbic system and basal ganglia underlies the different processes of attention (Greenberg, Esterman, Wilson, Serences, & Yantis, 2010; Mirsky, Anthony, Duncan, Ahearn, & Kellam, 1991; Nobre, Gitelman, Dias, & Mesulam, 2000; Peterson & Posner, 2012; Posner & Peterson, 1990; Stuss, 2006). The modulatory role of the amygdala with regard to attention is prominent in the literature (Gallagher & Schoenbaum, 1999; Holland & Gallagher, 1999; Holland, Han, & Gallagher, 2000; Vuilleumier, Richardson, Armony, Driver, & Dolan, 2004). The relationship between the amygdala and other attention systems was suggested to be bi-directional, in the sense that the amygdala sends biasing signals to other attention systems, while also receiving top-down modulation signals (Armony & Dolan, 2002; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002; Pessoa & Ungerleider, 2004). Specifically, the central nucleus of the amygdala has been suggested to play a role in modulating visuospatial attention (Holland et al., 2000), such as facilitating selective attention to visual stimuli. It has also been suggested that the amygdala plays a central role in modulating attention with regard to biologically, socially and emotionally salient cues (Adolphs & Spezio, 2006; Pessoa et al., 2002; Williams, Waiter, Perra, Perrett, & Whiten, 2005). It may also play a role in motivational aspects of attention, as part of the limbic system (Schaefer & Gray, 2007).

Selective and divided attention in persons with LiP. Some researchers reported deficits in selective and divided attention in adults with LiP (Talmi, Hurlemann, Patin, & Dolan, 2010; Thornton et al., 2008), while others found intact attentional functions in adults with the disorder (Brand et al., 2007). As bilateral calcification in the temporal lobes is often found in individuals with LiP (Markowitsch et al., 1994; Savage et al., 1988; Tranel & Hyman, 1990), amygdala damage may underlie these deficits in attention. Supporting this assumption, the literature suggests that temporal lobe pathology can disrupt the normal attention pathways (both the dorsal and ventral attention systems) and

that amygdala damage may disrupt general vigilance required during working memory tasks (Bocquillon et al., 2008; Zhang et al., 2009). Therefore, dysregulation of the modulatory role of the amygdala can cause attention dysfunction.

As the concept of shifting attention largely overlaps with the executive function concepts of cognitive flexibility, this aspect will be discussed under the section on executive function.

Social attention. Social attention refers to social orientation, joint attention and attention to the distress of others (Dawson et al., 2004). Social orientation refers to the effects of social cues on selective attention (Dawson, Meltzoff, Osterling, Rinaldi, & Brown, 1998; Greene, Mooshagian, Kaplan, Zaidel, & Iacoboni, 2009). The amygdala was found to be important for social orientation (Adolph & Spezio, 2006; Pessoa et al., 2002; Vuilleumier et al., 2004; Williams, Waiter et al., 2005). It was found that a woman who had bilateral amygdala lesions resulting from LiP, in comparison to controls, spent more time looking at the mouth than at the centre of the face during real conversations (Spezio, Huang, Castelli, & Adolphs, 2007). Adolphs, Gosselin, et al. (2005) concluded that this woman's impaired judgment of emotions from faces was possibly caused by a failure to attend to informative features of faces. These features include the eyes and especially the white regions of the eyes that are informative of fearful facial expressions (Adolphs et al., 2005). Adolphs and colleagues (Adolphs, 2007; Adolphs, Gosselin, et al., 2005; Atkinson & Adolphs, 2005) found that the role of the amygdala in orientation of attention to informative features of the face is the first step in efficient recognition of facial emotion. Therefore, amygdala pathology can contribute to deficits in recognising facial emotion.

Although research on LiP and social attention is limited to the studies by Adolphs and colleagues (Adolphs, 2007; Adolphs, Gosselin, et al., 2005), numerous studies have indicated the involvement of the amygdala in directing attention to gaze in the process of facial emotion recognition (Adams et al., 2003; Akiyama et al., 2007; Hooker et al., 2003; Young et al., 1995). The involvement of the amygdala in the process of social orientation has also been studied (Adolphs & Spezio, 2006; Pessoa et al., 2002). Modulation of the temporal visual cortex by the amygdala may influence the dorsal (location) stream, via

coarse visuospatial coding in these neurons to direct visuospatial attention to emotionally salient facial features, such as the eyes (Adolph & Spezio, 2006).

The ability to be attentive is an important function that influences a number of other cognitive functions such as memory and learning. The literature reviewed in this section suggests that attention in individuals with LiP can be impaired. This seems to be compatible with the neuroanatomy thought to underlie attention, as well as the neuropathology associated with LiP.

Executive Function

According to Klenberg, Korkman, and Lahti-Nuuttila (2001, p. 408) the concept of executive function "usually refers to cognitive abilities responsible for controlling and coordinating performance in complex cognitive tasks".

Several sub-domains of executive functioning, such as working memory, planning, self-regulation (fluency, shifting and inhibition), and effective performance have been mentioned in the literature (Baron, 2004; Garavan, Ross, Murphy, Roche, & Stein, 2002; Lezak, Howieson, Bigler, & Tranel, 2012; Miyake et al., 2000). Important theoretical and clinical distinctions can be made between these sub-domains.

The literature suggests that executive functioning is not exclusive to cognitive processes, but is also implicated in emotional responses (such as emotion regulation) and is dependent on emotional systems in the brain (Anderson, 2002; Rosso, 2004; Slattery, Garvey, & Swedo, 2001; Zelazo, Qu, & Müller, 2005).

Cortical connections and executive function. Although damage to the frontal lobes can result in significant dysfunction of various executive sub-domains (Carlin et al., 2000; Gouveia, Brucki, Malheiros, & Bueno, 2007; Jacobs, Harvey, & Anderson, 2007), these functions are not only associated with direct damage to the frontal lobes (Keller, Baker, Downes, & Roberts, 2009; Tulberg et al., 2004). The frontal lobes have bidirectional connections with the limbic (motivation) system, the reticular activating (arousal) system, the posterior association cortex (perceptual/cognitive processes) and the motor (action) regions of the frontal lobe (Lichter & Cummings, 2001; Middleton & Strick, 2001; Stuss, 2006). Therefore, the specific sub-components of executive function most likely have both common and divergent neural correlates. Accordingly, the executive functions are

suggested to be sensitive to damage in other parts of the brain such as white matter lesions that disrupt cortical-subcortical connections, as well as remote lesions that affect the development or structure of the frontal lobes (Campo et al., 2012; Lichter & Cummings, 2001; Tulberg et al., 2004). The amygdala has strong reciprocal connections to the prefrontal lobes (Aggleton & Saunders, 2000; Mega et al., 1997). Therefore, it seems likely that damage to the amygdala (such as in LiP) or to the direct and indirect connections of the amygdala with the prefrontal lobes may lead to functional alterations of these connections and consequently to deficits in executive function. Developmental alterations of brain structure associated with amygdala damage or damage to the connections of the amygdala with other brain structures may also occur, leading to altered or deficient executive function.

Executive function in persons with LiP. The results of studies on neuropsychological impairments associated with amygdala damage in LiP vary. Some studies show executive dysfunction (Brand et al., 2007; Thornton et al., 2008; Tranel & Hyman, 1990) and others indicate intact executive functions (Markowitsch et al., 1994; Siebert et al., 2003; Talmi et al., 2010), while a recent study indicates paradoxical facilitation of working memory in adults with LiP (Morgan, Terburg, Thornton, Stein, & Van Honk, 2012; Van Honk et al., 2013). The patient with LiP who was first reported by Tranel and Hyman (1990) and who had bilateral lesions of the amygdala ("SM") presented with deficient category formation, cognitive flexibility, set-shifting and verbal fluency. Although no other individuals with LiP were included in the study by Tranel and Hyman (1990), Thornton et al. (2008) examined a large group of individuals with LiP and found similar results to those reported by Tranel and Hyman (1990). The adults with LiP in the study by Thornton et al. (2008) performed significantly worse than controls in tasks measuring initiation, fluency, switching, abstract verbal reasoning and self-monitoring. Other researchers (Brand et al., 2007; Talmi et al., 2010) also reported deficits in category formation, shifting and verbal fluency in some individuals with LiP. The literature indicates that planning is generally unaffected in individuals with LiP (Brand et al., 2007; Talmi et al., 2010; Thornton et al., 2008). The particular areas of the frontal lobe and its connections affected by amygdala damage may be less involved in this function, explaining the finding of intact planning in individuals with LiP.

Decision making can also be viewed as an executive function (Lezak et al., 2012) and has been studied in LiP (Brand, Labudda, & Markowitsch, 2006; Talmi et al., 2010). Decision making where contingencies are known, appeared intact in individuals with LiP, but where the contingencies were not known, individuals with LiP took more risks than controls did and therefore made fewer advantageous decisions (Brand et al., 2006; Talmi et al., 2010). Therefore, individuals with LiP who had amygdala lesions tended to choose the risky option even when it had previously led to negative consequences (Brand et al., 2006). Similarly, two adult participants with LiP with bilateral amygdala damage showed a dramatic reduction in loss aversion compared to matched controls (De Martino, Camerer, & Adolphs, 2010). Talmi et al. (2010) notes reduced autonomic responses and attributed the reason for riskier choices in individuals with amygdala damage to their inability to learn from autonomic responses to rewards and losses. De Martino et al. (2010) suggest that the amygdala plays a key role in generating loss aversion by inhibiting actions with potentially deleterious outcomes.

There has been an ongoing debate about the role of other executive functions in decision-making in LiP, without any clear conclusions (Bechara, Damasio, & Damasio, 2000; Brand et al., 2007). Deficient decision making in risky situations correlated with deficient performance in tasks measuring categorisation, set-shifting and cognitive flexibility (Brand et al., 2007). This correlation between poor decision-making in risky situations and certain executive functions has also been found in studies with other populations (Bechara, Damasio, Damasio, & Lee, 1999; Brand et al., 2005). Brand et al. (2007) postulate that the onset and extent of amygdala degeneration could play a role in the development of executive dysfunction in individuals with LiP. This conclusion is in accordance with the assumption that the amygdala, through its indirect interactions with the prefrontal cortices, is part of a network through which emotional reactions are modulated and therefore indirectly plays a role in behaviour control and other executive functions (Delgado, Nearing, LeDoux, & Phelps, 2008; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003).

In contrast to the literature discussed so far, Morgan et al. (2012) found enhanced rather than deficient working memory in three women with LiP and basolateral amygdala damage. Morgan et al. (2012) hypothesise that enhanced performance in a working memory task in these individuals with LiP and basolateral amygdala damage may be

explained by an interactive model of brain function (Bressler & Menon, 2010; Raichle, 2010). According to such a model, brain function can be understood as interactions between diverse neural circuits and as a function of intrinsic activity (cellular and molecular neuroscience) rather than reflexive activity of one isolated neural system (Bressler & Menon, 2010; Raichle, 2010). Interaction between diverse neural circuits involves competition between these circuits. Competition between two neural networks is involved in working memory, namely the dorsal prefrontal cortex (effortful control) and a salience-sensitive basolateral amygdala-orbitofrontal circuit (vigilance). Thus, there is competition for attentional resources between working memory and salience surveillance (ongoing surveillance of the environment with regard to threat and reward). Therefore, damage to the basolateral amygdala was hypothesised to free the dorsolateral prefrontal cortex from having to compete for attentional resources and therefore result in enhanced working memory performance (Morgan et al., 2012).

In conclusion, bilateral amygdala lesions (and therefore disruption of connections between the amygdala and other brain regions) were postulated to be the cause of executive dysfunction (cognitive flexibility, shifting, initiation, fluency, abstract thinking, and decision making) in some adults with LiP. While amygdala damage was hypothesised to be the cause of poor working memory in some individuals with LiP, basolateral amygdala damage was suggested to be associated with enhanced working memory functioning in other individuals with LiP. Executive functions facilitate successful functioning in everyday life, and executive dysfunction can lead to inadequate adaptive behaviour, such as making poor decisions (Brand et al., 2007).

It is notable that tests of inhibition have not been included in the neuropsychological studies of individuals with LiP (Brand et al., 2007; Talmi et al., 2010; Thornton et al., 2008) and may be an important aspect of executive function to explore, as inhibition has been postulated to be one of the primary executive function components.

Psychiatric and Psychosocial Difficulties

Psychiatric Difficulties

Thornton (2006) found that neuropsychiatric diagnoses among a group of adults suffering from LiP were significantly more prevalent compared to matched controls.

Compared to controls, the individuals in the LiP sample reported significantly higher frequencies of anxiety disorders, mood disorders, suicidal ideation, psychosis and schizophrenia. The LiP individuals also reported a higher incidence of aggressive outbursts (Thornton, 2006). Similarly, other studies indicated depression (Babinsky et al., 1993; Claeys et al., 2007; Markowitsch et al., 1994; Van Rooy et al., 1991), increased risk for suicide (Van Rooy et al., 1991), panic disorder (Wiest et al., 2006), anger outbursts (Newton et al., 1971; Steenkamp, 1997) and psychosis (Emsley & Paster, 1985; Kleinert et al., 1987; Steenkamp, 1997) in adults with LiP. These findings (a higher incidence of certain psychiatric disorders in LiP compared to controls) are consistent with the current understanding of the amygdala and its role in mediating psychopathology (Adami, König, Vetter, Hausmann, & Conca, 2006; Drevets, 2007; Hayano et al., 2009).

The high prevalence of anxiety disorders in LiP is consistent with research findings confirming the central role of the amygdala in conditioned fear and the pathophysiology of anxiety disorders in adults (Adami et al., 2006; Davidson, 2002; Davis, 2000; Dityatev & Bolshakov, 2005). Anxiety and panic disorders were suggested to result from dysfunction in integrating the visceral amygdala functions with the internal state of the individual (Mega et al., 1997). Neuroimaging studies also indicated decreased amygdala volume and increased activity in the amygdala and temporal pole in individuals with anxiety disorders (Hayano et al., 2009; Rauch, Shin, & Wright, 2003).

The literature further suggests that abnormality of the orbitofrontal cortex (OFC) and its connections with the amygdala, medial prefrontal cortex, temporal lobe, striatum, thalamus and brainstem may lead to the signs and symptoms of depression (Davidson, Abercrombie, Nitschke, & Putnam, 1999; Drevets, 2007; Schaefer et al., 2002). Researchers (Aggleton, 1993; Davidson, Putnam, & Larson, 2000) further implicated the amygdala as an important brain structure involved in emotion regulation and aggression. Pathology in the brain circuits affecting the amygdala may lead to mental states where the misinterpretation of sensory input as threatening leads to aggressive outbursts (Aggleton, 1993; Van Elst, Woerman, & Lemieux, 2000).

Clinical similarities between schizophrenia and psychosis associated with temporal lobe lesions have been recognised (Seidman et al., 2003; Van Elst & Trimble, 2003). This supports the suggestion of an association between amygdala damage and a significantly

higher incidence of schizophrenia and psychosis in LiP. Consistent findings of abnormalities in the anatomy, physiology and function of medial temporal lobe structures and neural circuitry in schizophrenia provide further evidence of this association (Benes, 2010; Lawrie, McIntosh, Hall, Owens, & Johnstone, 2008; Niu et al., 2004). Neuropsychological studies have also found selective impairments in learning and memory in schizophrenia, consistent with medial temporal lobe dysfunction similar to LiP (Cirillo & Siedman, 2003; Yoo, Lee, Kim, Kang, & Lee, 2006).

In conclusion, review of the literature indicates a higher prevalence of depression, anxiety, psychosis and suicidal behaviour in individuals with LiP, and these findings are in line with the current understanding of the amygdala and its role in mediating psychopathology.

Psychosocial Functioning

The discussion of mucocutaneous and extracutaneous signs and symptoms of LiP has indicated the severe and chronic symptoms of the disorder. Chronic diseases carry important psychological and social consequences, demanding significant psychological adjustments (Stanton, Revenson, & Tennen, 2007). Research indicates that the quality of life, including personal relationships, social and leisure activities, emotions, daily routines, work and sexual relationships of adults with skin disorders, is affected negatively by their symptoms (Harlow, Poyner, Finlay, & Dykes, 2000; Krejci-Manwaring, Kerchner, Feldman, Rapp, & Rapp, 2006). Hoarseness, dysphagia and upper respiratory diseases in adults have been associated with poor quality of life due to interpersonal, psychological, emotional and employment-related difficulties (Baylor, Yorkston, & Eadie, 2005; Hurst, Wilkinson, Donaldson, & Wedzicha, 2004; Nguyen et al., 2005). Psychiatric disorders, especially anxiety and depression as well as epilepsy (conditions that are prevalent in LiP), have been associated with decreased quality of life and poor psychosocial functioning (Hansson, 2006; Taylor, Sander, Taylor, & Baker, 2011). In general, symptoms that are more severe were suggested to place greater demands on the inner resources of individuals with chronic conditions and may therefore lead to significantly decreased quality of life (Cao et al., 2013; Lewis-Beck, Abouzaid, Xie, Baser, & Kim, 2013). Therefore, the signs and symptoms of LiP (such as skin conditions, hoarseness, neurological symptoms and neuropsychiatric disorders) and their effect on appearance, communication, physical

health, cognition and mental health are very likely to have a negative effect on the psychosocial functioning and quality of life of individuals with this disorder.

In line with the literature, researchers (Steenkamp, 1997; Van Rooy et al., 1991) indicate that adults living with LiP often develop feelings of depression and low self-esteem related to their appearance. Steenkamp (1997) also found associations between increased severity of the symptoms of LiP and increased anxiety, lowered self-esteem and decreased social interactions in adolescents and young adults with LiP (Steenkamp, 1997). Aspects of people's lives often viewed as affecting their satisfaction with life, such as work performance (Van Hougenhouck-Tulleken et al., 2004) and meaningful long-term relationships (Thornton et al., 2008), seem to be affected negatively by LiP.

In contrast to the literature discussed so far, Thornton (2006) found no noteworthy evidence of differences in quality of life or satisfaction with life as reported by individuals with LiP and controls on the Short Form-36 and Impact of Epilepsy Scale, adapted to Impact of LiP (Thornton, 2006). However, these findings are inconsistent with other markers for quality of life (such as negative effect on work performance and long-term relationships). An explanation for these findings could be that the specific measure is not well suited to the LiP population or the specific South African context. The study focused on one geographical area (and predominantly one cultural group); therefore, the seeming homogeneous quality of life may be the result of environmental (socio-emotional) influence rather than the effect of the illness on the sufferer. Therefore, there are limitations with regard to the generalisability of the findings.

In conclusion, there are several indications of psychosocial difficulties among adults with LiP. There are limitations with regard to the generalisability of some findings with regard to quality of life.

Conclusion

In this chapter, LiP has been described as a rare genetic disorder affecting the skin, voice, nervous system and several other organs of the body. The literature indicates that LiP is caused by mutation in the CM1 gene, leading to the deposition of hyaline material in the skin and other organs. CNS involvement in LiP primarily includes epilepsy and intracranial calcifications. Bilateral, circumscribed intracranial calcification in the

temporal lobe, specifically the amygdala, is one of the primary symptoms or signs of the disorder and has been associated with certain neuropsychological deficits and psychiatric conditions in LiP. The most prominent neuropsychological deficits associated with LiP, as identified in this chapter, include attention, executive function, memory and social cognition deficits. There is a higher incidence of psychiatric diagnoses and psychiatric symptoms that are more severe among individuals with LiP than they are among controls. Psychiatric diagnoses associated with LiP include psychosis, schizophrenia, affective disorders, anxiety disorders and suicidal behaviour. Although very little research has been conducted with regard to the psychosocial adjustment of individuals with LiP, it can be expected that these individuals will experience increased stressors associated with their symptoms that may affect their psychosocial adjustment and quality of life. The next chapter will deal with LiP in children and adolescents.

Chapter 3

Lipoid Proteinosis in Children and Adolescents

The goal of this chapter is to discuss the prevalence, onset, presentation and progression of LiP signs and symptoms in children and adolescents and to document what is known about their psychosocial and neuropsychological development. Very few individuals identified with LiP have been systematically monitored over a meaningful period of time (Brajac et al., 2004); therefore, very little is known about the specific difficulties of children and adolescents in the different developmental phases. It is not apparent at what stage the neuroanatomical signs of lipoid proteinosis become evident, with some studies (Newton et al., 1971; Omrani et al., 2012) suggesting that children may already be symptomatic with associated neuropsychiatric and neuropsychological sequelae from early childhood. Other investigations (Kachewar, Singh, Sasane, & Bhadane, 2011; Rahalkar et al., 2001; Teive et al., 2004) suggest that this may be in late adolescence or early adulthood. On the assumption that there may be early neuroanatomical involvement, one must consider the literature on other children and adolescents who have displayed similar or matching lesions. However, bilateral amygdala lesions are very rare in children, adolescents and adults. The lack of research on the psychosocial development of children and adolescents with LiP also makes it imperative to gain knowledge about the difficulties of children with skin and voice disorders in order to develop an understanding of the psychosocial problems that children and adolescents with LiP may have.

Prevalence of LiP in Children

No rigorous prevalence studies on LiP have been conducted. Owing to the nature of the available literature (i.e. mostly case studies making use of very small samples), it is difficult to determine the prevalence of the disorder. Consequently, the international prevalence of LiP in children and adolescents is not known. Two hundred and twenty-nine reported cases of LiP in children and adolescents younger than 19 years could be found in the available literature dating from 1941 (Wolfram, 1941) to 2013 (Abbas et al., 2013; Al-Ekrish & Al-Sadhan, 2012; Al-Faky et al., 2012; Dogramaci et al., 2012; Parmar, Krishna, De, Kanwar, & Saikia, 2013). This figure (229 cases) suggests that LiP is a rare disorder among children and adolescents worldwide. It is possible that some of these cases have

been reported more than once. However, the different periods in which these cases were reported and the different regions from which these children and adolescents originated seem to indicate that most of these cases were in fact not reported more than once.

According to Thornton (2006), only five out of 37 individuals with LiP in the Northern Cape – the area in the world known to have the highest prevalence of LiP – were younger than 19 years, emphasising the rarity of the disease among children and adolescents. In the urban communities in South Africa (Johannesburg and surrounds), no children and only one adolescent with the disorder were known (Thornton, 2006). It was assumed that with every generation the frequency of the incidence of LiP decreased because affected individuals produced fewer offspring than the average individual in the population did (Stine & Smith, 1990). It was suggested that the decrease in the frequency of the incidence of LiP was due to natural selection; thus, fewer people with the illness married or had fewer children (Stine & Smith, 1990).

Progression of Signs and Symptoms of LiP

The progression of cutaneous signs and symptoms of LiP are generally better understood due to its visibility compared to signs and symptoms in the nervous system (Farolan, Ronan, Solomon, & Loeff, 1992; Kumar, Ramesh, Beena, Misra, & Mukherjee, 2002; Van Hougenhouck-Tulleken et al., 2004). Fluctuations (Kaya et al., 2003) and variability (Nasiri et al., 2008; Salih et al., 2011; Van Hougenhouck-Tulleken et al., 2004) of skin signs and symptoms and hoarseness among individuals are evident during the course of LiP (Hurlemann et al., 2010; Nagasaka et al., 2000; Siebert et al., 2003). Generally, the progression of skin symptoms and signs and hoarseness from birth onwards seems to be protracted, developing slowly during childhood, accelerating during adolescence and possibly stabilising in early adulthood (Brajac et al., 2004; Cohen, Vardy, Cagnano, Zvulunov, & Naimer, 1999; Masood, Aman, & Kazmi, 2008).

Over the last decade, research on the neurological and neuropsychiatric signs and symptoms of LiP has increased (Morgan, 2008; Morgan et al., 2012; Thornton et al., 2008), but the progression of nervous system signs and symptoms remains underresearched. The literature suggests that certain neurological and neuropsychiatric signs and symptoms (such as epilepsy) are evident in children, but these signs and symptoms were observed more frequently in adolescents and adults (Cowan, Alexander,

Vickers, & Cowdell, 1961; Kachewar, 2010). Psychosis has only been reported in adolescents and adults (Emsley & Paster, 1985; Steenkamp, 1997). Recent research indicates more extensive bilateral symmetrical calcification of the amygdalae in older individuals compared to less extensive amygdala lesions in younger individuals (Appenzeller et al., 2006). Therefore, it was hypothesised that intracranial lesions are progressive and that neuropsychiatric signs and symptoms have a later onset, or that these signs and symptoms increase with age.

The progression of LiP as a whole seems to be variable, but certain trends in the progression of symptoms are also evident. Provision should be allowed for the neurological, neuropsychiatric and neuropsychological symptoms that are not so visible. The available literature on symptom progression in LiP among children and adolescents will now be reviewed.

Mucocutaneous Signs and Symptoms

Hoarseness. Hoarseness is usually the first and most common clinical sign of LiP (Feiler-Ofry et al., 1979; Hofer, 1974; Piérard, Van Cauwenberge, Budo, & Lapiere, 1988; Ramos-e-Silva, Tanus & Cestari, 2002; Ramsey, Tschen & Wolf, 1985; Savage et al., 1988). It is generally reported in the literature that individuals with LiP have voice changes and hoarseness at birth or in early infancy (Acar et al., 2004; Grosfeld et al., 1964; Hofer, 1974). However, some authors (Amichai et al., 1996; Doğru et al., 2008; Wollina, Konrad, & Schonlebe, 2004) reported cases where individuals developed hoarseness only during adolescence. Progressive hoarseness that eventually led to aphonia, has been reported (Black, 1988; Blodi et al., 1960; Savage et al., 1988), while other studies found that the degree of hoarseness and hyaline formation in LiP seldom progress (Van Rooy et al., 1991. MacKinnon (1968) reported a general thickening of the tongue, epiglottis and all parts of upper aperture of the larynx from the age of two to 15 years in a child with LiP. Therefore, variable onset and progression of hoarseness in LiP seem evident. Despite this variability, most reports indicate that hoarseness develops during early childhood. Furthermore, dysphonia in LiP seems to be a chronic condition in the majority of children and adolescents with LiP.

Many studies indicate that most children and adolescents with LiP suffer from speech problems associated with hoarseness, woody or thickened tongue, thick lips, reduced

movement of tongue, thick sublingual frenulum and soft palate abnormalities (Batra, Safaya, & Aggarwal, 2008; Toosi & Ehsani, 2009; Uchida et al., 2007). Finkelstein, Hammond and Jones (1982) reported a 5-year-old child with LiP and otitis media, who was found to have bilateral mediotympanic hearing loss and articulation difficulties secondary to hearing loss. It is not clear if the otitis media was attributed to LiP or not, although conditions such as blockage of the Eustachian tube is known to occur in LiP. However, decreased tongue mobility due to LiP was suggested to cause lateralisation of consonants and consonant blends such as "s", "sh", and "ch". Therefore, it is evident that children and adolescents with LiP may have hoarseness and, speech and hearing difficulties, which can contribute to communication difficulties.

Skin signs. Skin lesions in LiP individuals usually develop during the first few years of life (Hamada, 2002; Horev et al., 2005; Ramos-E-Silva et al., 2002), but can also appear later (Cowan et al., 1961; Van Hougenhouck-Tulleken et al., 2004) or not at all (Omrani et al., 2012). Skin manifestations are sometimes precipitated by illnesses of benign nature or by vaccination (Ramos-E-Silva et al., 2002), but often appear in children with LiP when they start crawling and walking because they become active and are therefore more likely to hurt themselves (Scott & Findlay, 1960). As in adults, the skins of children with LiP are sensitive to exposure to the sun (Calnan & Shuster, 1962), and skin areas habitually exposed to the sun may have a progressively more severely scarred appearance (Sander et al., 2006). Changes in the skins of individuals with LiP may lead to a lack of pain sensation (Beury, Neimann, Pierson, Tridon & Sapelier, 1963).

Skin fragility and minor trauma or friction not only lead to scars on the face and extremities of children with LiP, but also cause alopecia on the scalp (Ringpfeil, 2005). Generally, alopecia in LiP is progressive and can be scarring (Vedamurthy, 2003) or non-scarring (Holme, Lenane, & Krafchik, 2005) and can become extremely severe as illustrated by the case of a 15-year-old girl with LiP who eventually had to wear a wig (Brajac et al., 2004). While alopecia of the scalp is generally reported from a very young age (Pursley & Apisarnthnarax, 1981; Shivaswamy, Thappa, Laximish, & Jayanthi, 2003; Yesudian & Bhasker, 1972), alopecia of the eyelashes and eyebrows frequently occurs somewhat later during adolescence (Al-Bitar & Samdani, 2004).

Beaded eyelid lesions, frequently mentioned in the literature and suggested to increase gradually in prominence, normally occur after the age of three years (Al-Faky et al., 2012; Mukhija, Singh, Singh, & Mukhija, 2006). Another skin sign associated with LiP is pruritis or chronic skin itching (Van Hougenhouck-Tulleken et al., 2004), which was reported in approximately 50% of children and adolescents who participated in two separate South African LiP studies (Heyl, 1963; Van Hougenhouck-Tulleken et al., 2004) and develops in children as young as three months to one year of age (Hafeez & Hussein, 1996; Masood et al., 2008). Pruritis may be provoked by heat or occur without any apparent cause (Heyl, 1963).

Notwithstanding some cases in which variable progression was noted, skin lesions in LiP seem to have an early onset and chronic course in the majority of children and adolescents suffering from the condition (Hamada, 2002; Keipert, 1970; Ramos-E-Silva et al., 2002), while alopecia seems to be progressive (Vedamurthy, 2003).

Extracutaneous Signs and Symptoms of LiP

Certain symptoms of LiP, other than cutaneous symptoms and hoarseness, have also been observed in children. These include chronic upper respiratory infections (Parimalam et al., 2009), recurrent parotitis (Al-Ekrish & Sadhan, 2012), nasal infiltration leading to anosmia (Konstantinov, Kabachiev, & Karchev, 1992; Kumar, Seethamm, Singh, & Vaswani, 1986) and certain congenital abnormalities (Barthelemy, Mauduit, Kanitakis, Cambazard, & Thivolet, 1986; Rook, 1976). Ophthalmological signs and symptoms such as pseudomembranous conjunctivitis, keratoconus and trichiasis were reported in children and adolescents (Acar et al., 2012; Al-Faky et al., 2012; Barthelemy et al., 1986). Al-Faky et al. (2012) conducted a longitudinal study (beginning in infancy and early childhood) of the ophthalmological difficulties of children and adolescents with LiP and followed it up every six months. Results indicate that the children's vision was normal, but that moniliform blepharosis (beaded eyelids) appeared after the age of four years in all cases. Prominent corneal nerves (more apparent in children with genetic mutations that were more severe) were detected in all the children regardless of their age, whereas moniliform blepharosis (beaded eyelids) was suggested to be dependent on age (Al-Faky et al., 2012). This research shows that certain ophthalmological signs and symptoms of LiP (such as

moniliform blepharoris) progress with age, while others are less dependent on age. The research also suggests that some phenotype-genotype correlations may be evident in LiP.

Aplasia of the teeth, additional teeth, underdevelopment of teeth, and gingival hyperplasia have been reported in several individuals with LiP, including children (Mainali, Nayak, & Gaur, 2011; Marta et al., 2008; Rook, 1976). Multiple carious teeth may be present due to hypo- salivation (Kurtuluş, Onur, Olgaç, Balik, & Batur, 2006); therefore, teeth often need to be extracted at an early age (Finkelstein, Hammond, & Jones, 1982; Rook, 1976; Simpson, 1972). Overall, the literature indicates that extracutaneous signs and symptoms of LiP that do not involve the CNS are present from birth (such as abnormalities of the teeth) or may develop at any age.

CNS Signs and Symptoms

No information about the foetal brain development of individuals with LiP is available, although Srinivasan et al. (2009) reported that an MRI of the brain of a 7-year-old boy with LiP did not indicate any signs of glial cell migration errors, which is normally a sign of abnormal early prenatal brain development. However, a generalisation to other cases cannot be made based on this one case. Several authors reported normal neurological status in children and adolescents with LiP (Acar et al., 2004; Aubin, Blanc, Badet, & Chobaut, 1989; Baykal et al., 2007). However, intracranial calcifications and other CNS complications such as epilepsy (Newton et al., 1971; Omrani et al., 2012), and headaches (Kumar et al., 2002; Wang et al., 2006) in children and adolescents with LiP have also been reported. Therefore, variable reports about the presence of CNS involvement in LiP among children and adolescents exist. However, it may be important to note that the majority of studies that either report an absence of CNS involvement or do not list CNS-related symptoms in children and adolescents with LiP did not make use of radiological investigations or neuropsychological measures (Barthelemy et al., 1986; Baykal et al., 2007; Ehsani et al., 2006; Hamada et al., 2003; Yakout et al., 1985). Consequently, the prevalence of intracranial manifestations and neurological and neuropsychological complications among children with LiP may be underreported.

The prevalence and progression of epilepsy and intracranial calcifications will be discussed next in more detail.

Epilepsy. While adults with LiP often suffer from epilepsy (Claeys et al., 2007; Hofer, 1973; Newton et al., 1971; Thornton, 2006), only 9 out of 229 (3,9%) reported cases of children and adolescents younger than 19 years with LiP were mentioned to have seizures (Desmet et al., 2005; Hafeez & Hussain, 1996; Ito et al., 2000; Kini et al., 2006; Miziara, Gondim, Takeuti, & Mitini, 1992; Nagasaka et al., 2000; Omrani et al., 2012; Steenkamp, 1997). However, it was not possible to access detailed information (full articles) with regard to all cases (Fochem, Geschnait, & Klumair, 1983; Irkeç, Orhan, Orhan, Durgun, & Can, 1996; Pavlinec & Bucek, 1979). Therefore, in many cases, it is unknown if the children and adolescents with LiP had epilepsy or not. Thornton (2006) found that none of the five South African children and adolescents with LiP evaluated by her had epilepsy.

A history of seizure onset during childhood or adolescence was reported in case descriptions of at least 11 adults with LiP (De Lima et al., 2003; Fabrizi, Porfiri, Borgioli, & Serri, 1980; Johnson & Hepler, 1989; Şenol et al., 2007; Yesudian & Bhasker, 1972). However, a history of the progression of symptoms such as seizures is often not included in case reports of adults with LiP. The youngest age of onset of epilepsy mentioned in the literature was infancy (0-24 months). Desmet et al. (2005) and Newton et al. (1971) reported that the individuals they described had presented with epilepsy at the age of three. The woman with LiP that Newton et al. (1971) examined, reported an increase in the frequency of seizures during adolescence. Appenzeller et al. (2006) hypothesise that epilepsy may be more common in the advanced stage of LiP, as evidenced by the presentation of seizures in the oldest of three patients examined by them. Overall, the general age of onset or the true incidence of seizures in children and adolescents with LiP is unknown, but it is evident that several children and adolescents with LiP are reported to have epilepsy, in some cases starting as young as three years.

Statistics reported by Eriksson and Koivikho (1997), Leonard and George (1999) and Sander (2003) indicate that, in developed countries, epilepsy affects approximately 0.0037% to 0.05% of individuals younger than 16 years. In resource-poor countries, the incidence is likely to be higher (approximately 0.57%) due to factors such as the lack of medical facilities and technology (Placencia et al., 1994; Senanayake & Román, 1993). Therefore, several factors can play a role in the incidence of epilepsy in a given sample of children.

Apparently, the prevalence of epilepsy among children and adolescents with LiP has not been studied; therefore, it is unclear if epilepsy is more prevalent among these individuals than among the general population. However, a small number of children and adolescents with LiP were reported to have epilepsy. Literature on adults indicates that the prevalence of epilepsy in LiP is greater than in the general population (Thornton, 2006). This suggests that the onset of epilepsy may be in late adolescence or adulthood in most cases.

Intracranial calcifications

Prevalence of intracranial calcifications in children and adolescents with LiP. Intracranial calcifications, specifically bilateral, circumscribed, symmetrical lesions in the temporal lobe (mostly the amygdala, hippocampus, parahippocampal gyrus or striatum), are considered characteristic of LiP (Appenzeller et al., 2006; Friedman et al., 1984; Gonçalves et al., 2010; Kleinert et al., 1987). The prevalence of intracranial calcifications in individuals with LiP older than 10 years of age has been reported being 50%-75% (Aroni et al., 1998; Hofer, 1973). The prevalence of brain calcification in LiP during childhood (0-12 years) and adolescence (13-18 years) is not known. A search of the available literature from 1941 to 2013 indicates that thirty-two (29%) of 111 adolescents (individuals between the ages of 13 and 18) with LiP exhibited brain calcifications. These studies are too numerous to list, but they include reports by Emsley and Paster (1985), Gonçalves et al. (2010), Omrani et al. (2012), Salih et al. (2011) and Pradhan, Mahadik, Karekar, Bhat & Desmukh (2013). However, imaging results were not available for all the reported cases; therefore, this figure (29%) may be an underestimation of the true prevalence of intracranial calcifications among adolescents with LiP.

A literature search indicates that 117 out of a total of 229 children and adolescents with LiP (51%) who were reported in the available literature spanning from 1941 to 2013 were younger than 13 years (Abbas et al., 2013; O'Blenes et al., 2013; Raymond-Jones, 1965; Scott & Findlay, 1960). Neuroimaging results were reported in 51 of these 117 cases, with intracranial calcifications present in 13 (25,5%) of the children. Examples of articles referring to the neuroimaging results of 51 children and adolescents with LiP include case reports by König, Hausser, Anton-Lamprecht, Schröter, and Petzoldt (1994), Lupo et al. (2005), Matisonn (1972) and Sainani et al. (2011). Radiographic results for 14

LiP children of the ages six and younger were available, and none of them had brain calcifications (Cinaz, Güvenir & Gönlüşen, 1993; Feiler-Ofry et al., 1979; Haneke, Hornstein, Meisel-Stosiek & Steiner, 1984; Marone et al., 1991; Van Rooy et al., 1991). Thus, intracranial calcifications have been observed in a number of children with LiP. This includes a number of reports of intracranial calcifications in children below the age of 10 years. However, the incidence of intracranial calcifications in children with LiP has not been established formally.

It may be pertinent to consider whether certain methodological issues in the available LiP research could have influenced the estimation of the apparent prevalence of intracranial calcification among children and adolescents affected by the condition. First, X-rays were used in many of the studies (Rao, Prabhu, Scripathi, & Gupta, 2008; Shivaswamy et al., 2003; Vedamurthy, 2003), and Atlas et al. (1988) cautioned that X-rays might be less effective than CT or MRI in detecting structural brain pathology. Consequently, it is possible that intracranial calcifications existed in a number of the children and adolescents described in these studies, but that the neuroimaging techniques employed were inadequate. Furthermore, obtaining a reliable neuroimaging result for young children is often problematic due to their inability to remain immobile for an extended period of time. Therefore, methodological and logistical factors may have caused an underestimation of the prevalence of intracranial calcifications in children and adolescents with LiP. It is also important to note that not all children and adolescents with LiP are reported in the literature; therefore, it is not known what the real incidence of intracranial calcifications among unreported individuals is.

Progression of intracranial calcifications in children and adolescents with LiP. In a number of studies involving children and adolescents with LiP who had undergone radiological investigations, calcifications were observed in the hippocampus (Van Rooy et al., 1991), amygdala (Ito et al., 2000, Omrani et al., 2012; Poyrazoglu et al., 2008), deep internal temporal lobes, parts of the hippocampal gyrus (Allani et al., 2005), temporal horn (Bahadir et al., 2006), suprasellar area (Yakout et al., 1985) and temporal lobes (Allani et al., 2005; Nagasaka et al., 2000; Srinivasan et al., 2009). Almost without exception, these calcifications were described as bilateral, symmetrical, bean-shaped (Gonçalves et al., 2010; Ito et al., 2000; Kaya, Gunduz, Kokturk, Tursen, & Ikizoglu, 2002; Kumar et al., 2002) and, in some cases, as hypo intense (Gonçalves et al., 2010). It would thus appear

that the location of intracranial calcifications noted in children and adolescents with LiP (predominantly in the temporal lobe), is similar to that of the location reported for adults (Friedman et al., 1984; Kleinert et al., 1987). Therefore, it can be reasoned that this pattern of calcification in children and adolescents affects similar neuropsychological functions as in adults, such as memory, facial emotion recognition and executive function. Consequently, these neuropsychological functions are of particular interest in the current study.

The age of onset and the progression of lesions may have important implications for the cognitive and psychosocial development of children and adolescents with LiP (Prather et al., 2001). It has been hypothesised that brain calcifications in individuals with LiP are generally more common after the age of 10, presumably due to pericapillary degenerative changes in the area of the anterior choroidal artery (Al-Natour, 2008; Appenzeller et al., 2006; Rahalkar et al., 2001). However, some studies indicate bilateral temporal lobe calcifications in a number of children younger than 10 years (Rahalkar et al., 2001; Scott & Findlay, 1960; Shivaswamy et al., 2003). Therefore, these findings indicate that temporal lobe calcification in persons with LiP does not occur exclusively during adolescence and adulthood.

Recently, Appenzeller et al. (2006), Hurlemann et al. (2010) and Terburg et al. (2012) suggest that the degree of calcification in LiP may be progressive and related to the duration of the disease. Appenzeller et al. (2006) base their conclusion on the observation of more extensive bilateral symmetrical calcification of the amygdalae in two older individuals (23 and 44 years old), compared to no amygdala lesions in a five-year-old child with LiP. However, Omrani et al. (2012) report significant calcification and atrophy in the bilateral amygdala of a 14-year-old girl, indicating extensive amygdala damage in early adolescence.

Hurlemann et al. (2010) conducted repeated MRI scanning of two adults with LiP and found that their bilateral temporal lesions progressed over time. Initially, the lesions in these two individuals were located primarily in the basolateral subregion alone, but after a period of approximately three years, their lesions progressed to incorporate the whole amygdala region. Similarly, Feinstein et al. (2011) report that SM (the often studied case first described by Tranel & Hyman in 1990) initially presented with focal bilateral

amygdala lesions and a circumscribed area of white matter damage in the area of the amygdala and the anterior entorhinal cortex, but that these lesions eventually extended to the putamen. Terburg et al. (2012) found calcified tissue localised in the basolateral amygdala of the three younger adult women participating in their study, and found that the lesions in the two oldest women that participated in the study extended beyond the basolateral amygdala into the borders of the right superficial amygdala. Overall, the mentioned studies (Feinstein et al., 2011; Hurlemann et al., 2010; Terburg et al., 2012) indicate progression of brain lesions during adulthood in persons with LiP. It has to be remembered that the results of these studies, while demonstrating the progressive nature of bilateral temporal lobe calcification in some adults with LiP, do not necessarily suggest that similar progressions occur in children and adolescents or all individuals with the condition.

The literature reviewed suggests that intracranial calcifications are prevalent in individuals with LiP older than 10 years of age. In addition, cases of intracranial calcifications in children younger than 10 years of age have also been reported. Therefore, some evidence suggesting the presence of intracranial lesions (which may increase in size or invade other areas) in children and adolescents with LiP exists. However, the prevalence of intracranial calcifications in this developmental phase has not been established clearly. Evidence, mostly obtained through scanning adults with LiP and amygdala lesions, suggests that the degree of calcification in persons with LiP might be progressive and related to the duration of the disease.

Intracranial lesions and epilepsy may have a negative effect on the neuropsychological development of children and adolescents with LiP. In the next section, these potential negative effects will be discussed.

Neuropsychological Deficits in Children and Adolescents with LiP

Bilateral calcification in the temporal lobe, often the amygdala, in persons with LiP has been associated with specific cognitive problems in areas of memory, executive function, decision making and social cognition (Adolphs, Gosselin, et al., 2005; Adolphs, Tranel, et al., 2005; Brand et al., 2007; Buchanan, Tranel, & Adolphs, 2003). Since calcification in the temporal lobe in children and adolescents with LiP has also been described (Lupo et al., 2005; Rahalkar et al., 2001; Staut & Naidich, 1998), similar deficits

or difficulties may occur in children with the condition. However, given the rapid neural development taking place during childhood, the neuropsychological profile of children and adolescents with LiP may differ from that noted among adults with the condition (Karmiloff-Smith, 1997; M. Thomas & Karmiloff-Smith, 2002). It has also been suggested that intracranial calcifications commonly associated with LiP may develop or enlarge with age, thus resulting in a progression of neuropsychological deficits (Appenzeller et al., 2006; Hurlemann et al., 2010; Terburg et al., 2012). Therefore, the influence of the developmental context of children on the specific presentation of brain injuries needs to be taken into account. The outcome may depend on several factors, which will be explored briefly.

It is important to consider the age of acquisition and the progression of the lesion (Allman & Scott, 2013; Anderson, Damasio, Tranel, & Damasio, 2000; Eslinger, Flaherty-Craig, & Benton, 2004). There appears to be increasing consensus in the literature that brain damage suffered in early childhood tends to increase the likelihood of serious cognitive deficits and adaptive behavioural difficulties throughout childhood and adolescence (Anderson et al., 2000; Eslinger et al., 2004; Tranel & Eislinger, 2000). However, variability in the outcome of early-onset or congenital brain damage has also been noted (Anderson et al., 2000; Chugani, Müller, & Chugani, 1996; Spilkin, Ballantyne, Babchuk, & Trauner, 2007). Lidzba, Staudt, Wilke, and Krägeloh-Manna (2006) and Allman and Scott (2013) suggest that deficits associated with early focal lesions may be the consequence of complex processes such as a crowding effect. *Crowding effect* refers to a neuronal scarcity in the damaged hemisphere, affecting the development of functions associated with that and the opposite hemisphere (Lidzba et al., 2006). This scarcity leads to functional reorganisation, where deficits are observed in functions not normally associated with the damaged hemisphere. Therefore, deficits associated with early focal lesions may lead to atypical functioning due to reorganisation.

It was suggested that developing brain regions are less specified; therefore, injury to the child's brain is far more likely to result in generalised or global deficits (Anderson, Northam, Hendy, & Wrennall, 2001). An early lesion can have a widespread effect, not only on the local site, but also on the maturation of interacting areas mediating the acquisition of several functions (Eslinger et al., 2004; Kolb, Gibb, & Gorny, 2000). When using the traditional methodology of comparing function in the hypothesised area to other

domains, the apparent milder effect of the injury on a child's brain may be a measurement error due to the omission of the possibility of global reductions in function (Stiles, Reilly, Paul, & Moses, 2005).

Another factor that may affect the outcome and profile of neuropsychological deficits in children and adolescents with focal lesions is plasticity. It has been suggested that plasticity and periods of vulnerability during childhood play a role in the eventual outcome and development of children with focal brain lesions or brain abnormalities (Karmiloff-Smith, 2007; Stiles, 2000; Stiles et al., 2005; Thompson et al., 2009). Plasticity effects were observed in an adult with LiP who appeared to have developed a functional social neural network, despite amygdala damage (Becker et al., 2012; Hurlemann et al., 2010). Normal responses to fear signals and negatively valenced social stimuli (functions normally associated with the amygdala) were observed. This was hypothesised to be the result of partial functional compensation involving the mirror-neuron system (Becker et al., 2012; Hurlemann et al., 2010). It was suggested that the mirror-neuron system had taken over some of the functions normally ascribed to the amygdala. Nevertheless, this phenomenon was observed in an adult with LiP, and it is possible that children with LiP will not show the same functional compensation.

Another phenomenon affecting the cognitive functioning of individuals with focal lesions, *paradoxical functional facilitation* (Kapur, 1996, p. 1776), has been described. Paradoxical functional facilitation refers to the fact that a lesion or second lesion of the brain may bring about an improvement in functioning (Pilato et al., 2009; Toomela, Tomberg, Orasson, Tikk, & Nõmm, 1999). An example of paradoxical functional facilitation is when a second lesion in an affected hemisphere determines a plastic change of the unaffected hemisphere by switching off a maladaptive modulation exerted by the affected hemisphere on the contralateral hemisphere (Pilato et al., 2009). In a study by Morgan et al. (2012), adults with LiP outperformed controls on a measure of working memory. Their basolateral amygdala damage appeared to have caused enhanced working memory performance. An interactive model of brain functioning described by Stevens (2009) was suggested to explain this phenomenon. It was hypothesised that reduced vigilance, caused by amygdala damage, allowed the individuals with LiP to perform better in a working memory task (Morgan et al., 2012). It means that if a function (such as vigilance) subserved by a specific brain region normally interferes with the function in

another brain region (such as working memory), subsequent damage to the first brain region (vigilance) would remove the interfering effect of this brain region. Overall, the phenomenon of paradoxical facilitation was observed in adults with LiP. Therefore, paradoxical enhancement (better performance compared to healthy individuals) in certain cognitive measures may also be observed in children and adolescents with LiP.

Owing to the factors described in the previous paragraphs, focal brain injuries or lesions acquired during childhood and adolescence have been shown to result in deviations from the typical neuropsychological developmental trajectories (Anderson et al., 2000; Anderson & Catroppa, 2007; Eslinger & Biddle, 2000; Eslinger et al., 2004). Focal lesions may result in atypical or abnormal cognitive development, as is evident in slower and atypical development, stagnation or plateaus in cognitive development (Scott et al., 2001; Stiles et al., 2005) and even loss or regression of previously attained functions (Copeland, DeMoor, Moore III, & Ater, 1999; Fisch et al., 2007). It is not clear if a progressive lesion may also cause increasingly enhanced performance in certain cognitive measures, in line with the paradoxical facilitation phenomenon described in the previous paragraph (Pilato et al., 2009; Terburg et al., 2012).

Although amygdala lesions were observed in children and adolescents with LiP (Appenzeller et al., 2006; Ito et al., 2000, Omrani et al., 2012), very little information could be found on the neuropsychological functioning of children and adolescents with the disorder. A few researchers have investigated some aspects of cognitive functioning in children and adolescents with LiP, focusing mainly on deficits in declarative memory and facial emotion recognition (Emsley & Paster, 1985; Savage et al., 1988; Teive et al., 2004; Thornton, 2006). To date, however, no specific neuropsychological profile of children and adolescents with LiP has been compiled. Moreover, several domains of neuropsychological functioning reported being affected by LiP in adults or associated with amygdala damage in adults – such as ToM, emotional memory and learning, moral reasoning, social attention, executive function and affective decision making – have remained unexplored in children and adolescents with the condition. Additionally, no information on the progression of neuropsychological functioning of children and adolescents with the disorder could be found.

The available literature on the neuropsychological and psychosocial functioning of children and adolescents with LiP will be reviewed within the context of typical development and with specific reference to the effect of temporal lobe damage on cognitive development.

Memory and Learning

To understand the effect of paediatric LiP and the associated temporal lobe or amygdala lesions on the development of memory functions, it is necessary to discuss the neurological substrate underlying memory development briefly.

The neurological substrate underlying declarative memory development. Learning and memory in children progress from simple habituation, adaptation and conditioning - implicit memory processes associated with the subcortical regions - to increasingly cortical control of memory and learning processes. The maturation of the temporal and prefrontal lobe structures and the connections between them has been linked to the development of episodic memory (Bauer, 2008; Cycowicz, Friedman, & Duff, 2003; Newcombe, Lloyd, & Ratliff, 2007; Ofen et al., 2007). Changes in neurochemistry, structure and dynamic processes (such as synaptogenesis, myelination and pruning, and brain network integration) during specific developmental periods contribute to maturation, fine-tuning and specialisation of the declarative memory system (Casey, Galvan, & Hare, 2005; Casey, Giedd, & Thomas, 2000; Munakata, Casey, & Diamond, 2004). Rudimentary explicit (but not necessarily episodic) memory functions start developing earlier than what was proposed initially (at approximately six months), due to hippocampal maturation, which was suggested to continue until as late as five years of age (Bauer, Larkina, & Deocampo, 2011; Gogtay et al., 2006). Developmental changes in the temporal lobe structures affect the efficiency of encoding, stabilisation of long-term storage, rate of forgetting and the ease and speed with which appropriate information is retrieved (Bauer, 2008). The development of the dentate gyrus is related specifically to improvement in the consolidation of new information (Bauer et al., 2011). Place learning and memory for spatial location depends on the hippocampus, and improvement in this function between 18 and 24 months is linked to a general transition in spatial representation occurring towards the end of infancy (Sluzenski, Newcombe & Satlow,

2004). These changes might be associated with the retrieval of the first autobiographical memories (Newcombe et al., 2007).

It was suggested that memory development occurs within the context of the development of other cognitive functions (Ghetti & Angelini, 2008; Sluzenski, Newcombe, & Kovacs, 2006; Tulving, 2002). Children initially depend more on visual memory strategies due to their underdeveloped verbal abilities (Newcombe et al., 2007). The development of language skills makes the acquisition of factual knowledge possible and forms the basis for symbol formation, which is associated with the functions of the parietal lobe (Welzer & Markowitsch, 2005). The consequential ability to hold mental images in short-term memory (parietal lobe development) contributes to improved working memory (Baddeley, 2001). Similarly, when attention span and processing speed increase, more information can be held and processed in the working memory (Visu-Petra, Miclea, Cheie, & Benga, 2009).

All memory processes (from encoding to retrieval) are influenced by the protracted development of the prefrontal cortex and its connections (Bauer, 2008). The maturation of the frontal lobe and the frontal-medial temporal circuit is specifically important for the development of source memory and strategic memory (using strategies to learn and retrieve information), which improve between four and six years of age (Newcombe et al., 2007). During this developmental stage, the ability to bind information develops. *Binding* refers to the process of encoding relations among stimuli, ensuring cohesion of the details that are remembered (Cohen & Eichenbaum, 1993). This ability of binding enables the formation of complex memories and is related to the formation of episodic memory (Sluzenski et al., 2006). Overall, the development of the frontal lobe and the frontal-temporal connections initiates a transition from primary reliance on simple recognition and associative memory to strategic memory (Becker & Lim, 2003). Therefore, executive function is the main contributor to improvement in memory functions during middle childhood.

Memory development occurs in interaction with the environment (Bauer, 2010; Durston et al., 2006; Farah et al., 2006; Kroupina, Bauer, Gunnar, & Johnson, 2010); therefore, socio-economic factors and trauma may affect memory development (Bauer, 2010; Cowan, 2009; Kroupina et al., 2010). An example of the effect of the environment

on memory development, is the relationship between trauma and hippocampal plasticity. Stressful environmental conditions (pre- or postnatal) lead to high levels of cortisol and have profound effects on neurogenesis in the dentate gyrus, which provides an index of hippocampal plasticity; these alterations are associated with impaired performance in spatial memory tasks and altered behaviour (Coe et al., 2003; Lemaire, Koehl, Le Moal, & Abrous, 2000; Noble, Houston, Kan, & Sowell, 2012).

The role of the amygdala in memory development. Pinabiaux et al. (2013) indicate that the amygdala is important for the development of normal interactions between emotions and memory, and the integration of emotion and memory continues to develop from early childhood through adolescence when interactivity between the brain systems improves due to myelination in the frontal lobe. Development of emotional memory is affected by changes in the neurochemistry of the amygdala, for example norepinephrine, GABA, opioid, peptidergic and cholinergic systems involved in the neuromodulation of memory storage (Fellous, 1999). The ability to remember the gist of a story or relevant details was shown to be dependent on the intact functioning of the amygdala (Adolphs, Denburg, & Tranel, 2001; Adolphs, Tranel, et al., 2005). Pre-school children often have difficulty remembering the gist of a story or event and focus too much on details or unimportant information due to immature interaction between the amygdala and hippocampus and the temporal and frontal lobes. Markowitsch (2008) suggests that the amygdala plays an important role in autobiographical memory and that this kind of memory represents the highest level of integrative memory functioning, as it is dependent on interaction between emotion, social maturity and self- and temporal awareness. Development of autobiographical memory in interaction with the social environment takes place gradually from approximately two years of age (Welzer & Markowitsch, 2005). The development of autobiographical memory is dependent on temporal awareness and theory of mind and requires interaction between the temporal pole and the frontal lobe (Welzer & Markowitsch, 2005).

Overall, the maturation of the temporal and prefrontal lobe structures and the connections between them can be associated with a cascade of declarative memory development, with the culmination in complex forms of memory such as strategic and episodic memory, which is reliant on frontal-temporal lobe connections. The amygdala appears to play a specific role in the development of emotional and autobiographical

memory and memory for the gist of a story. Owing to the importance of the temporal lobe brain regions, including the amygdala, in the development of declarative memory across the different age groups, it can be expected that temporal lobe lesions in children and adolescents may have a negative effect on the development of this function. The effect of temporal lobe damage on the development of memory will be discussed next.

Temporal lobe damage and memory in children. Several authors have reported declarative memory deficits in children with temporal lobe lesions (Bonelli et al., 2010; Cronel-Ohayon et al., 2006; Gleissner et al., 2002; Leunen et al., 2009; Nolan, Redoblado, & Lah, 2004). Deficits pertaining to consolidation and verbal learning seem to be characteristic of temporal lobe resection during childhood (Bonelli et al., 2010; Cronel-Ohayon et al., 2006; Leunen et al., 2009), although there is still uncertainty about the different effects of left hemisphere versus right hemisphere lesions on memory functioning (Carpentieri & Mulhern, 1993; Kar, Rao, Chandramouli, Thennarasu, & Satishchandra, 2010; Lee et al., 2010; Mabbott & Smith, 2003). Left hemisphere resection during childhood was often found to be associated with deficits in verbal learning and verbal delayed recall (Bonelli et al., 2010; Gleissner et al., 2002; Leunen et al., 2009; Szabó et al., 1998), although lateralisation did not always predict the type and extent of memory deficits (Gonzalez, Anderson, Wood, Mitchell, & Harvey, 2007; Kar et al., 2010; Mabbott & Smith, 2003). Memory deficits in the context of widely distributed neuropsychological deficits were often present despite lesion side (Kar et al., 2010). This may be because visual and verbal memory does not seem to be as clearly dissociated in children as in adults (Lendt, Helmstaedter, & Elger, 1999). It is also possible that children with complex partial seizures may develop atypical language and other dominance due to brain plasticity, which may explain why lesion side does not predict specific verbal or visual memory deficits (Brázdil, Zákopčan, Kuba, Fanfrdlová, & Rektor, 2003; Everts et al., 2010; Helmstaedter, Brosch, Kurthen, & Elger, 2004).

The literature suggests that acquired bilateral hippocampal lesions in children and adolescents (such as bilateral hippocampal atrophy associated with hypoxic-ischemic episodes) are associated with anterograde amnesia (Gadian et al., 2000; Martins, Guillery-Girard, Jambaqué, Dulac, & Eustache, 2006; Vargha-Kadem et al., 1997; Vargha-Kadem et al., 2003). Deficits in immediate and delayed memory for verbal and visual material as well as paired associate recall were reported (Cormack, Vargha-Khadem, Wood, Cross, &

Baldeweg, 2012; Gadian et al., 2000; Vargha-Kadem et al., 1997). Interestingly, several reports suggest that children with amnesia due to hippocampal damage early in life has at least partially preserved abilities to acquire semantic knowledge, despite the lack of a premorbid knowledge base (Brizzolara, Casalini, Montanaro, & Posteraro, 2003; Gardiner, Brandt, Baddeley, Vargha-Khadem, & Mishkin, 2008; Martins et al., 2006; Vicari et al., 2007). Adults and children with developmental amnesia due to perinatal hippocampal damage were also found to be less impaired in familiarity-based recognition memory than they were in recollection (Brandt, Gardiner, Vargha-Khadem, Baddeley, & Mishkin, 2009; Vargha-Khadem et al., 2001). A reason for this dissociation is suggested to be that the perirhinal-entorhinal regions support familiarity-based recognition and remain intact in developmental amnesia (Düzel, Vargha-Khadem, Heinze, & Mishkin, 2001). Therefore, these findings suggest dissociation between semantic and episodic memory as well as between familiarity and recall processes.

The age of onset of temporal lobe and bilateral hippocampal lesions is suggested to play a role in the effect on memory functioning (Gleissner, Sassen, Schramm, Elger, & Helmstaedter, 2005; Lee et al., 2010). Onset of temporal lobe lesions in childhood is associated with outcomes that are more positive when compared to onset in adulthood (Gleissner et al., 2005; Lee et al., 2010). It is suggested that plasticity during infancy and early childhood promotes superior recovery of memory function after temporal lobe resection in children (Gleissner et al., 2005; Seidenberg et al., 1997). However, the type of underlying pathology in Temporal Lobe Epilepsy (TLE) was not taken into account consistently when research results were interpreted (Gonzalez et al., 2007; Lee et al., 2010). Cormack et al. (2012) found distinct presurgical profiles of memory impairment that depended on the underlying pathology in paediatric TLE.

In general, early-onset bilateral hippocampal damage (before the age of one year) yielded significant functional and structural reorganisation of the neural substrate underlying memory (Maguire, Vargha-Khadem, & Mishkin, 2001; Manning, 2008), leading to less severe memory impairment compared to memory impairment with lesion onset during later childhood (Braun et al., 2008; Vargha-Kadem et al., 2003). However, Isaacs et al. (2003) found that the volume of the hippocampus predicted the severity of memory impairments among a group of adolescents who were born preterm and among a group with developmental amnesia. When the volume of the hippocampus was reduced

below normal by 20-30% on each side (such as in the amnesic group), the memory impairment was disabling. Memory impairment was less pronounced in the group of adolescents that were born preterm (hippocampal volumes ranged from 8-9%). Therefore, it is likely that the severity of memory difficulties in children and adolescents with LiP may also be affected by the degree of temporal lobe calcification.

The presence of seizures is suggested to have an effect on the outcome of memory development in children with early-onset bilateral hippocampal lesions. Bilateral hippocampal atrophy due to *status epilepticus* is suggested to lead to severe global developmental deficits when onset is early (DeLong & Heinz, 1997) and less severe cognitive delay and specific memory deficits are found with later onset (Jambaqué et al, 2006). Hippocampal atrophy due to *status epilepticus* possibly prevents plasticity effects due to epileptic brain activity (Jambaqué et al., 2006). Bilateral hippocampal atrophy due to chronic generalised epilepsy (including episodes of *status epilepticus*) may also have a general slowing effect on the brain and thus affect encoding and recall, caused by encumbered processing speed (Lopes, Simões, Robalo, Fineza, & Gonçalves, 2010). Therefore, children and adolescents with LiP and associated epilepsy may have worse memory functioning compared to individuals without epilepsy.

Only three studies could be found with regard to the effect of temporal lobe and amygdala lesions on emotional memory in children (Pinabiaux et al., 2013). Jambaqué et al. (2009) and Pinabiaux et al. (2013) found reduced enhancement of memory for emotional stimuli (recall and recognition) in children and adolescents with TLE and temporal lobe resection, while facilitation of memory for emotional material in typically developing children is evident. Early damage to the amygdala is also associated with a lack of enhancement of memory for emotional stimuli compared to neutral stimuli during adulthood (Shaw, Brierly, & David, 2005). The recognition of fearful faces was the exception in the study by Pinabiaux et al. (2013). Memory enhancement for fearful faces, but not for other emotional expressions, was evident in children and adolescents with temporal lobe resection in this study. Pinabiaux et al. (2013) was of the opinion that fearful expressions might possibly increase memory for faces through familiarity rather than through recollection in children and adolescents with temporal lobe resection, compared to memory enhancement through recollection in healthy individuals.

From the above literature, it is evident that early-onset temporal lobe lesions or resection, bilateral hippocampal sclerosis and early amygdala damage in children are associated with memory deficits. The age of onset and volume of temporal lobe and bilateral hippocampal lesions is suggested to play a role in the effect on memory functioning. *Status epilepticus* in very young children who have hippocampal lesions prevents plasticity and has a detrimental effect on memory and global development. Early temporal lobe or amygdala damage is suggested to cause a lack of enhancement of memory for emotional stimuli compared to neutral stimuli. Overall, the literature suggests that temporal lobe lesions in children and adolescents cause declarative memory deficits; therefore, temporal lobe lesions in children and adolescents with LiP may cause similar difficulties.

Memory in children and adolescents with LiP. LiP in adults has been associated with deficits in declarative memory (Maruani et al., 2007; Thornton et al., 2008) and emotional memory (Adolphs, Tranel & Buchanan, 2005). Some reference to the memory functioning of children and adolescents with LiP could be found (Brand et al., 2007; Emsley & Paster, 1985; Omrani et al., 2012; Savage et al., 1988). Savage et al. (1988) reported poor performance in memory tests by a 5-year-old girl with LiP who had extensive parasellar calcifications located in the amygdala and hippocampus. Neuropsychological testing showed evidence of impairment of visual and verbal memory in the context of otherwise normal cognitive abilities. The memory impairments were not described in any detail, and the information did not provide clarity on the nature of the memory deficits (such as short term or long term). The case report suggests that memory impairments may already be noticeable in young children with LiP who have calcifications in the amygdala and hippocampus.

Emsley and Paster (1985) were the first to report on the memory functioning of an adolescent with LiP. The short-term visual memory of this 18-year-old female was impaired in the face of relatively intact visuomotor abilities. A CT scan showed intracranial calcification in both temporal lobes, anteromedial to the tip of the inferior horn of the lateral ventricle. No verbal memory tests were administered; therefore, no further deductions can be made with regard to verbal memory. Omrani et al. (2012, p. 150) reported that a 14-year-old adolescent with LiP, suffering from bilateral amygdala lesions and presenting with epilepsy since the age of five years, had normal “recent and remote

memories". No further detail with regard to the nature of the memory impairment was provided. Brand et al. (2007) reported normal visual delayed recall, but a deficit in delayed free recall of affective words in a 17-year-old adolescent with LiP and bilateral amygdala damage.

The case descriptions by Brand et al. (2007), Emsley and Paster (1985) and Omrani et al., (2012) indicate variable memory functioning in adolescents with LiP. The wider literature supports the likelihood of deficits in visual and verbal declarative memory as well as emotional memory in children and adolescents with temporal lobe lesions or abnormality (Gadian et al., 2000; Kesler et al., 2004; Reiss, Lee, & Freund, 1994; Vargha-Kadem et al., 2003). Therefore, it is very likely that the memory deficits of the child and adolescents with LiP described in the previous paragraphs were associated with their observed temporal lobe calcifications. The nature of the intracranial lesions and the onset and progression of the lesions may explain the variable results. The affective nature of the content may also affect the performance of adolescents with LiP.

Markowitsch and Staniloiu (2011) propose that memory impairment in interconnected processing of affective and cognitive aspects in individuals with LiP may lead to difficulties in the development of an integrated personality. Therefore, amygdala damage and memory impairments in children and adolescents with LiP may lead to difficulties in the development of a self-concept. Memory impairment may further limit learning, social adjustment and the acquisition of skills (Anderson, Northam, et al., 2001; Jambaqué et al., 2006) and the development of extensive personal (autobiographical) memories (Lysaker & Buck, 2007). Subsequently, limited skills acquisition and poor self-concept may lead to poor adaptive functioning (Lysaker & Buck, 2007).

In summary, there is a marked paucity of research regarding memory functioning in children and adolescents with LiP. With regard to the few studies available, the literature indicates variable results with regard to memory functioning, which is possibly dependent on the type of lesion and the nature of the material to be remembered. Several limitations, such as the limited number of reported cases and the absence of fine-grained measurement of memory in most of the studies, prohibit a definite conclusion.

Recognition of Facial Emotion

Neural mechanisms underlying recognition of facial emotion

The neurological substrate of development of recognition of facial emotion. Although research is available with regard to brain structures and processes underlying recognition of facial emotion in adults, very little research has been conducted on the development of neuroanatomical structures underlying recognition of facial emotion during childhood (Baird et al., 1999; Killgore, Oki, & Yurgelun-Todd, 2001; Thomas, De Bellis, Graham, & LaBar, 2007). It is possible that different cortical areas mediate recognition of facial expression during different developmental stages (McClure, 2000). Tonks et al. (2008) propose a model for the development of recognition of facial emotion, based on the identification of three levels of processing of facial emotion. Tonks et al. (2008) suggest that these processes come on line and continue to operate, starting with the most basic intrinsic arousal system and culminating in higher levels of executive control of emotion perception and regulation of emotion. It was suggested that neural processes involved in processing facial emotional expressions, as measured by ERPs, develop in a staggered fashion throughout childhood, with the adult pattern appearing only late in adolescence (Batty & Taylor, 2006; Calder et al., 2003).

The first level of processing facial emotion involves intrinsic arousal in reaction to emotional cues. This level of processing is functional at birth and consists of a fast recognition response system, dependent on subcortical structures, primarily the amygdala and hippocampus (Adolphs, 2002a). The next level of processing is more sophisticated and involves confirmation of initial non-conscious recognition through analysis. Spatial and information processing pathways and structures (including the right inferior parietal cortex, the occipital and posterior temporal visual cortices, the fusiform gyrus and the superior temporal gyrus) converge on the amygdala and triggers an appropriate non-conscious emotional reaction (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000; Adolphs, Damasio, Tranel, & Damasio, 1996). This process enables reward-based and associative learning of visual and auditory emotional displays. The sensory and spatial analysis system develops rapidly during the first 18 months of life and continues to develop (especially evident in the right hemisphere of the brain), with a further significant

growth spurt observed around the age of 10 to 13 (Batty & Taylor, 2006; Tonks et al., 2008).

The third level of processing facial emotion involves the integration of affect perception and cognition, leading to action or thought (Tonks et al., 2008). This level of processing requires executive control and modulation of emotional reactions. Development of the latter executive system occurs throughout childhood and adolescence and is based on continued maturation of the frontal lobe (especially the orbitofrontal lobe) and its connections with the subcortical structures. The results of functional MRI studies (Batty & Taylor, 2006; Monk et al., 2003; Nelson, Parker, & Guthrie, 2005), as well as scores of measures on recognition of facial emotion (Herba, Landau, Russell, Echer, & Phillips, 2006; Thomas et al., 2007), confirm that frontal lobe development and progressive changes in cortical-subcortical connections may underlie the development of recognition of facial emotion from an early age (Herba & Phillips, 2004; Herschkowitz, 2000; Thomas et al., 2007). Improved connectivity between the cortical and subcortical structures is also suggested as important for the inhibitory control and regulation of emotion processing (Hariri, Bookheimer, & Mazziotta, 2000; Hariri et al., 2003; Phillips, Drevets, Rauch, & Lane, 2003a).

From the discussion so far, it is evident that the amygdala is part of several brain networks that underlie different levels of processing facial emotion. The amygdala is suggested to be vital during development by establishing the neural networks necessary for emotion expression and recognition (Adolphs, 2006). However, once these neural networks have been established, they may function more independently (Adolphs et al., 1996). Golouboff et al. (2008) postulate that a crucial period, possibly before the age of five years, exists for establishing the neural networks underlying recognition of facial emotion. Once these neural systems have been established, processing of emotions may continue, despite damage to the subcortical areas that are critical for establishing the processing of facial emotion expressions. Herba and Phillips (2004) propose that this may be due to the increasingly important role of the cortical-subcortical connections in the processing of facial emotional expressions. Through these connections, the processing of emotions elicits cognitive processes such as attention and memory (Sato & Murai, 2004). It is suggested that the continued myelination of the frontal lobes of the brain coincides with the development of templates for emotional matching and processing, which

contributes to the acquisition of abstract knowledge of emotions (Batty & Taylor, 2006). On this level of processing, it is evident that the development of recognition of facial expression occurs in tandem with daily personal experiences in a certain cultural environment, which modifies perceptions of personal emotion (Batty & Taylor, 2006). Although the ability to recognise different facial expressions emerges early in life, ongoing development of these skills throughout childhood and adolescence is suggested (Batty & Taylor, 2006; De Sonneville et al., 2002; Durand, Gallay, Seogneuric, Robichon, & Baudouin, 2007).

Recognising different expressions of facial emotion. It is suggested that different neural mechanisms underlie the recognition of different facial expressions in adults (Damasio, Grabowski, Bechara, Damasio, & Ponto, 2000; Grosbras & Paus, 2006; Schroeder, Henenlotter, Erhard, Haslinger, & Stahl, 2004). It is suggested that the amygdala in particular is involved in ascribing emotional significance to stimuli, particularly in processing fearful facial expressions (Calder et al., 2001; Calder et al., 1996; Damasio et al., 2000; Morris, Ohman & Dolan, 1999). However, other studies show that the amygdala also plays a role in recognising other emotional expressions, such as sad and happy facial expressions (Blair, Morris, Frith, Perrett & Dolan, 1999; Morris et al., 1996).

Limited research on the neural basis of recognising different facial expressions during childhood and adolescence has been conducted (Monk et al., 2003; Yang et al.; 2003). Research findings suggest that children recognise happiness earlier in development in comparison with other facial expressions (Boyatzis, Chazzan & Ting, 1993; Golouboff et al., 2008). Typically developing children very seldom confuse negative and positive facial expressions, but most often confuse two negative facial expressions such as angry versus sad (Simonian, Beidel, Turner, Berkes & Long, 2001; Vieillard & Guidetti, 2009; Williams, Wishart, Pitcairn & Willis, 2005). It is postulated that efficient discrimination between happy and negative facial expressions (especially happy facial expressions versus fearful or angry expressions) may have an important evolutionary function in terms of signalling potential environmental threat (Batty & Taylor, 2006; Gao & Maurer, 2010) and reward (Green, 2004; Phillips et al., 1998). For the same reason, it is suggested that children are able to recognise fearful faces at a young age. It is postulated that the amygdala underlies the rapid discrimination between negative and positive facial expressions and the recognition of threat during childhood and adolescence (Monk et al.,

2003; Yang et al.; 2003). The connections between the amygdala and the developing hippocampus possibly explain the emergence of the amygdala response to fearful stimuli (Herschkowitz, 2000).

The discussion emphasises the importance of the amygdala in the development of processes of recognising facial emotion, especially in children younger than six years. The amygdala is suggested to underlie the ability to distinguish rapidly between positive and negative emotions at a very young age. Frontal lobe development (such as myelination in the frontal lobe) and progressive changes in cortical-subcortical connections may underlie the development of recognition of facial emotion throughout childhood. Overall, owing to the suggested importance of the amygdala in the development of recognition of facial emotion, amygdala damage may have a negative effect on the development of this skill.

Recognition of facial emotion by children with temporal lobe damage. Deficits in recognition of facial emotion have been demonstrated in different groups of children with temporal lobe and amygdala pathology (Castelli, 2005; Golouboff et al., 2008; Henry, Phillips, Crawford, Ietswaart, & Summers, 2006; Meletti et al., 2003; Plesa-Skwerer, Faja, Schofield, Verbalis, & Tager-Flusberg, 2006). An association between early-onset amygdala lesions and deficits in recognition of facial emotion has been suggested (Adolphs et al., 1996). In this regard, Adolphs et al. (1996) indicate that an adult with early bilateral amygdala damage found it difficult to recognise facial expressions of fear, whereas two subjects who had sustained bilateral amygdala damage in adulthood were not impaired. Deficits in recognition of facial emotion were also reported in individuals with early onset (before the age of five), TLE and medial temporal lobe sclerosis (Benuzzi et al., 2004; Meletti et al., 2003), whereas no deficits were observed in individuals with seizure onset after five years of age (Meletti et al., 2003). Meletti et al. (2003) postulate that epileptic activity since early childhood may disrupt physiologic phenomena of plastic reorganisation of the temporal lobe, which may prevent the development of recognition of facial emotion and other cognitive skills.

Meletti et al. (2003) suggest that the presence of right-sided as opposed to left-sided medial temporal sclerosis and a history of early onset seizures may be the main factors leading to severe impairment in recognising facial expressions. However, in a more recent article, Meletti et al. (2009) indicate that recognition of facial emotion appears to be more

severely impaired by early onset TLE with bilateral epileptic foci as opposed to unilateral epileptic foci.

Additional research on the effect of early-onset bilateral TLE on recognition of facial emotion in children suggests variable results with regard to the recognition of specific facial expressions. Meletti et al. (2009) found that deficits in the recognition of all basic facial expressions (except happiness) were evident in individuals with early-onset bilateral TLE. Localisation of lesions is suspected to be of importance with regard to deficits in recognising specific emotions, but research results in this regard vary (Golouboff et al., 2008; Meletti et al., 2003; Meletti et al., 2009). Golouboff et al. (2008) found that some children exhibited deficits in the recognition of more than one negative emotion, while other children presented with emotion-specific deficits (Golouboff et al., 2008). McClelland et al. (2006) found that individuals with early-onset TLE and right amygdala damage were impaired in recognising expressions of fear, but not angry or happy expressions. The authors (McClelland et al., 2006) speculate that the development of the right amygdala may be necessary for adequate recognition of fear. Research on children with temporal lobe lesions who do not have epilepsy is lacking, and children who do not have epilepsy may have intact recognition of facial emotion skills or may present with a different pattern of deficits.

Overall, the literature indicates that early amygdala lesions or temporal lobe lesions associated with TLE have a negative effect on the development of recognition of facial emotion. Earlier onset of damage or seizures tends to have a more detrimental effect than later injury or onset of seizures does. The presence of seizures increases the possibility of deficits in recognition of facial emotion due to its disruption of the plastic reorganisation of the temporal lobe. Variable results with regard to specific patterns of deficits in recognition of facial emotion in children with temporal lobe lesions or pathology were reported, although the recognition of happiness was generally not affected. Based on the literature reviewed in this section, it seems possible that bilateral temporal lobe lesions in children and adolescents with LiP may have a negative effect on the development of their ability to recognise different facial expressions.

Recognition of facial emotion by children and adolescents with LiP. Thornton et al. (2008) reported that adults with LiP displayed deficits in recognition of facial emotion

with regard to all the basic positive and negative emotions. Thornton (2006) utilised the Ekman Facial Emotion Recognition Test, requiring testees to name facial emotion expressions displayed by actors in photos. Thornton (2006) notes a possible difference between the performance of adults and children with LiP on the Ekman Facial Emotion Recognition Test. Analysis of the research results of a group of LiP individuals (children, adolescents and adults) indicates an intact ability to recognise happiness compared to controls. When the data for the adults (individuals 17 years and older) were analysed separately from the test results of the three individuals between the ages of 10 and 17 years, it was noted that their ability to recognise positive facial expressions, in addition to difficulty recognising all the negative facial expressions, was impaired. The author (Thornton, 2006) deduced that the ability to recognise happiness might deteriorate with age (due to the possible later onset of temporal lobe calcification). However, the small sample size of the children's group (one child and two adolescents below the age of 17 years) could have affected the validity of the research results. The deficits in the ability to recognise negative facial emotions in the group of children and adults with LiP in Thornton's (2006) study corresponds with a study associating early amygdala damage and difficulties in the recognition of all the negative emotions (Meletti et al., 2009). As Thornton (2006) did not include brain scans, the presence or absence (as well as the extent) of intracranial calcifications could be neither confirmed nor denied. Therefore, an association between the findings related to recognition of facial emotion and the presence or extent of brain lesions could not be established.

Other research on the recognition of facial emotion of children and adolescents with LiP could not be found, except for a case study reported by Brand et al. (2007). Brand et al. (2007) reported that a 17-year-old adolescent with LiP and associated bilateral amygdala damage and epilepsy obtained scores within the normal limits on a test measuring facial affect discrimination, including naming and attribution, as well as affective prosody discrimination and naming. Separate scores reflecting the adolescent's ability to recognise or name specific facial expressions (such as fear or happiness) were not calculated; therefore, it cannot be deduced if this adolescent's test results support Thornton's (2006) findings or not.

Overall, variable results on recognition of facial emotion measures for a few children and adolescents with LiP have been reported. Different instruments to measure

recognition of facial emotion were used, which may explain the inconsistent results. Owing to the small sample sizes, the findings can also not necessarily be generalised to all children and adolescents with LiP. In one study (Thornton, 2006), no radiological results were available; therefore, an association between the findings and the presence of brain lesions could not be established definitively.

ToM

The neural network underlying ToM development. ToM is defined as the ability to attribute mental states (beliefs, desires, intentions, imagination and emotions) to oneself, to understand that others have mental states that are different from one's own, and to predict behaviour in terms of these states (Baron-Cohen, 2001b; Bellerose et al., 2012). It is suggested that the core neural circuit underlying ToM consists of the medial prefrontal cortex, the superior temporal sulcus, bilateral temporoparietal junctions, and para- and anterior cingulate cortex (Amodio & Frith, 2006; Pfeifer et al., 2007), while it is proposed that the amygdala also plays a role (Baron-Cohen, O'Riordan, Stone, Jones, & Plaisted, 1999; Fine et al., 2001). The same regions involved in the adult configuration of ToM seem to be involved in the development of ToM in children and adolescents, but certain changes in the functional activity of these brain regions occur with age. For example, the right temporoparietal junction seems to be active when younger children think about mental and physical facts about people, but activation is evident in older children only when processing facts that are not related to people (Saxe, Whitfield-Gabriele, Pelphrey, & Scholz, 2009).

Some researchers view ToM as an innate module that emerges in infancy (Onishi & Baillargeon, 2005; Wellman, 2011), while others view ToM as the result of general domain processes such as executive function (Bull, Phillips, & Conway, 2008; Sabbagh, Xu, Carlson, Moses, & Lee, 2006; Zelazo, Qu, & Kesek, 2010). It is also possible that ToM involves both modular processes and general domain processes (Leslie, Friedman, & German, 2004). It was suggested that the integrity of the circuitry of the early developing amygdala system is necessary for the emergence and development of ToM (Baron-Cohen, O'Riordan, et al., 1999; Carrington & Bailey, 2009; Siegal & Varley, 2002). The rapid and automatic response of the amygdala to socially significant stimuli plays a prominent role in the development of ToM (Winston et al., 2002) but becomes less important in the

maintenance of this ability (Baron-Cohen et al., 1999; Carrington & Bailey, 2009; Siegal & Varley, 2002).

Tager-Flusberg and Sullivan (2000) suggest that ToM reasoning may be divided into early and late developing components that rely on distinct cognitive and neural mechanisms, and that these mechanisms remain important in adulthood (Saxe et al., 2004; Saxe et al., 2006). Understanding concepts related to mental state, such as feelings and desires, is seen as a separate ToM function compared to reasoning about the contents of mental states, such as beliefs (Saxe et al., 2004; Tager-Flusberg & Sullivan, 2000). This distinction between early and later developing ToM functions appears to overlap with the hypothesised distinction between affective ToM (sharing and understanding another's emotion state) and cognitive ToM (understanding intentions), dependent on partly dissociable neural structures (Shamay-Tsoory, Tibi-Elhanany & Aharon-Peretz, 2006). *Affective ToM* is hypothesized to require cognitive ToM (understanding intentions and beliefs) and empathy (relying on the processing of affective cues), while *cognitive ToM* does not rely on the processing of emotionally salient cues (Sebastian et al., 2012; Shamay-Tsoory, Harari, Aharon-Peretz & Levkovitz, 2010). The ventromedial prefrontal cortex is involved in understanding affective but not cognitive ToM stories. Ventromedial lesions were suggested to cause difficulties with affective ToM, while dorsolateral prefrontal lesions were associated with deficits in cognitive ToM (Shamay-Tsoory & Aharon-Peretz, 2007).

The ability to decode others' mental states from observable cues as a function of the early developing ToM system may rely on contributions from the amygdala, right anterior insula and orbitofrontal/medial temporal circuit (Sabbagh, 2004; Sebastian et al., 2012; Tager-Flusberg & Sullivan, 2000). In contrast, the ability to reason about others' mental states (inferential reasoning) may rely on left medial frontal, left and right temporoparietal and posterior cingulate regions (Saxe et al., 2004; Saxe & Powell, 2006; Tager-Flusberg & Sullivan, 2000). According to a componential understanding of ToM (Saxe & Powell, 2006; Sabbagh, 2004), the ability to decode mental states develops first, whereas inferential reasoning develops only at approximately four years of age when the frontal areas mature. Wang, Lee, Signan, and Dapretto (2006) found activity that is more robust in the medial pre-frontal cortical regions of children processing ToM compared to that of adults. Therefore, Wang et al. (2006) hypothesise that, as children develop, their ToM

understanding becomes increasingly more automatic and less reliant on the medial pre-frontal region (Wang et al., 2006).

Furthermore, studies indicate that mirror neurons may provide the basis of ToM abilities due to control of shared representations (Carrington & Bailey, 2009). Research indicates that the same brain circuits are activated when a person is thinking about his or her own mental states as when the person is reflecting on other people's mental states (Kaplan & Iacobone, 2006; Rizzolatti & Craighero, 2004). Not all researchers agree with the premise that mirror neurons provide the neural basis for ToM (Frith & Frith, 2003), and some suggest that mirror neurons merely facilitate learning through imitation and provide a precursor to the development of ToM (Melthoff & Decety, 2003; Somerville & Decety, 2006). According to this view, the young child's ability to imitate others represents the origins of ToM and other social-cognitive abilities, while further development of these abilities does not depend on the imitation of others (Meltzhoff, 2002; Melthoff & Decety, 2003).

Baron-Cohen (1994) devised a theoretical model to explain the development of ToM during the first four years of life. The model contains four components that explain the ontogenesis of ToM. The components of Baron-Cohen's model comprise the intentionality detector, the eye direction detector, the shared attention mechanism and the theory of mind mechanism (Baron-Cohen, 1994; Baron-Cohen & Chakrabarti, 2008). Later, Baron-Cohen (2005) added the component of an emotion detector and empathising system to his model of ToM development. It has been suggested that empathy is closely related to ToM but includes an experiential component and may also include action. This means that an individual experiences a similar affective response to the person with whom he or she interacts and understands the reasons for the other person's mental state and perspective (De Waal, 2008).

Overall, different perspectives on the development of ToM have been proposed. In general, there seems to be agreement that ToM develops in stages, with early development consisting of the emergence of the following skills: decoding others' mental states, imitating others, processing eye direction and intention and sharing attention. Later development includes the development of complex functions, such as reasoning about mental states. It has been proposed that the amygdala is especially involved in the early-

developing, affective ToM system; therefore, damage to the amygdala or medial temporal lobe during childhood may lead to ToM deficits.

ToM and temporal lobe damage. Literature on TLE or temporal lobe lesions and ToM in children is limited. Structural damage to the brain associated with early-onset TLE comprises reduction in brain connectivity, especially in the temporal and parietal regions (Hermann et al., 2006; Hermann et al., 2002). Laurent, Arzimanoglou, and De Schonen (2005) found socioperceptive deficits (facial identity recognition) in children with TLE, but they did not investigate ToM.

The existing literature on amygdala damage and ToM consists of studies on adults who acquired amygdala lesions during early childhood (Adolphs, Tranel, & Damasio, 1998; Fine et al., 2001; Shaw et al., 2004), while no research results of similar studies on children were found. These studies on adults (Adolphs et al., 1998; Fine et al., 2001; Shaw et al., 2004) suggest an association between ToM difficulties and early-onset amygdala lesions. Adults with early-onset or congenital amygdala damage (left or right) have deficits in ToM skills that are more advanced, such as second-order false belief (usually understood by children aged six to seven years) and advanced understanding of non-literal utterances such as white lies, especially when the amygdala lesions act as epileptogenic foci in childhood (Adolphs et al., 1998; Shaw et al., 2004). The deficits include lack of understanding of the beliefs and emotional states of others.

Research with regard to ToM abilities in children and adolescents with temporal lesions is lacking, but findings suggest the possibility that children and adolescents with LiP and amygdala damage may have ToM deficits.

ToM in children and adolescents with LiP. Although research results of studies on ToM in adults are variable, it seems that certain aspects of ToM development (such as decoding of social emotions) may be affected by amygdala lesions (Adolphs et al., 2002; Brand et al., 2007). Reports on ToM abilities of children and adolescents with LiP are scarce; only one report on the ToM ability of an adolescent with LiP could be found (Brand et al., 2007). A 17-year-old adolescent with LiP, bilateral amygdala damage and epilepsy obtained a score in the low average range (12th percentile) on a measure of ToM, which does not necessarily indicate a ToM deficit. The ToM Eyes Test presented to the adolescent measures the recognition of social emotions, an ability that is associated with

affective ToM. The score on the test was not compared to a matched control group. This case report seems to suggest that adolescents with LiP may not necessarily have severe deficits in the recognition of social emotions. However, because the study involved only one adolescent, the results cannot be generalised to all children and adolescents with LiP.

Overall, one report of an adolescent with LiP and amygdala damage indicates that she did not have a severe deficit in recognising social emotions (a component of ToM). Nevertheless, the research results of a study that included an adult with LiP provide at least some indication that children and adolescents with LiP may also have ToM deficits related to amygdala damage.

Executive Function

The neural substrate of executive function development. Executive functions can be viewed as integrative functions that exert control over cognition, behaviour and emotions (Powell & Voeller, 2004). Currently, it is accepted that executive functions in adults are associated with different regions of the frontal lobe, sharing reciprocal connections with cortical, subcortical and limbic regions of the brain (Fuster, 2002; Lezak et al., 2012; Powell & Voeller, 2004; Stuss, 2011). The major cortical-subcortical circuits were identified as the anterior cingulate, orbitofrontal and dorsolateral brain circuits (Lichter & Cummings, 2001; Powell & Voeller, 2004; Taber & Hurley, 2011). These circuits are active in several distinct executive functions (Lichter & Cummings, 2001; Powell & Voeller, 2004). Circuits involving the ventral striatum process emotion and autonomic responses via its connection with the limbic system. The ventral striatum circuits involve the anterior cingulate, medial orbitofrontal cortices, amygdala and hippocampus (Lichter & Cummings, 2001). The anterior cingulate circuit appears to have a primary role in attention, arousal, emotion and motivation (Powell & Voeller, 2004). It is suggested that the orbitofrontal circuit mediates socially appropriate behaviour, impulse control, decision making, and empathy (Taber & Hurley, 2011). The dorsolateral circuit mediates executive functions such as organisation, planning and attention (Taber & Hurley, 2011). The cingulate, orbitofrontal and dorsolateral frontal brain circuits also facilitate several other executive functions such as working memory, inhibition, switching and maintaining set, divided attention, error detection, self-monitoring and initiation, and flexibility goal-directedness (Moll, Zahn, De Oliveira-Souza, Krueger, & Grafman, 2005;

Pickens, Saddoris, Setlow, Holland, & Schoenbaum, 2003; Powell & Voeller, 2004; Völlm et al., 2006; Wallis, 2007).

Research indicates a correlation between the age-related protracted maturation of the frontal lobe circuitry and its neurotransmitter systems and the age-related development of executive function and its component processes (Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Eslinger & Biddle, 2008; Fuster, 2002; Lamm, Zelazo, & Lewis, 2006; Steinberg, 2005). In contrast to the adult brain, the developing brain is characterised by diffuse representation of executive function (Jacobs, Harvey, & Anderson, 2011; Long et al., 2011; Spencer-Smith & Anderson, 2009). Progressive focal activation of frontal regions, as suggested by functional MRI studies, reflects the increasing efficiency of the longer fibre tracks and the increasing specialisation of executive function (Tamm, Menon, & Reiss, 2002).

The trajectory of executive function development. Differences in the maturation of various brain areas in the frontal cortex are reflected in the timing of the emergence and development of specific executive skills (Anderson, 2002; Duncan et al., 1997; Kar, Rao, Chandramouli, & Thennarasu, 2011; Waber et al., 2007). It has been suggested that periods of rapid changes in frontal lobe maturation (as reflected in EEG coherence studies, functional and structural imaging, normative studies and metabolic analyses) reflect a non-linear trajectory for executive function development (Anderson, et al., 2001; Klimkeit, Mattingley, Sheppard, Farrow, & Bradshaw, 2004; Nagy, Westerberg, & Klingberg, 2004). Ongoing postnatal brain changes that occur parallel to executive function development include increased cell and neurotransmitter maturation, synaptogenesis, myelination and pruning (Blair, 2002; Fossella, Sommer, Fan, Pfaff, & Posner, 2003; Halliwell, Comeau, Gibb, Frost, & Kolb, 2009; Steinberg, 2005). Sequences of synaptic overproduction followed by synaptic pruning are responsible for growth spurts in development of executive function (Andersen, 2003; Anderson, 2002; Friedman, Miyake, Robinson, & Hewitt, 2011; Hudspeth & Pribam, 1992; Thatcher, 1992).

Progression of executive function development is based on the notion of hierarchical development of the brain and frontal lobes, consistent with processes such as myelination, progressing from primary and sensory cortical regions to association areas and finally to frontal regions (Sowell et al., 2004; Stuss & Alexander, 2000). The development of

executive functions progresses through three levels: inhibition of automatic responses based on sensory/perceptual input on the first level; executive and supervisory functions on the second level; and self-reflection (metacognition) and awareness on the third level (Stuss & Alexander, 2000).

Development of functions on the first level (regulation of several autonomic, motor and subcortical functions) is associated with an initial growth spurt throughout the first year of life due to frontal metabolic changes. These functions include rudimentary attention control, behaviour inhibition, regulation of arousal and reactivity and self-regulation of affect/motivation (Anderson, 2002; Barkley, 1997; Chugani, 1999; De Luca & Leventer, 2008; Friedman et al., 2011; Garon, Bryson, & Smith, 2008). The autonomic nervous system and hypothalamic-pituitary-adrenal axis are involved in the regulation of arousal and reactivity, while the orbitofrontal, ventral prefrontal cortex, frontostriatal control system and connections between the prefrontal regions and the amygdala and nucleus accumbens were postulated to be particularly important for affective regulation (Galvan et al., 2006; Hare & Casey, 2005; Monk et al., 2003; Nomura et al., 2004; Ochsner & Gross, 2005; Thomas et al., 2001; Zelazo, Muller, Frye, & Marcovitch, 2003). The orbitofrontal and ventral prefrontal regions become myelinated before the dorsolateral areas and therefore emotional regulation develops before cognitive control (Luciana, Conklin, Hooper, & Yarger, 2005; Slattery et al., 2001).

Rudimentary cognitive control functions (inhibition and working memory) emerge during the first year (Anderson, 2002; Barkley, 1997; De Luca & Leventer, 2008; Friedman et al., 2011; Garon et al., 2008) and executive functions that are more complex are suggested to build on these early executive processes (Marcovitch & Zelazo, 2009; Senn, Epsy, & Kaufman, 2004; Smidts, Jacobs, & Anderson, 2004). In the preschool years, there is a steady increase in the volume of gray and white matter in the frontal lobe (Sowell et al., 2004) and an increase in brain metabolism is evident between the ages of six and seven years (De Luca & Leventer, 2008). These changes accompany an improvement in preschool children's processing capacities, inhibition and sustained attention (De Luca & Leventer, 2008; Posner & Rothbart, 2005; Reuda et al., 2005).

There are significant changes in cortical gray matter development in the frontal lobes between 7 and 12 years of age, accompanied by development of cognitive control

processes. There is a spurt or second wave of cortical gray matter development peaking around the age of 11 years in girls and around the age of 12 years in boys (Andersen, 2003; Giedd & Rapoport, 2010). In line with these brain changes, there is rapid improvement of all executive functions, especially verbal working memory, strategic thinking, fluency, goal-directed behaviour, response inhibition and selective attention (Anderson, et al., 2001; Brocki & Bohlin, 2004; Klimkeit et al., 2004; Luciana & Nelson, 2002). By late childhood, several skills reach adult levels of maturity (Anderson, et al., 2001; Brocki & Bohlin, 2004; Casey et al., 2000; De Luca & Leventer, 2008; De Luca et al., 2003; Klimkeit et al., 2004; Luciana & Nelson, 2002). White matter development and myelination also progress steadily between 7 and 12 years of age. The continued development of the ability to inhibit responses depends on the development of white matter and connectivity in fronto-subcortical tracts (Liston et al., 2003; Stevens, 2009).

After the peak in gray matter development at the ages of 11 and 12 years, gray matter slowly declines during adolescence due to a pruning process (Andersen, 2003). An overall shift from subcortical to cortical recruitment during cognitive tasks was suggested to occur during adolescence (Killgore et al., 2001) due to quantitative and qualitative changes in prefrontal cortex development (Brown, 2006; De Luca & Leventer, 2008; Gogtay et al., 2004; Luciana et al., 2005; Luna, 2009; Luna & Sweeney, 2004). The adolescent brain becomes more efficient, processing speed increases and monitoring, working memory and self-organisation improve due to the elimination of redundant or unused synapses, the myelination of longer fibre tracks and increased connectivity between brain regions (Anderson, et al., 2001; Blakemore & Choudhury, 2006; Gogtay et al., 2004; Killgore et al., 2001; Sowell et al., 2004; Sowell, Thompson, Tessner, & Toga, 2001). The constant myelination in the prefrontal cortex and increasing brain connectivity still continues in late adolescence and early adulthood, while executive function skills, such as working memory, planning and inhibition, peak at the same time (Best, Miller, & Jones, 2009; De Luca et al., 2003; Klingberg, Forssberg, & Westerberg, 2002; Nagy et al., 2004; Olesen, Westerberg, & Klingberg, 2004).

Development of executive functions that involve affective processes will be discussed in more detail in the section on the neural substrate and trajectory of psychosocial development.

The discussion of executive function development in this section focused on the neural substrate of executive function development and the trajectory of executive function development. The maturation of the frontal lobe circuitry seems to underlie the development of executive functions. Developmental changes in the frontal lobe and its major cortical-subcortical circuits, such as sequences of synaptic overproduction followed by synaptic pruning, are responsible for the protracted, non-linear changes in executive functions. Development progresses from the emergence of basic autonomic, motor and emotional regulation to mature cognitive control functions, self-awareness and self-reflection. Connections between the frontal lobe and subcortical structures, including the amygdala, appear to play an important role in the maturation of executive functions, including emotional control and motivation. Therefore it can be expected that children and adolescents with temporal lobe or amygdala damage may have executive function deficits.

Executive function in children and adolescents with temporal lobe damage. Children and adolescents with LiP sometimes have focal lesions in the temporal lobe, which were suggested to cause disconnection and structural and functional changes in surrounding brain areas in LiP (Boes et al., 2011; Morgan, 2008). It was illustrated that the amygdala and temporal lobe connect either directly or indirectly with different prefrontal pathways. Disruption or impaired development of the neural structures and pathways of the prefrontal lobe system during any of the developmental stages was suggested to underlie executive deficits in developmental disorders, epilepsy syndromes, diffuse injuries, focal injuries and other CNS disorders during childhood (Baron, 2004; Channon & Crawford, 2000; Levin & Hanten, 2005; Marlow, Rose, Rands, & Draper, 2005; Riva et al., 2005). Therefore, children and adolescents with temporal lobe damage may have executive function deficits.

Research results of studies on executive function in paediatric TLE and early amygdala damage are inconsistent (Culhane-Shelbourne, Chapieski, Hiscock, & Glaze, 2002; Kar et al., 2010; Stretton & Thompson, 2012). One study suggests normal executive function in children with TLE, although difficulties in sustained attention were evident (Culhane-Shelbourne et al., 2002). Another study shows no executive function deficits during adulthood due to early left amygdala damage (Fine et al., 2001). Although the latter study did not focus on children, the findings suggest that amygdala lesions acquired during childhood do not necessarily lead to executive function deficits in later life.

Further research indicates associations between early onset TLE and executive dysfunction such as working memory deficits during childhood (Kar et al., 2010; Lopes et al., 2010; Rzezak et al., 2009; Stretton & Thompson, 2012). Early age TLE onset also predicts poor performance on a working memory index during adulthood (Black et al., 2010). Lopes et al. (2010) found that children and adolescents with TLE performed poorly on measures of phonemic verbal fluency and planning. It was suggested that executive function deficits in paediatric TLE might be the consequence of damage to the mesial region of the temporal lobe and consequently damage to the temporofrontal circuit (Drake, Allegri, & Thomson, 2000). White matter abnormality in cortical and subcortical areas following widespread synchronised neuronal firing was also suggested to be one of the mechanisms leading to executive dysfunction in children with TLE (Meng et al., 2010).

The discussion indicates inconsistent findings with regard to executive dysfunction in children with TLE and adults with early onset amygdala damage. This may be due to difference in underlying pathology. However, some evidence of executive deficits in children and adolescents with temporal lobe lesions seems to exist. Although the underlying pathology in paediatric LiP is different from paediatric TLE, damage to the temporal lobe in LiP may also disrupt the frontotemporal pathways that facilitate executive function and thus lead to executive function deficits.

Executive function in children and adolescents with LiP. LiP is associated predominantly with temporal lobe lesions, and researchers have reported executive difficulties such as deficits in working memory, cognitive flexibility, fluency, initiation and decision making in adults with LiP (Brand et al., 2007; De Martino et al., 2010; Stretton & Thompson, 2012; Thornton et al., 2008). Although it was apparent that the LiP subjects' frontal lobes had not been implicated, it was suggested that amygdala damage in LiP cause damage in brain areas connected with this structure (Boes et al., 2011). Therefore, it was assumed that these brain abnormalities affect executive functions normally associated with the frontal lobe. Damage to or abnormality of the orbitofrontal or ventromedial prefrontal cortex may affect certain executive functions such as behaviour regulation, inhibition of prepotent responses, decision-making and flexibility in changing reinforcement contingencies (Anderson, Wisnowski, Barrash, Damasio, & Tranel, 2009; Zald & Andreotti, 2010). These executive deficits may emerge only later in life in LiP due to progressive changes in the brain, but no information is available on the onset and

progression of brain changes in LiP during childhood and how it relates to executive function. However, one adolescent with LiP and amygdala damage presented with low scores on measures of letter and semantic fluency, suggested to depend partially on executive functions such as working memory, self-monitoring, shifting, and inhibition (Baron, 2004; Brand et al. 2007).

Taken together, the literature indicates that adults with LiP have executive deficits; hence children and adolescents with LiP and amygdala damage may also experience the same difficulties. However, evidence indicating an association between executive dysfunction and paediatric LiP is limited to one case report of an adolescent with LiP. Therefore, the hypothesis that paediatric LiP may be associated with executive dysfunction is based largely on results of studies on adults with the disorder.

Psychosocial Development

The Neural Correlate of Psychosocial Development

Despite the central importance of social interaction in human life, the neural mechanisms underlying social cognition and emotional processing remained poorly understood until the last decade when research integrating approaches from neuroscience and social psychology begun to unravel these processes (Adolphs, 2003; Ochsner, 2004; Ochsner & Lieberman, 2001). Researchers suggest that neural structures such as the amygdala, medial frontal cortex (including orbitofrontal cortex and anterior cingulate cortex) and their connections underlie social-emotional behaviour and social cognition in adults (Amodio & Frith, 2006; Holland & Gallagher, 2004; Ochsner & Gross, 2008). These brain structures and their connections facilitate the development of social-emotional processing and regulation during childhood and adolescence (Adolphs, 2009; Brink et al., 2011; Frith, 2007; Heimer & Van Hoesen, 2006; Mesulam, 2000; Pascalis, Kelly, & Schwarzer, 2009; Rizzolatti & Craighero, 2004; Saxe et al., 2006; Skuse, Morris, & Lawrence, 2006). Some neural structures underlying social emotional development (such as the amygdala) come into effect very early in development (De Haan & Gunnar, 2009). The functional organisation of these brain structures continues to change with age (Blair, Marsh, Finger, Blair, & Luo, 2006; Choudhury, Charman, & Blakemore, 2009); therefore, social cognition and emotional processing continue to develop with increasing age

(Bechara, 2004; Coccaro, McCloskey, Fitzgerald, & Phan, 2007; Davidson et al., 2000; Happaney, Zelazo & Stuss, 2004; Zelazo & Müller, 2010).

Researchers have suggested that the amygdala play an important role in the development of several social-emotional processes such as attachment, social-emotional information processing and *hot executive functions* (Blair, 2003, 2010; Coccaro et al., 2007; Decety et al., 2011; Moll & Schulkin, 2009; Raine & Yang, 2006; Scheele et al., 2012). Attachment is not a focus of the current study and will not be discussed further. The development of specific social information processing skills such as facial emotion recognition and ToM have already been discussed under the headings "Recognition of Facial Emotion" and "ToM" and will not be repeated here; therefore, the ensuing discussion will briefly focus on the development of *hot executive functions*.

Hot executive function (Zelazo et al., 2005, p. 314) is a term that refers to executive functions requiring high affective involvement or tasks demanding flexible appraisal of the emotional significance of stimuli. The term *cool executive function* refers to the purely cognitive aspects of executive function such as working memory, associated with the dorsolateral prefrontal cortex (Zelazo & Müller, 2005, p. 314). It has been suggested that there is a close connection between hot and cool executive functions and that these functions are important for social adaptation (De Luca & Leventer, 2008; Zelazo et al., 2005). However, the hot executive functions (Zelazo & Müller, 2005, p. 314), such as emotional regulation, are especially relevant to social adjustment (De Luca & Leventer, 2008) and to start developing earlier than the cognitive or cool executive functions do (Hongwanishkul, Happaney, Lee, & Zelazo, 2005). However, these functions eventually lag behind the development of other cognitive skills due to the protracted development of brain structures underlying them and the continued functional reorganisation of these structures (Prencipe et al., 2011; Zelazo & Carlson, 2012). For instance, Choudhury et al. (2009) observed that brain activity during social-cognitive processing move from anterior (medial prefrontal) regions during adolescence to posterior temporal regions in adulthood. Therefore, the shift is from areas underlying effortful control (medial prefrontal) to areas underlying automatic responding (posterior temporal regions). Another example of functional changes in the development of social-emotional processing is the following: Pfeifer & Blakemore (2012) found less prefrontal cortex activity in the context of peer influence in adolescent boys than in the prefrontal cortices of adults in the same situation

(Pfeifer & Blakemore, 2012). Pfeifer & Blakemore (2012) hypothesized that this reflected ineffective regulatory control in the context of peer influence during adolescence.

Some researchers view ToM and empathy as hot executive functions (Zelazo & Müller, 2005). ToM and empathy are also often seen as related processes (Baron-Cohen, 2005; Brink et al., 2011). Baron-Cohen (2005) includes empathy in his model of ToM development while Brink et al. (2011) suggests that ToM is one of two components of empathy. Brink et al. (2011, p. 1) defines empathy as "the ability to understand and share another person's inner life" and suggests that empathy consists of two components: affective (emotion-sharing) and cognitive empathy (theory of mind)". Empathy depends on shared neural representations, affective arousal, self-awareness, insight into emotions and regulation thereof (Decety, 2010 & Jackson, 2004; Hurlemann et al., 2010). Emotional regulation includes effortful control (inhibiting), initiating feeling states and adjusting feeling states and physiological processes according to the social situation (Eisenberg, Champion, & Ma, 2004; Monopoli & Kingston, 2012). Decety (2010) suggests that certain neuroendocrine and autonomic processes and a network of interacting neural regions facilitate the differential development of the components of empathy (Decety, 2010). The neural regions involved in empathy include the superior temporal sulcus, insula, medial and orbitofrontal cortices, amygdala and anterior cingulate cortex (Brink et al., 2011; Decety, 2010; Hurlemann et al., 2010). Shared neural representations rely on the connection between the limbic system with mirror neurons (Birbaumer et al., 2005; Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Sterzer, Stadler, Krebs, Kleinschmidt, & Poustka, 2005). Regulation of emotion processing was suggested to depend on the development of the anterior cingulate, the ventromedial prefrontal cortex and increased connectivity between the cortical and subcortical brain structures (Hariri et al., 2000; Lamm, Granic, Zelazo, & Lewis, 2011; Phan, Wager, Taylor, & Liberzon, 2002; Phillips et al., 2003a). Coccaro et al. (2007) and Davidson et al. (2000) suggest that amygdala-orbitofrontal interaction is especially critical for effective regulation of emotion and control of aggression.

Decety, Michalska, and Kinzler (2011) and Eisenberg (2000) suggest that the amygdala functions as part of the motivational-emotion system. Amygdala functions include generation of emotion states, arousal and reward processing. Amygdala function facilitates emotional learning, judgement of arousal level and generates emotions such as

guilt, shame and empathy (Blair, 2003, 2010; Blair et al., 2006; Decety et al., 2011; Luo et al., 2006; Moll & Schulkin, 2009; Raine & Yang, 2006; Scheele et al., 2012). These functions are closely connected to processes such as moral behaviour and affective and moral decision making as it motivates prosocial behaviour and reparation. Researchers demonstrated that the prefrontal cortex facilitates affective decision making in adults. However, the amygdala system appears to facilitate affective decisions and caring reactions during childhood and adolescence, as the prefrontal cortex is still immature (Bechara, 2004; Blair, 2008; Blair et al., 2006; Eslinger & Robinson-Long, 2010). Children's social cognition and their capacity for empathy improve with age. This enables them to form friendships, show cooperate behaviour, inhibit aggression, allow the sharing of experiences and facilitate prosocial behaviour and moral reasoning (Carr et al., 2003; Decety, 2010; Eisenberg & Eggum, 2009; Webster-Stratton & Reid, 2004). A shift from less integrated brain functioning to more efficient cortical-subcortical interaction and the increasing efficiency of the prefrontal lobe underlies increasingly diverse, complex and integrated social behaviour during adolescence (Rubin, Bukowski, & Parker, 2006; Yeates et al., 2007).

Taking into account the importance of the amygdala in the development of processes that underlie healthy psychosocial functioning, amygdala damage may affect the psychosocial adjustment of children and adolescents. The next section focuses on temporal lobe damage and psychosocial development.

Temporal Lobe Damage and Psychosocial Development

Pathology of the amygdala and the temporal lobe is evident in disorders affecting social behaviour and emotional stability (Bachevalier, 2000; Bachevalier & Loveland, 2006; Baron-Cohen et al., 2000; Blumberg et al., 2003; Munson et al., 2006; Schultz, 2005). However, the effect of these types of injuries on the psychosocial development of children has not been researched often. This is due to the rarity of circumscribed amygdala and temporal lobe lesions. Research on the effect of early temporal lobe injuries, specifically amygdala lesions, primarily consists of animal studies (Bachevalier, 1991, 1994; Malkova, Mishkin, Suomi, & Bachevalier, 2010; Prather et al., 2001). Although the human nervous system is more complex than the nervous systems of animals, it evolved from older phylogenetic brain structures shared by other mammals. Consequently, humans

share a wide repertoire of social and emotional behaviours with other species (Panksepp & Biven, 2012; Porges & Carter, 2010; Striedter, 2004). Therefore, studies of social development and emotional reactivity in young mammals with temporal lobe and amygdala lesions can provide insight into the social development and behaviour of children and adolescents with similar brain lesions (Mega et al., 1997; Panksepp & Biven, 2012; Porges & Carter, 2010).

Animal studies. Literature on early bilateral amygdala lesions in macaque monkeys suggests that the lesions affect the development of social behaviour negatively, without causing severe social impairment (Amaral, 2003; Bauman et al., 2004b; Prather et al., 2001). Social difficulties were more apparent in certain social situations, such as in complex groups (Machado & Bachevalier, 2006). Monkeys with lesions received social attention in dyads but were avoided in groups that were more complex (Machado & Bachevalier, 2006).

Bachevalier (1994) reported that social difficulties were more severe when the amygdalae of monkeys had been injured early in development compared to adulthood (Bachevalier, 1994). Compensatory mechanisms did not ensure recovery of functions after early brain damage, possibly because the damage had affected other neural systems remotely located to the site of the lesions (Bachevalier, 2000). Young, neonatal monkeys with amygdala lesions demonstrated all expected age-appropriate social behaviour, but showed more social fear than adult monkeys with bilateral amygdala lesions (Amaral, 2003; Bauman, Lavenex, Mason, Capitanio, & Amaral, 2004a; Prather et al., 2001). Bachevalier (1991) suggests that the social fear may be related to difficulties in recognising facial emotion. In contrast to increased social fear, decreased fear of dangerous situations is apparent in neonatal monkeys with amygdala lesions (Amaral, 2003; Bauman et al., 2004a; Prather et al., 2001). Despite species-typical mother-infant interaction, the monkeys with amygdala lesions did not seek the proximity of their mothers or vocalise their distress after separation from their mothers at six months, as developing monkeys typically do (Bauman et al., 2004a). Therefore, the monkeys' impaired ability to perceive potential danger led to atypical social behaviour (Bauman et al., 2004a).

Bauman, Toscano, Mason, Lavenex & Amaral (2006) further found that monkeys with neonatal amygdala lesions showed fewer aggressive gestures in reaction to social cues than

healthy controls and controls with neonatal hippocampal lesions. Bauman et al. (2004b) highlight the possibility that excessive fear shown by the monkeys with amygdala lesions may have resulted in a diminished capacity to compete, form coalitions and subsequently obtain high social status in early development. Thus, early-onset amygdala lesions may cause dysregulation of aggression, affiliation and fear responses in complex social interactions, leading to diminished capacity to compete for social rank.

A recent study (Malkova et al., 2010) on monkeys with medial temporal lobe and inferotemporal lesions indicates more severe outcomes in monkeys with early medial temporal lobe lesions compared to outcomes described for the monkeys with amygdala lesions. Infant monkeys with neonatal medial temporal lobe lesions displayed severe social and emotional deficits in infancy that persisted into adulthood. Furthermore, these infant monkeys with medial temporal lobe lesions had social-emotional difficulties that were more severe relative to adult monkeys with similar lesions. In contrast to medial temporal lesions, infant monkeys with inferotemporal lesions exhibited less severe social deficits that were resolved by adulthood (Malkova et al., 2010). The deficits were still more severe than those observed in animals with similar lesions in adulthood were. Thus, differences in the severity and trajectories of psychosocial development were apparent in relation to the type of lesion. Compared to inferior temporal lobe lesions (excluding the amygdala), medial temporal lobe lesions, including the amygdala, produced long-term social-emotional difficulties.

Malkova et al. (2010) suggest that the severe social-emotional difficulties of the monkeys with amygdala lesions in their study to some extent may be attributed to the detrimental effect of amygdala lesions on the development of the prefrontal cortex (Kolb, 2010). According to Herschkowitz (2000), the amygdala develops earlier than cortical association areas do; therefore, damage of the amygdala may prevent functional development of the association cortex, including the prefrontal cortex (Kolb, 2010). It is suggested that the prefrontal cortex plays an important role in social behaviour. It also possible that poor recovery in the monkeys with medial temporal lesions can be ascribed to impaired ability of the brain to compensate after injury (Kolb, 2010). Despite poor recovery, environmental experience appears to modulate the severity of the psychosocial symptoms of the monkeys with medial temporal lobe lesions in the study by Malkova et al. (2010).

Overall, literature on amygdala lesions in monkeys indicates that the amygdala plays an important role in psychosocial development. Damage to this structure may lead to permanent social-emotional deficits of varying degree, depending on the presence or absence of injuries that extend into the medial temporal lobe and the timing of the lesion. These studies suggest that amygdala or more extensive temporal lobe lesions that include the amygdala in humans may also cause social-emotional deficits, with severity possibly depending on the time of onset and progression of the lesion.

Human studies. Animal studies, as discussed in the previous section, suggest that the medial temporal lobe plays an important role in regulating social behaviour (Adolphs, 2003; Brothers, Ring, & Kling, 1990; Marin et al., 2008). Baron-Cohen et al., (2000) propose an amygdala theory of autism (a condition in which processing of social behaviour is profoundly affected). Baron-Cohen et al., (2000) propose that the amygdala is one of several brain regions that are abnormal in autism. His conclusion is based on studies of animals with amygdala lesions such as the study by Bachevalier (1991, 1994) and studies suggesting structural and functional abnormalities of the amygdala in autistic persons (Baron-Cohen et al., 1999). Structural and functional abnormality of the amygdala in persons with autism is associated with social perception deficits (Schultz, 2005). In support of the theory of Baron-Cohen et al. (2000), studies on children with genetic conditions affecting the temporal lobes (such as tuberous sclerosis) suggest an association between temporal lobe abnormality and autism (Curatolo, Napolioni, & Moavero, 2010; Curatolo, Porfirio, Manzi, & Seri, 2004; Jansen et al., 2008; Numis et al., 2011). The autistic behaviour in persons with tuberous sclerosis is described as deficits in play, impairment in communication and social interaction and poor quality of eye contact. Other behavioural problems in these persons include overactivity, repetitive and ritualistic behaviour and temper tantrums (Jeste, Sahin, Bolton, Ploubidis, & Humphrey, 2008).

One explanation for the development of autistic symptoms in individuals with temporal lobe lesions or abnormalities is the possibility of a critical early stage of brain development. Temporal tubers, lesions or epileptiform activity possibly interrupts the development of brain systems that underlie social cognition and behaviour (Curatolo et al., 2004; Curatolo et al., 2010; Marin et al., 2008). This hypothesis corresponds with literature on the effect of early medial temporal lobe lesions in monkeys: Worse outcomes were associated with medial temporal lobe lesions in neonatal monkeys, compared to

monkeys that sustained lesions during adulthood. Thus, the stage at which medial temporal lobe lesions appear may play an important role in the severity of social deficits and symptoms of psychopathology in individuals with these types of lesions.

Researchers reported less severe socio-emotional outcomes (not compatible with a diagnosis of autism) in children with temporal lobe lesions in TLE (Caplan et al., 2004; Golouboff et al., 2008; Schoenfeld et al., 1999). Golouboff et al. (2008) found a correlation between poor recognition of fearful expressions and internalising problems in children with TLE and right-sided temporal lobe lesions. This result supports the findings in animal studies that indicate increased social anxiety, presumably associated with social perception deficits, in monkeys with early amygdala lesions. However, it has to be remembered that several factors (such as the physiological effects of seizures, medication and living with a chronic illness) can potentially influence the behaviour and psychosocial development of children with TLE (Caplan et al., 2005; Caplan et al., 2004; Oguz, Kurul, & Dirik, 2002). Therefore, research results in this regard will not only reflect the effect of temporal lobe lesions on psychosocial development.

The only report that could be found on the behaviour of a preschool child with bilateral amygdala lesions was published recently (Freeman & Luby, 2013). A five-year-old Chinese boy who was adopted from an orphanage at the age of 18 months presented with aggressive behaviour, inappropriate affect, little or no fear, cognitive delays and no interest in food since the age of 22 months. Parents also reported minimal interaction with other children, very limited shared play and very simple, mostly mechanistic, persevering play (manipulation of his toys for minutes or even hours). Neuroimaging before the age of five years indicated atrophy of medial temporal structures, and two years later, progression of the lesions was observed. Extensive loss of these structures (including the amygdala) bilaterally was reported. He was diagnosed with electrical *status epilepticus* of sleep (ESES) of unknown aetiology. Screening indicated clinically meaningful scores on measures of autistic behaviour, but a wide variety of social behaviours were still evident. He made eye contact readily, enjoyed the company of his family and shared play activities. The authors thought that aggressive behaviour and disinterest in food were of significant interest, as the kind of lesion he had (bilateral amygdala lesions) was typically associated with apathy and hyperphagia in the Klüver-Bucy syndrome (Schraberg & Welberg, 1978). Freeman and Luby (2013) further found clearly impaired social interactions in the boy with

amygdala damage, but he was still able to interact meaningfully, showed preference for primary caregivers, showed anxiety of strangers and shared play with a stranger. This led to the conclusion that an intact amygdala is not required for these complex behaviours. Freeman and Luby (2013) argue for the plasticity of the cortical substrates that serve emotional processing in the human brain. Although the presence of some preserved social behaviour in a five-year-old boy with amygdala lesions possibly indicated the robustness of the emotional brain system early in life, it is still apparent that the boy's social deficits were quite severe (given the clinically significant scores on measures of autism). This accentuates a strong connection between bilateral amygdala lesions (among further structural damages to the temporal lobe) and social-emotional deficits. A longitudinal study of this child's development would point out what his eventual social competence would be, given that the progression of social competence also depends on the further development of other brain structures such as the orbitofrontal area of the brain. The description of the social behaviour of this child shows some similarity with the severe social-emotional deficits in monkeys with early medial-temporal lobe lesions (Malkova et al., 2010). However, the results of the study by Freeman and Luby (2013) were complicated by two issues. The first is the fact that the boy suffered from electrical *status epilepticus* of sleep (ESES), which might have affected synaptogenesis due to abnormal neuronal activity during a critical period of brain development (Nickels & Wirrell, 2008). Secondly, the boy not only had amygdala damage, but also spent the first 18 months of his life in an orphanage, which could have affected his attachment relationships and social-emotional development profoundly. The question of how circumscribed amygdala damage would affect a child's psychosocial development is still not answered.

Overall, studies on animals, children with conditions such as tuberous sclerosis, autism and TLE and a child with bilateral amygdala damage provide evidence of a connection between temporal lobe lesions and problematic social development. The conclusions are complicated by the presence of other factors, such as the onset of the lesion, the extent of the damage, the effect of seizures on the brain, the effect of early social deprivation and the psychological effect of having a chronic illness. In LiP, similar to TLE, it may be difficult to distinguish social-emotional difficulties caused by the effect of brain lesions from the effect of living with a chronic illness. Therefore, the discussion in the next section will focus on the effect of disfigurement and hoarseness (symptoms and signs of LiP) on psychosocial development.

The Effect of Disfigurement and Hoarseness on Psychosocial Development

The effect of amygdala damage on social cognition and psychosocial development has been discussed in the previous section, but living with a chronic illness and having visible physical symptoms or disabilities also have psychosocial implications (self-esteem and interpersonal relationships). Therefore, the effect of disfigurement and hoarseness on psychosocial development will be discussed.

Psychosocial development of children and adolescents with voice disorders. The ability to use their voices effectively enables individuals to participate in various social and occupational domains (Baylor et al., 2005; Krischke et al., 2005). Very few studies describe the psychosocial functioning of children with dysphonia. Poor voice quality has a negative influence on children's interpersonal communication and the extent to which they are accepted socially (Baylor et al., 2005; Markham & Dean, 2006). Takeshita, Aguiar-Ricz, Isaac, Ricz, and Anselmo-Lima (2009) indicate that voice alterations correlate with social performance and affective-emotional development of children. Connor et al. (2008) conducted a qualitative study on the psychosocial adjustment of children and adolescents with dysphonia and found that a large proportion of the children, including children as young as six years of age, expressed concerns and an awareness of their dysphonia. Toddlers, young children and school-aged children are mostly concerned with the physical problems related to dysphonia and for instance ask why they cannot speak in a normal voice. Emotional concerns, such as anxiety about speaking in front of others, are more evident in school-aged children and adolescents (Conner et al., 2008). Feelings of anger, sadness and embarrassment are especially prominent during adolescence. Children and adolescents often feel that their dysphonic voices receive undue attention and also limit their participation in important events. The study by Conner et al. (2008) illustrates the likelihood that dysphonia may contribute to poor psychosocial adjustment in children and adolescents with LiP.

Psychosocial development of children and adolescents with skin conditions. Skin conditions can have a negative effect on children's lifestyle, psychosocial functioning and quality of life due to their cosmetic effect on appearance, although some individuals adapt better than others do (Beattie & Lewis-Jones, 2006; Gupta & Gupta, 1998; Lewis-Jones, 2006; Lund & Gaigher, 2002; Purvis, Robinson, Merry, & Watson, 2006; Saunders &

Edwards, 2004). An example of the effect of skin conditions on lifestyle is children who are sensitive to the effect of the sun (similar to children with LiP), who may enjoy only limited participation in outdoor activities (Lund & Gaigher, 2002). Another example is itching and pain related to eczema that can cause sleeplessness and fatigue, which in turn may cause mood changes and impaired psychosocial functioning (Lewis-Jones, 2006).

Studies on the psychosocial adjustment of children with neurocutaneous skin conditions suggest that the degree of noticeability of disfigurement is more relevant to psychological impact than the extent or severity of the disfigurement is (Graf, Landolt, Mori, & Boltshauser, 2006; Krab et al., 2008; Oostenbrink et al., 2007). This is particularly true when the face and hands are affected (Blakeney et al., 1998; Bradbury, 2007). Children affected by visible disfigurement may be ignored, teased, bullied and ostracised (Lewis-Jones, 2006). Most children and adolescents with LiP have extensive visible scarring on their faces – the appearance of their skin is often described as similar to a person with severe acne (Newton et al., 1991). Purvis et al. (2006) found that adolescents in secondary school, who considered their acne to be a severe problem, were at increased risk of being affected by significant anxiety, depression, suicidal thoughts and suicide attempts.

Behavioural problems and depression in children with skin conditions are prevalent (Krab et al., 2008; Rumsey & Harcourt, 2004) and frequently involve spirals of negative emotions (such as social anxiety), maladaptive thought processes (such as fear of negative social evaluation), unfavourable self-perceptions (such as lowered self-esteem and negative body image) and negative behaviour patterns such as social avoidance (Rumsey & Harcourt, 2004). A cycle of anticipatory anxiety, withdrawal, avoidance and a decrease in the number of opportunities to practise and develop social skills may evolve (Walters, 1997). When there are additional difficulties (such as hoarseness) in LiP, social communication may be affected further (Broder, Smith, & Strauss, 1994).

Overall, the literature suggests that noticeable skin lesions (especially in the facial area) and dysphonia in children and adolescents (such as in LiP) may contribute to several social-emotional difficulties such as poor self-esteem, poor interpersonal communication, depression, anxiety, social withdrawal and negative behaviour affecting the development of social skills. Therefore, children and adolescents with LiP who have dysphonia and

severe, chronic skin scarring may be vulnerable to developing social and emotional difficulties.

The Psychosocial Development of Children and Adolescents with LiP

Psychosocial adjustment. The direct effects of genetic abnormalities on brain and behaviour, as well as the indirect effects that stem from gene-environment interactions, are important to consider with regard to the psychosocial development of individuals with neurogenetic disorders (Simonoff, Bolton & Rutter, 1996; Yeates et al., 2007). Researchers were interested in the day-to-day social behaviour of adults with LiP due to the characteristic bilateral amygdala lesions of individuals with this disorder (Kennedy, Glascher, Tyszka & Adolphs, 2009; Paul et al., 2010). However, no research on the effect of amygdala lesions in LiP on the psychosocial development of children and adolescents with LiP could be found. Research focused on the effect of a different appearance and hoarseness on their psychosocial functioning.

Literature (Buchan & Kemble, 1974; Juberg et al. 1975; Steenkamp, 1997; Thornton et al., 2008; Van-Hougenhouck-Tulleken et al., 2004) indicates that appearance and hoarseness have a negative effect on the psychosocial functioning of children and adolescents with LiP. They are often teased and called names due to their hoarse voices (Juberg et al., 1975; Steenkamp, 1997). Hoarseness specifically causes self-consciousness, lack of confidence and poor self-esteem (Steenkamp, 1997). Difficulties with communication and embarrassment are also associated with hoarseness (Steenkamp, 1997). Skin symptoms cause children and adolescents to feel different and unattractive (Steenkamp, 1997). Owing to their self-perception of unattractiveness and their struggles with socialisation and relationships with the opposite sex, adolescents and young adults with LiP fear that they will not marry and have children (Steenkamp, 1997).

Steenkamp (1997) observes a possible association between the severity of symptoms of LiP and poor self-esteem, increased anxiety and decreased quality of social relationships in adolescents with the disorder. Social withdrawal, isolation and continuing difficulties in making friends have been observed (Brajac et al., 2004; Emsley & Paster, 1985; Keipert, 1970; Steenkamp, 1997). Brajac et al. (2004), Emsley and Paster (1985) and Steenkamp (1997) describe severe depression, anxiety and suicidal ideation (internalising behaviour) in adolescents with LiP. Steenkamp (1997) also describes impulsivity, anger outbursts and

aggression (externalising behaviour) in two of the three adolescents who participated in her study.

Overall, the available literature suggests that the psychosocial adjustment of children and adolescents with LiP may be affected negatively by the disfigurement and hoarseness that are typical of the disorder. Some of the adolescents and young adults in the study by Steenkamp (1997) presented with bilateral amygdala lesions; therefore, difficulties such as anxiety, depression, aggression, and social withdrawal may be related to the effect of the brain lesions on their behaviour and mood.

Psychopathology in children and adolescents with LiP. A high incidence of mood and anxiety disorders, psychosis and schizophrenia has been reported in a population of adults with LiP (Thornton et al., 2008). Impulse control disorder has also been diagnosed in some adults with LiP (Thornton, 2006). A few inconsistent reports of psychopathology in children and adolescents with LiP could be found (Bahadir et al., 2006; Brand et al., 2007; Emsley & Paster, 1985; Omrani et al., 2012; Steenkamp, 1997; Thornton, 2006). Paranoia and suspiciousness (Emsley & Paster, 1985; Steenkamp, 1997), anxiety, depression (Bahadir et al., 2006; Steenkamp, 1997; Thornton, 2006) and suicidal ideation in adolescents with LiP have been described. In her study, Thornton (2006) conducted a psychiatric interview with a 12-year-old LiP participant and his mother. Psychiatric diagnoses of bipolar affective disorder, conduct disorder, attention deficit hyperactivity disorder, anxiety disorder and suicidal behaviour were apparent (Thornton, 2006). In contrast to descriptions of psychopathology in the mentioned studies, Omrani et al. (2012) and Brand et al. (2007) did not find clinically relevant symptoms of depression or other psychiatric disorders in two adolescents with LiP and bilateral amygdala lesions (one of these adolescents also had epilepsy).

Overall, the sparse literature suggests that various psychiatric difficulties can be identified among children and adolescents with LiP. Available literature should be considered critically, as it is limited and focuses only on a few children and adolescents with the disorder. However, the general literature on psychopathology in children and adolescents supports the likely link between mood disorders, anxiety disorders, psychosis and temporal lobe pathology in children and adolescents with LiP (Caetano et al., 2007; MacMaster & Kusumakar, 2004; Pine, 2007; Rosso, Cintron, Steingard, & Renshaw,

2005). Depression, anxiety and anger outbursts (impulse control disorder), as identified in individuals with LiP (Thornton, 2006), are generally characterised by problematic regulation of self control, mood (depression) and fear (Coccaro et al., 2007; Pine, 2007). These regulatory difficulties have been linked to abnormalities in the cortico-limbic system (Todd & Lewis, 2008), medial temporal lobe (Caetano et al., 2007; MacMaster & Kusumakar, 2004; Rosso et al., 2005; Van Elst et al., 2000) and specifically the amygdala (Coccaro et al., 2007; Matthies et al., 2012). Psychosis in adults and children has also been associated with medial temporal lobe pathology and injury (Caplan et al., 2008; Coccaro et al., 2007; Takahashi et al., 2009; Van Elst & Trimble, 2003). In general, the literature on psychopathology associated with abnormality of the temporal lobe or cortico-limbic system in adults and children appears to support the likelihood of psychopathology in children and adolescents with LiP.

Children and adolescents with amygdala damage, like adults with amygdala damage, may have the following challenges: poor decision making in risky situations, difficulty in learning from negative feedback, difficulty recognising facial emotions, executive dysfunction and anger outbursts (Brand et al., 2007; Thornton, 2006; Thornton et al., 2008). These deficits in children may be associated with aggressive, impulsive, risky and rule-breaking behaviour (Blair, Monson & Frederickson, 2001; Kambam & Thompson, 2009). However, only one out of the five children in the Thornton study (Thornton, 2006) presented with rule-breaking behaviour suggestive of conduct disorder.

Overall, sparse literature suggests that children and adolescents with LiP may have similar psychopathology (anxiety disorders, mood disorders, psychosis and poor regulation of anger) as has been observed in adults with the disorder. Disorders that have not been specifically identified in adults with LiP thus far (such as attention deficit hyperactivity disorder – ADHD) may also be present. However, research involving more children and adolescents with LiP is necessary to confirm the possible association between LiP and certain psychiatric disorders.

Conclusion

The discussion of the literature suggests that children and adolescents with LiP have the same cutaneous and extracutaneous symptoms as described for adults with the disorder. The physical symptoms and signs of LiP, such as skin scarring and hoarseness, occur as

early as birth. Children and adolescents with LiP grow up with extensive and noticeable skin, voice and other systemic symptoms and signs. The age of onset of the CNS manifestations often found in individuals with LiP (epilepsy and bilateral temporal lobe calcifications) is not clear, but it is suggested that calcifications possibly have paediatric onset and are progressive. Epilepsy most often (with a few exceptions) has been described in adolescents and adults with LiP; therefore, it seems possible that epilepsy has a later onset in this disorder. Bilateral temporal lobe calcifications have been described in some children with LiP younger than 10 years and have often been observed in adolescents and adults. Neuropsychological deficits (executive functioning, memory and social perception) and neuropsychiatric problems (depression, increased risk of suicide, psychosis and anxiety disorders) in adults with LiP have been associated with bilateral amygdala lesions.

The limited literature on the neuropsychological functioning of children and adolescents with LiP discussed in this chapter (Emsley & Paster, 1985; Thornton, 2006) suggests the presence of neuropsychological difficulties in children with this disorder (deficits in memory and recognition of facial emotion), although no conclusive evidence is present. Limited research on psychopathology in children and adolescents with LiP suggests that these individuals may have similar pathology (mood disorders, anxiety and suicidal behaviour) as adults with the disorder. Additional difficulties (including ADHD and rule-breaking behaviour) were observed in one child with LiP, but these difficulties might have been unrelated to LiP. To date, only one study specifically explored the social and emotional difficulties of adolescents with LiP (Steenkamp, 1997). The study shows that these adolescents are teased, are depressed, feel self-conscious, have low self-esteem and poor communication skills and struggle to form satisfactory interpersonal relationship, partly because of their skin scarring and hoarseness.

Overall, the literature reviewed in this chapter suggests limited and inconclusive evidence that children and adolescents with LiP have the same neuropsychological and psychosocial difficulties as adults with the disorder. There is a lack of understanding of the trajectory of neuropsychological and psychosocial development of children and adolescents. The limited literature makes it difficult to compare children with LiP to children with other similar conditions (TLE and medial temporal damage). It is evident that no study has been undertaken to extend the limited existing knowledge on children and adolescents with LiP (Steenkamp, 1997; Thornton, 2006). The question whether

children and adolescents with LiP have more neuropsychological and psychosocial deficits compared to typically developing children remains unanswered. It is also not clear how the neuropsychological and psychosocial development of these individuals may present across the different age groups. Consequently, the current study aims to expand the current knowledge on the neuropsychological functioning (memory and learning, social perception and executive functioning), adaptive abilities and behaviour of children and adolescents with LiP. The primary focus of the study is to investigate how the neuropsychological and psychosocial functioning of children and adolescents with LiP differs from that of typically developing children and adolescents. The secondary focus is on differences in the trajectory of neuropsychological and psychosocial development of children and adolescents with LiP compared to typically developing peers. As the majority of children and adolescents with LiP in South Africa come from a significantly economically deprived area, it was imperative to compare their functioning to matched controls (develop norms for location, education, language and culture).

Based on the literature, the expectation was that children and adolescents with LiP would have similar difficulties as adults with this condition have, such as difficulties with memory, recognition of facial emotion and executive function, as well as neuropsychiatric disorders (maladaptive behaviour) and social difficulties. As the neuropsychological and neuropsychiatric difficulties in adults with LiP were presumed to be related to mesial temporal lobe (and especially amygdala) calcifications, it was further expected that the presentation of neuropsychological and neuropsychiatric difficulties in children and adolescents with LiP might be variable or even absent in some cases. This was postulated to be due to the presence or absence and types of lesions, age of onset, progression and extent of lesions. Environmental influences were also expected to affect the functioning of children and adolescents with LiP. Factors such as social rejection and self-consciousness were expected to increase the likelihood of internalising, externalising and social problems. The method of study will be described in the next chapter.

Chapter 4

Method of Study

The aim of this chapter is to outline the research hypotheses, discuss the type of research as well as the research design and to provide information about the sampling of participants. This is followed by an explanation of the procedures for screening and data collection. A description of each instrument, the rationale for its inclusion, the administration procedures, and its psychometric properties are then presented. This is followed by an explanation of the procedures for the translation of the measuring instruments. Ethical considerations are also discussed. Finally, the approach to data analysis is explained.

Hypotheses

The primary focus of this study was to describe the neuropsychological functioning and psychosocial development of LiP participants and to compare their functioning and adjustment with typically developing peers (control group). To compare these groups, the following null and alternative hypotheses were investigated:

H_0: Scores of the LiP participants on each of the neuropsychological tests and behaviour rating scales are not significantly different from the mean scores of the control and norm group.

H_1: Scores of the LiP participants on each of the neuropsychological tests and behaviour rating scales are significantly different from the mean scores of the control and norm group.

The secondary aim of the study was to explore whether any developmental or age-related trends were apparent in the neuropsychological and psychosocial functioning of the LiP participants across age and/or to what extent such developmental age-related trends may differ between the LiP participants and typically developing children and adolescents.

The type of research and research design will be discussed next.

Type of Research and Design

Non-experimental research has been done. A cross-sectional cohort study design (De Vaus, 2001), based on age and involving two groups (LiP participants and controls), was used. This design allowed the researcher to explore the neuropsychological and psychosocial functioning of a small heterogeneous population of children with LiP. The sampling method and the participants will be discussed next.

Sampling Method

Sampling is associated with the external validity, or generalisability, of research findings (Miller & Salkind, 2002; Rosnow & Rosenthal, 2012). As this study aimed to assess all the children and adolescents with LiP residing in South Africa, a purposive sampling method was used (Rosnow & Rosenthal, 2012). In the context of the current research, participants were chosen purposely based on their LiP diagnosis and age (younger than 18 years). This sampling methodology yielded five individuals with LiP, representing the total known population of children and adolescents diagnosed with LiP in South Africa. How they were identified will be discussed in the next paragraph.

Participants

First, the focus was to identify children and adolescents with LiP and then to match them with children and adolescents (control group) with typically developing status. During the data-collection procedure, information was also gathered from their guardians and teachers. The different participating groups will be discussed next.

LiP Participants

Four individuals with LiP (two children and two adolescents) were identified and recruited through the Urbach-Wiethe Disease (UWD) study group database, and a fifth child was identified via a family member with LiP who participated in another UWD study. The extensive UWD database has been compiled over several years and is consistently updated in collaboration with the local municipal and outpatient clinics across the country (Thornton et al., 2008). A medical practitioner diagnosed all of these LiP participants with LiP. A brief description of each LiP participant – intended to provide an

impression of how LiP has manifested in each individual, as well as to note the presence of any neurological problems, developmental difficulties or psychopathology – follows.

Participant 1 was a right-handed, 4-year-old girl from an urban middle-class environment. A dermatologist diagnosed her with LiP at the age of three years, following the diagnosis of her older sister (Participant 2) by the same medical practitioner. This child presented with pruritis, skin lesions and a hoarse voice. According to her parents' responses on the Structured Developmental History (SDH) form, they were concerned about her language and motor functioning during her early development. Her sentence construction was incorrect and the stories she told were very confusing. Her mother, who is a gymnastics teacher, noticed that her motor skills were somewhat delayed. The results of her EEG were normal, while her MRI results were inconclusive due to excessive movement during the scan. The child's Full Scale IQ (FSIQ = 103), Verbal IQ (VIQ = 95) and Performance IQ (PIQ = 112) on the Wechsler Pre-primary and Primary Scale of Intelligence-III (WPPSI-III) fell within the average to high average range. Furthermore, her parents' responses to items on the DSM-oriented Scales of the Child Behavior Checklist (CBCL) did not suggest any psychiatric disorder. However, this participant's teacher and parents expressed concern (on the Caregiver-Teacher Report Form [C-TRF] and Child Behavior Checklist for Ages 1.5-5 [CBCL/1.5-5]) that she was often in her own world and that she wandered off. However, she was not abnormally withdrawn and she did interact with others. Her teacher noted that she often refused to eat, picked her skin, masturbated excessively at school and she had little fear. However, the 4-year-old participant's parents observed that she was afraid of the dark. Finally, it was noted on the SDH form that the 4- and 6-year-old LiP participants, who were sisters, had an uncle (their mother's brother) who was cognitively impaired.

Participant 2 (the sister of the 4-year-old girl) was a 6-year-old, right-handed girl who came from an urban, middle-class environment. She had presented with a hoarse voice since birth. She was diagnosed with LiP at the age of five years. She had septic dermatitis, skin lesions, beaded papules on the eyelids and pruritis since infancy. In response to the questions of the SDH form, her parents indicated that she had been hospitalised on numerous occasions due to septic dermatitis related to LiP. The results of her EEG were normal, while the results of the MRI were inconclusive due to excessive movement during the scan. This child's performance on the WPPSI-III fell within the

average to high average range (FSIQ: 112; VIQ: 100; and PIQ: 119). Furthermore, her parents' responses to items on the DSM-oriented Scales of the CBCL/1.5-5 did not suggest any psychiatric disorder. This 6-year-old LiP participant's teacher was concerned (mentioned on the C-TRF form) that the girl often questioned authority. She was disobedient and overactive. Her teacher also indicated that she showed little fear of getting hurt and that she was consequently often injured. Her parents also remarked that she was overactive, needed constant supervision and that she often wandered away. She was scared of doctors and injections (she was hospitalised often due to skin infections). Her parents indicated that she was often teased at school due to her hoarseness and that they planned to home-school her instead. They were concerned about the effect of LiP on her self-esteem in the future.

Participant 3 was an 8-year-old, right-handed boy from an impoverished rural environment. He had been hoarse since birth, and had frequent rashes, skin lesions and septic dermatitis since infancy. He had alopecia and skin lesions on his scalp. He often had sores in his mouth. He was hospitalised due to respiratory infections and had a very high fever (above 39) on such occasions. This child's EEG was normal, but the MRI scan showed partial bilateral amygdala calcification. His maternal aunt was diagnosed with LiP. However, neither his younger sister nor his two older half-sisters were diagnosed with the condition. This participant's performance on the Wechsler Abbreviated Scale of Intelligence (WASI) fell within the low average range (PIQ of 87). The WASI VIQ and FSIQ could not be calculated because an Afrikaans translation of the WASI Vocabulary test was not available at the time of testing. However, the 8-year-old participant's performance on the short form of the Senior South African Intelligence Scale (Revised) [SSAIS(R)] indicated that his FSIQ was in the low average range (FSIQ = 88). According to the Child Behavior Checklist for Ages 6-18 (CBCL/6-18) DSM-oriented scales, he had symptoms suggesting an anxiety disorder, although a formal diagnosis of an anxiety disorder had not been made by a mental health practitioner. This participant's teacher was concerned (mentioned on the Teacher Report Form [TRF]) that he was sometimes very quiet and withdrawn. He was generally self-confident at school, but self-conscious when teased (which happened often). The 8-year-old participant's teacher noted that he scratched and picked his skin. His mother noted that he often had anger outbursts and that he would throw or destroy things when he lost his temper. She expressed concern about his future and how to deal with his illness.

Participant 4 was a 15-year-old, right-handed male from an impoverished rural environment. He had presented with a hoarse voice since birth, had frequent rashes, skin lesions, acneiform scars and septic dermatitis, and he bruised easily. He suffered from chronic parotitis. His parents did not give their consent for the administration of any medical tests; therefore no MRI or EEG results were available. He was one of three children, and both his siblings (21 and 23 years old) had also been diagnosed with LiP. His siblings were not included in the current study, as they were older than 18 years. His performance on the WASI fell within the low average range (PIQ of 87), but his VIQ and FSIQ could not be established because an Afrikaans version of the Vocabulary test of the WASI was not available. The WASI was administered to him during a previous research project when he was 10 years old, and on that occasion the PIQ was 77. On the day of the SSAIS(R) assessment, he refused to be tested. He was concerned about being stigmatised, as the assessment was scheduled to take place at school. The school principal did not want him to leave the school premises in order to be tested during school time. Therefore, the SSAIS(R), which was supposed to be administered on that day, was not completed. Initially, the 15-year-old LiP participant's mother was also distrustful of the researcher, despite giving permission for her child to be involved in the study. She explained that a television crew had previously interviewed individuals with LiP and had promised not to broadcast recordings of the interviews, but subsequently did. After being reassured that results of the current study would be published only in professional journals, the 15-year-old participant's mother cooperated willingly. The 15-year-old LiP participant's parents' responses to items on the DSM-oriented Scales of the CBCL/6-18 did not suggest any psychiatric disorder. This participant's parents remarked (on the CBCL/6-18) that he was easily influenced by friends. His teacher did not mention any concerns on the TRF form.

Participant 5 was a 17-year-old, right-handed male from an impoverished rural environment. EEG results of this participant were normal, but extensive bilateral amygdala calcification was observed on MRI. He had had a hoarse voice since birth and had frequent rashes, skin lesions, acneiform scars and pruritis, and he bruised easily. He also presented with upper respiratory complications associated with LiP and suffered from chronic parotitis. According to his mother's responses on the SDH form, he presented with delayed language development and articulation problems during his early development. He left school during Grade 9 at the age of 15 and was employed as a farm labourer on a part-time basis. According to his mother, he left school due to emotional

problems. He was often teased at school. He was the only LiP participant whose parents were divorced. He had a younger brother who did not have LiP. The 17-year-old participant's performance on the WASI fell in the borderline to average range (FSIQ: 87; VIQ: 78; PIQ: 99). He had been assessed previously by means of the WASI at the age of 12 during another research project. His PIQ at that stage was 84. The reason for the difference in performance on the WASI PIQ scale during the first and the second assessments was not clear. Scores in the clinical range on the DSM-oriented Scales of the CBCL/6-18 indicated that he had symptoms that suggested several psychiatric disorders: affective disorder, somatic disorder, attention deficit hyperactivity disorder (ADHD), conduct disorder and oppositional defiant disorder. Clinically significant scores on these scales do not necessarily indicate conclusively that specific psychiatric diagnoses are present. However, these results correlate with previously identified psychopathology (identified by means of the MINI Neuropsychiatric Interview during previous research). Some of the somatic problems indicated on the CBCL/6-18 DSM-oriented Somatic Disorder Scale (such as skin problems) were related to the symptoms of LiP. The 17-year-old LiP participant's mother expressed concern about his anger outbursts (she noted this on the CBCL/6-18 form). He often acted impulsively and was unable to control himself when he became angry. However, his angry moods did not last long. The 17-year-old LiP participant's mother indicated on the SDH form that he was extremely self-conscious. During the process of collecting data, this participant did not keep the first two appointments with the researcher. His mother explained that he was self-conscious about his hoarseness and skin scarring and he had to be reassured.

None of the LiP participants reported epilepsy, traumatic brain injury, additional serious illness or a history of physical or sexual abuse, factors that could potentially have influenced research results.

Apart from the LiP participants, it was necessary to employ a group of typically developing children (control group) in the current study to ensure that differences in measurement data could be ascribed primarily to the effects of LiP rather than measurement errors related to differences in age, gender, race, language, right- or left-handedness, intelligence and geographical environment (urban/rural). These factors represent cultural, socio-economic and neurological differences that may have affected test

performance (Braga, 2007; De Agostini & Dellatolas, 2001; Korkman, Kemp, & Kirk, 2001; McClure, 2000; Razani, German, Tabares, & Wong, 2006; Sobeh & Spijkers, 2013).

Control Group

Two matched control participants for each LiP participant were recruited, even though one control for each subject is often used in neuropsychological studies (Cavanagh, 2002; Pijnacker, Vervloed, & Steenbergen, 2012; Wheeler, Stevens, Sheard, & Rovet, 2012). In a large sample, variables tend to regress to the mean, and normal distribution of scores can be assumed. In a small sample the chance of a significant difference between the control participants and the clinical participant is increased. In addition, given that FSIQ and VIQ scores are not available for all participants, the chance that the controls may not be well-matched with the LiP participant with regard to intelligence is increased. Increasing the number of controls reduces the likelihood of such an error. Having two controls for every participant reduces the chance of a significant difference between the control and the clinical participants. However, the results of such a small control group ($n = 2$) may still have negative implications with regard to external validity.

Controls for the children and adolescents with LiP from the Northern Cape (rural area) were recruited through the municipal primary healthcare clinics in their respective towns. Staff at the clinics identified a cohort of children (three rural 8-year-old boys and seven rural male adolescents) who were all the same gender and age as the children and adolescents with LiP. Controls for the two children with LiP from an urban area (Gauteng) were recruited from preschools in another urban metropolis (Cape Town). They were from socio-economic backgrounds similar to those of the LiP children from Gauteng. Teachers at the relevant preschools identified 16 urban preschool girls of the same gender and age as that of the two children with LiP. The final group of ten control participants were identified by matching their demographic and IQ data with that of the LiP participants. Both groups will now be discussed in terms of their demographic variables, IQ and developmental history.

Demographic Data and IQ of Participants

Table 4.1 provides information regarding the age, gender, race, home language, right- or left-handedness, intelligence and geographical environment (urban or rural) of the LiP

and control participants. Information about their school attendance and siblings is also presented.

Table 4.1

Demographic Data for the LiP Participants and Control group with respect to Age, Gender, Handedness, Language, Race, Geographical Environment and IQ, Family Composition and Family History of LiP (n=15)

Variable	LiP group (*n* = 5)	Control group (*n* = 10)
Age at testing (years)		
Mean (*sd*)	10.4 (5.7)	10.4 (5.5)
Median	8.1	8.0
Range	4.6-17.8	4.3-17.8
Gender (Male/female)	3/2	6/4
Handedness (RH/LH)	5/0	10/0
Home language		
Afrikaans/English	3/2	6/4
Race/ethnicity		
Mixed race/Caucasian	3/2	6/4
Geographic environment		
Rural/Urban	3/2	6/4
Mean FSIQ		
4-year-olds (WPPSI-III)	103	109
6-year-olds (WPPSI-III)	112	102
8-year-olds (SSAIS-R)	88	93
17-year-olds (WASI)	87	84
Mean PIQ (WASI)		
8-year-olds	80	84
15-year-olds	87	80
Current school attendance		
Pre-school	2	4
Primary school	1	2
High school	1	4
Employed part time	1	0
Number of siblings		
One sibling	3	7
Two siblings	1	3
Three siblings	1	0
Sibling with LiP	3	0
Other family member with LiP	3	0

In Table 4.1, it is apparent that the mean ages (LiP: 10.4 years; Control: 10.4 years) and median ages (LiP: 8.1 years; Control: 8.0 years) for the two groups are similar. This is to be expected, given that age is one of the matching criteria. Similarly, the matching

methodology employed in the study has resulted in Afrikaans first language speakers, males, individuals of mixed ancestry and people from rural communities comprising 60% of both the LiP participants and the control group. English first language speakers, females, Caucasians and urban dwellers make up 40% of the LiP and control participants.

The level of education reported for the sample ranged from Grade 00 (pre-primary) to Grade 8 for the LiP participants and from Grade 00 to Grade 11 for the controls. In all but one instance, the two controls matched to each LiP participants were at the same grade level as that individual. The 17-year-old male with LiP was the exception, as it was not possible to refine the matching criteria further to include only individuals who had left school at the same age and grade level as this individual, and who were employed part-time as unskilled labourers. Consequently, controls for this individual could be matched only based on age, right- or left-handedness, gender, home language, race, residential area and IQ. Consequently, one individual matched to the 17-year-old LiP participant was in Grade 10, while the other was in Grade 11.

The family composition of the two groups differed to some extent. The majority of LiP participants (three) and controls (four) had one sibling. However, three of the controls had two siblings, while one of the LiP participants had two siblings. In contrast, one of the LiP participants had three siblings compared to none of the controls. Given that a diagnosis or suspicion of LiP was an exclusion criterion for the control group, it is not surprising that none of the controls reported familial incidences of LiP. However, three LiP participants reported siblings affected by the condition and three reported other family members with LiP.

As this study aimed to investigate the differences in the neuropsychological and psychosocial development of children and adolescents with LiP compared to typically developing children, it seems appropriate to report data on the early development of the LiP and control participants. This will provide a developmental context for the exploration of their cognitive functioning and psychosocial adjustment.

Developmental History of Participants

Table 4.2 indicates how the variables of the developmental history of the LiP research participants and controls compare.

Table 4.2

Developmental History of the LiP and Control Participants

Variable	LiP Group (*n* = 5)	Control Group (*n* = 10)
Primary caregivers		
Parents/Grandparents	5/0	9/1
Birth weight		
Mean (*sd*)	3.2 (0.7)	3.1 (0.6)
Median	2.9	3.2
Range	2.6-4.2	2.3-4.1
Neonatal complications	1	0
Early development (0-4 years)		
Concern about gross motor/fine-motor development	1/2	0/0
Feeding problems	1	0
Concern about social relatedness	0	1
Concern about language development	2	0
Separation anxiety	0	0
Poor emotional regulation	3	0
Enuresis	2	0
Seizures/epilepsy	0	0
Speech problems		
Unclear speech	0	1
Other speech problem (hoarse voice)	5	0
Vision problems (wears glasses)	2	1
School adjustment		
Adjustment problems preschool	2	0
Repeated a grade	0	1
Special needs education	0	0
Left school before Grade 12	1	0
Therapeutic intervention		
Speech therapy	0	0
Occupational therapy	1	0
Psychotherapy	2	1

Table 4.2 indicates that, with the exception of one control participant who was raised by his grandparents, the primary caregivers of all the LiP participants were their biological parents. This control participant's mother died when he was a child, and his father was not involved in his life. The mean birth weights of the clinical and control groups were very similar (3.2 kg for the LiP group and 3.1 kg for the control group). The median birth weight and range of birth weights of the two groups were similar, indicating that prenatal and neonatal growth was comparable. One parent indicated that her child with LiP had neonatal complications when he aspirated amniotic fluid. Consequently, he was ventilated in the neonatal ICU for approximately one week and was hospitalised for approximately two months. The neonatal complications of this child were not related to LiP, however: therefore, they cannot be viewed as a typical complication of the disorder. None of the control participants had neonatal complications.

The parents of three of the LiP participants were of the opinion that their children's fine and gross motor development was delayed, while none of the controls' parents expressed concerns in this regard. One of the LiP children had feeding problems as an infant due to LiP-related sores in his mouth. None of the LiP participants had difficulty with social relatedness during their early development. The mother of one of the control participants was concerned about the child's social relatedness during the early developmental stage, but confirmed that the quality of his social interaction had improved over time and normalised during the later stages of his development. For this reason, the early social problems were not viewed as a sign of a developmental disorder or other mental disorder; therefore, he was not excluded from the study.

Two out of five parents of the LiP participants were of the opinion that their children had delayed language development compared to typically developing children, while none of the control participant parents expressed this concern. Only one control participant's parents mentioned that his/her child had unclear speech (lisping) as a younger child, but all parents of LiP participants reported a hoarse voice (one of the prominent signs or symptoms of LiP).

Three of the LiP participants' parents reported that their children presented with poor emotional regulation (anger outbursts) during their early development (from birth to four years of age), while none of the control participants' parents noted a particular problem

with emotional regulation. These difficulties may have been related to many aspects of LiP, such as neuropsychiatric difficulties or frustration with the skin and voice symptoms of LiP (hoarseness, pruritis, septic dermatitis, hospitalisation or pain related to skin symptoms) and consequent difficulty in communicating their needs.

Enuresis was a problem during the development of two of the LiP participants. It is not clear what the association between LiP and enuresis could be; therefore, its co-existence may be coincidental.

Seizures were not reported for any of the LiP participants. Thornton (2006) reported that not one of the five children and adolescents that formed part of the population of individuals with LiP that she had assessed, had presented with seizures. However, Thornton (2006) reported that 35% of individuals older than 17 years, who lived in the same community as the current research participants, had reported epilepsy. Therefore, the prevalence of epilepsy in adults with LiP in this community seems to be high. The absence of seizures among the children and adolescents reported in the Thornton (2006) study and the children and adolescents with LiP in the current study may be explained by generally later onset of epilepsy in LiP, possibly during late adolescence or early adulthood.

Two of the LiP participants had marked adjustment problems during preschool. Both these LiP participants were teased about their hoarse voices. The first of the two LiP participants who had adjustment problems (6-year-old), was taken out of pre-school and taught at home. The second LiP participant (17-year-old) remained in school until Grade 9, when he also left school due to emotional difficulties. Therefore, these adjustment difficulties seem to be related to LiP. In addition to being teased and leaving school, the 17-year-old LiP participant also presented with behaviour problems. In contrast, none of the control participants had adjustment problems during their preschool years.

None of the LiP or control participants attended a special needs school, which may indicate a lack of serious developmental delay, as was also confirmed by the results of the cognitive assessments. None of the LiP participants failed a grade, while one control participant had to repeat Grade 10. This participant was a control for the adolescent who dropped out of school; therefore, he was not excluded from the study. Parents of LiP and control participants in the impoverished rural (Northern Cape) area, in response to

questions about the educational environment of their children, reported concern about the poor quality of education that might have affected their children's school performance.

Three of the LiP participants had been referred to professionals for therapy. One child received occupational therapy for fine motor difficulties. Two LiP participants had been referred to psychology. One of these children had experienced emotional difficulties due to rejection and teasing by peers. The other child had been experiencing scholastic and behavioural difficulties and had been referred for a psycho-educational assessment. The mother of this last child had been referred for counselling to help her deal with the child's behaviour. One of the control participants previously attended psychotherapy sessions when his parents had divorced, but he adjusted well thereafter and was not experiencing emotional difficulties at the time of the study.

Parents or Caregivers as Participants

Certain information could be obtained only from the participants' guardians (parents or caregivers). Table 4.3 outlines a comparison of the guardians' biographical variables for the LiP and control participants.

Table 4.3

Parent/caregiver characteristics of LiP and control participants

Variable	LiP group (*n* = 5)	Control group (*n* = 10)
Parent completing questionnaires: Father/mother/grandmother (*n*)	1/4/0	0/9/1
Age of parent who completed forms		
Mean (*sd*)	42.2 (8.9)	44.2 (9.9)
Median	39.0	39.5
Range	34.0-54.0	26.0-60.0
Marital status of parents		
Married	4	8
Divorced	1	1
Single	0	1
Maternal/caregiver employment		
Teacher/professional	1	1
Business	0	1
Sports coach/youth pastor/HIV counselor	1	3
Unskilled (Cleaner)	0	2
Homemaker	2	2
Pensioner	0	1
Maternal level of education		
Median (years)	12	12
Range (years)	9-15	4-15
<10	1	3
10-12	3	4
13-15	1	3
Paternal level of education		
Median (years)	13	12
Range (years)	9-16	9-16
<10	1	2
10-12	1	2
13-15	0	2
≥ 16	2	1
Unknown	1	3
Paternal employment		
Professional	2	2
Business	0	1
Pastor	0	1
Semi-skilled	1	4
Unskilled	0	1
Pensioner	1	1
Unemployed	1	0

Table 4.3 indicates that one father and four mothers of the LiP participants completed questionnaires, while nine mothers and one grandmother of the control participants completed questionnaires. The grandmother who completed the questionnaire raised the participant; therefore, she was able to provide adequate information. The mean age of LiP participants' caregivers who completed forms ($\overline{X}$ = 42.2) was nearly similar to the mean age of the parents of the control participants ($\overline{X}$ = 44.2), while the age range of parents and caregivers of control participants (26-60 years) was somewhat wider compared to the age range for LiP participant parents (34-54 years). Four of the LiP participants' parents were married, while one participant's parents were divorced. The marital status of control participants' caregivers was nearly similar compared to the LiP participants' caregivers. Eight of the control participants' parents were married; one participant's parents were divorced, while one participant's mother never married.

There were clear differences between the urban and rural participants of the LiP and control groups. The urban parents generally had higher education levels, and more urban parents were employed as professionals or in business as opposed to semi-skilled or unskilled jobs, which can be explained by commonalities in geo-economic variables. Differences in educational level and quality in the rural areas versus those in the urban areas are due to the legacy of the Apartheid government and differences in opportunity, resource and facility demographics (Skuy, Schutte, Fridjhon, & O'Carroll, 2001). Level and quality of education has implications for socioeconomic attainment and cognitive development of children (Ferrett, 2011; Shuttleworth-Edwards et al., 2004; Skuy et al., 2001). These variables were controlled by geographic matching of the participants in each group.

The median for the acquired level of maternal education of both groups was 12 years. The number of years of acquired maternal education varied (due to differences between the rural and urban participants in each group) and differed slightly between the two groups (9-15 years in the LiP group and 4-15 years in the control group). The status of maternal employment among the research participants in each group also varied, for socioeconomic reasons already discussed.

Paternal education was similar in both groups (9-16 years). The median years of education was 13 in the LiP group and 12 in the control group. The level of education of three of the control fathers and one of the LiP fathers was unknown.

The father of two of the LiP participants (female, urban participants) was employed as a professional, one father was employed as a semi-skilled worker, one father was a pensioner, and one father was unemployed. Two of the fathers of children in the control group were professionals (accountants), one was a property manager, one was a pastor, four fathers were semi-skilled workers, and one grandfather was a pensioner. As a whole, the composition of the two groups (LiP and control parents) was very similar, as expected because the participants were matched.

Screening and Data-Collection Procedures

The screening and data-collection procedures for the LiP and control groups are shown in Figure 4.1.

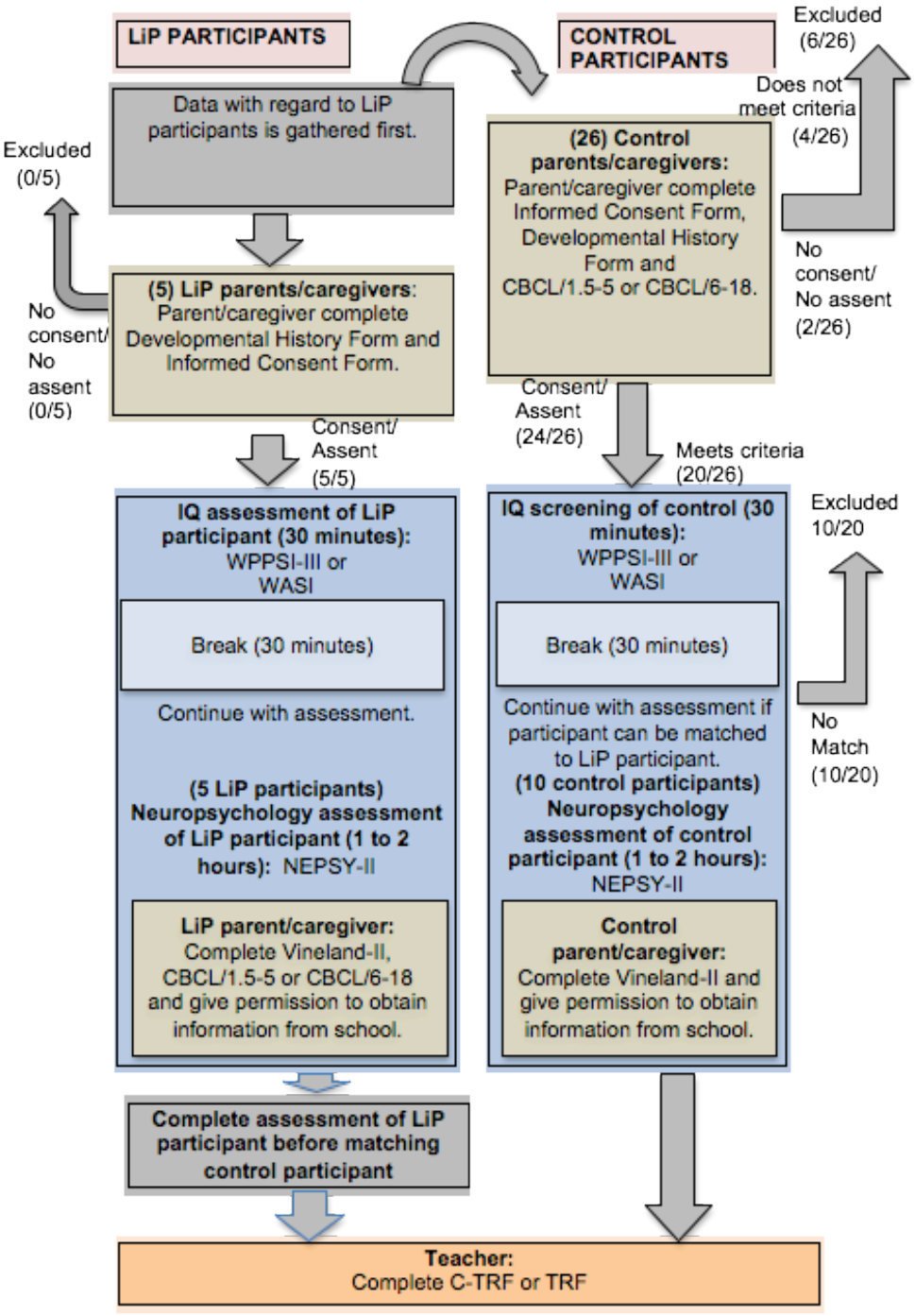

Figure 4.1. Data collection procedures.

Figure 4.1. Data-collection procedures

Figure 4.1 shows that the sequence of data collection and administration of tests for the LiP and control participants was similar. Data for the LiP participants were collected first in order to be able to match control participants to them. The data collection process for both groups started with parental consent and the completion of the SDH. Five LiP participants were recruited and all their parents and guardians gave permission for the inclusion of their children in the study. The pool of 26 potential control children and adolescents that were recruited initially consisted of 16 urban preschool girls, 3 rural 8-year-old boys and 7 rural male adolescents. The parents of these children and adolescents were contacted to request permission for their children to be screened for potential inclusion in the control group. Twenty-four out of the 26 potential control participants' parents and guardians gave permission for their screening and inclusion in the study.

The data obtained from the SDH form provided an overview of the characteristics and demographic details of each LiP and control participant. The SDH provided screening for a history of abuse, medical illness and neurological or developmental difficulties in the control participants. In addition to the SDH form, the Achenbach System of Empirically Based Assessment (ASEBA) checklists, namely the CBCL and C-TRF or TRF, were administered to parents of the control participants. The DSM-oriented scales of the CBCL (Achenbach & Rescorla, 2001) were used as a screening measure for psychiatric disorders among the potential control participants. After completion, the forms were perused and scored to determine if the particular child or adolescent was suitable for inclusion in the study. Potential control participants were excluded from the study if their scores on any of the DSM-oriented scales of the CBCL fell within the clinical range (T-score above 70).

Four potential control participants were excluded based on the initial screening process (SDH form and CBCL DSM-oriented scales). In the urban area, one potential control participant was excluded due to right- or left-handedness, one due to a metabolic disorder (diabetes), and one due to a psychiatric disorder (anxiety disorder). In the rural area, one potential control participant was excluded due to a neuropsychiatric disorder (ADHD). Subsequently, these children were referred to a neurologist (the child with ADHD) and psychologist (the child with an anxiety disorder), who confirmed the diagnoses. Following the exclusion of the four potential controls, an initial sample of 20 individuals (12 children and 8 adolescents), selected from the original sample of 24 individuals, met all the matching criteria except for IQ (PIQ or FSIQ). Once parental

permission had been granted and suitability for inclusion determined, consent was obtained from the children and adolescents to continue with the assessment. All the LiP and control participants gave their consent.

Figure 4.1 shows that the same sequence of administration of the intelligence tests and the NEPSY-II was followed for both the LiP and control participants. The WASI or WPPSI-III was administered to obtain a FSIQ or PIQ. The IQ tests were scored during a 30-minute break. Potential control participants who scored within one standard deviation of the FSIQ (4-, 6- and 17-year olds) or PIQ (8- and 15-year-olds) of the LiP participant for whom the individual would potentially serve as a control were retained as controls, while those who scored outside of this range were excluded. The process was repeated until two controls had been matched to each LiP participant in the sample. Eight potential controls between the ages of 4 and 6 years and two potential adolescent participants were excluded because they could not be matched to the corresponding LiP participants with regard to FSIQ or PIQ. The screening process yielded a total of 10 control participants suitable for inclusion in the study.

The completion of the intelligence testing was followed by the administration of the NEPSY-II, and (although not indicated in Figure 4.1) subtests were administered in the same order for all the participants in each age group. IQ testing by means of the WASI took approximately 15-30 minutes. The break was 30 minutes long, and scoring of the WASI took approximately 20 minutes. Administering the NEPSY-II subtests to the eight-, 15- and 17-year-old participants lasted approximately 90 minutes. The IQ testing by means of the WPPSI-III lasted approximately one hour, while the neuropsychological testing of the 4- and 6-year-olds by means of the NEPSY-II was also completed within one hour. Scoring of the WPPSI-III lasted approximately 20 minutes.

Parents completed the behaviour checklists (control participants: Vineland Adaptive Behavior Scales [2nd ed., Vineland-II], LiP participants: CBCL/6-18 or CBCL/1.5-5 and Vineland-II) either during the assessment of their children or at home, after which the forms were returned to the researcher. A permission form, indicating consent for obtaining data from the schools, was signed by parents and guardians of the 10 controls and 5 LiP participants The last step in the process was to obtain information from teachers by means of the C-TRF and TRF checklists. The TRF forms were given or sent to the headmasters

of the schools where the participants received their education. The nature of the study was explained verbally or in a letter. A letter containing the details of the researcher, an explanation of instructions and the parent's written consent for the school to release information regarding the child were attached to each form. The headmaster was asked to return the forms to the researcher after completion by the class teacher by means of post, fax or e-mail or by handing them to the research assistant (psychologist) who worked at one of the schools. All TRF forms were completed and received.

Geographical area, language, education, access to transport and work circumstances of parents dictated the practical aspects of data collection, but measures were put in place to help ensure consistency: All neuropsychological and IQ testing was completed by the researcher, and the same sequence of testing (as set out in Figure 4.1) was followed for all the participants. All participants were tested in one session, with a break of 30 minutes between the administration of the age-appropriate IQ test and the NEPSY-II. Two different research assistants, both bilingual psychologists registered with the profession's regulating body (HPCSA), were employed in the administration of behaviour checklists. To ensure consistency, the researcher trained both of them. Either the research assistants or the researcher were available to clarify instructions or questions of parents. The telephone number of the researcher was made available to parents who completed the forms at home.

Although measures were put in place to ensure consistency, certain difficulties were encountered in other aspects of data collection and caused some inconsistency in the collection of data. The details of these difficulties and inconsistencies will be described for the rural and urban research participants separately.

Owing to the long distances that rural LiP participants, potential control participants and the researcher had to travel and the consequent time restraints, the recruitment and testing of participants progressed in an unpredictable manner. This necessitated four visits to the rural area to complete the collection of data for the rural participants. The research assistant was able to travel on two occasions to assist with the administration of tests, while the researcher administered all the tests on the other occasions. Several other factors affected the data-collection process, such as parents working, participants not keeping

appointments, fear of being stigmatised, difficulty travelling to the clinic and children being refused permission to attend appointments during school time.

Some rural LiP and control participants and their parents and guardians were interviewed and tested at the local municipal clinics, while others were interviewed or tested at their homes. The latter arrangement was made because some of the parents refused or were not able to meet at the community clinics. The impression was that the 17-year-old male rural participant and the 15-year-old LiP participant's mother were concerned about being stigmatised and therefore did not want to meet at the clinic. Although the 17-year-old LiP participant gave his consent to being tested, he did not keep appointments on two occasions (he was not at home at the time agreed upon). He was then contacted again, and his reluctance to be tested was discussed. The impression was that he was self-conscious and consequently avoided the situation. This participant was reminded that he was not compelled to take part in the research, and he was reassured with regard to confidentiality and the fact that only one researcher would be present during the testing. He kept a subsequent appointment and was willing to be tested on this occasion. After the assessment of the 8- and 15-year-old rural LiP participants, it was decided that it would be wise to administer the short form of the SSAIS(R) in addition to the WASI, as it was not possible to obtain an FSIQ for the Afrikaans-speaking 8- and 15-year-old participants with this instrument. The plan was to administer the SSAIS(R) on a different day, as the participants were tired after the administration of the WASI and NEPSY-II. The 8-year-old participant and his parent cooperated, and it was possible to complete the administration of the SSAIS(R) on a subsequent day. However, the headmaster of the school where the 15-year-old received his education refused to give him permission to leave the school premises during school time; therefore it was suggested that the test be administered at school during break. However, the 15-year-old LiP participant refused to be tested at school, and it seemed as if he was concerned about being stigmatised by his peers. He refused any further assessment; therefore, the SSAIS(R) was never administered to him.

Behaviour rating, intelligence testing and neuropsychological testing were completed for most LiP participants on the same day, with the exception of one set of behaviour checklists, which was completed by the parent of a rural LiP participant the day before the participant was tested. It was possible to complete most of the screening, behaviour

checklists, intelligence and neuropsychological testing of a specific control participant on the same day. Only two rural control participants were screened before the actual assessment. One of these control participants' mother completed forms and questionnaires at her place of work, as she did not have permission to leave the residence where she worked. Her child (control participant) was tested at home on the following day. Another control participant's grandparents were old and sickly; therefore, the screening was conducted at their home, while the control participant was tested at the clinic on another day.

The urban participants were the 4- and 6-year-old LiP children and the 4 controls matched to them. As they lived in a different city as the researcher, the researcher had to travel by aeroplane and met them at their home. One urban LiP participant (6-year-old child) was then tested at her home. The other urban LiP participant (her 4-year-old sister) was uncooperative during the initial assessment attempt. The impression was that she found it difficult to concentrate and she was restless. Consequently, the 4-year-old child was tested at the researcher's office at a later stage when the family visited Cape Town. She also found it difficult to concentrate during this subsequent assessment, but her cooperation was sufficient to finish the assessment. The parents of the 4- and 6-year-old LiP participants completed the behaviour checklists while they were being tested. The C-TRF was handed to the teachers during the initial visit to the urban LiP participants' home town.

The control participants were tested either at the preschool they attended or at the researcher's office, depending upon practicality. A research assistant (a registered psychologist who worked at one of the preschools where some of the children were recruited) personally explained to parents how to complete the SDH form and the CBCL/1.5-5. Parents returned the completed forms to the school or the researcher's office. After perusal of the forms and checklists, the parents of children who met the criteria for inclusion in the study were contacted, and arrangements were made for the children to be tested at the respective preschools or at the researcher's office, depending on practical considerations.

Once a control participant had been matched to a LiP participant, the control participant's parents were requested to complete the Vineland-II Adaptive Behavior Scale.

Two urban control participant parents completed the Vineland-II at home (the research assistant explained the completion procedure to them), after which they returned the forms to the school. The researcher explained the procedure for completion of the Vineland-II form to two control participant parents who completed the form in the researcher's office while the NEPSY-II subtests were being administered to their children. The different measuring instruments will be discussed next.

Screening and Measuring Instruments

In Figure 4.1, it is clear that specific measuring instruments were used to screen the participants in terms of their background and development, the presence of psychiatric and developmental problems and intellectual ability. For this purpose, the SDH, the DSM-oriented scales of the CBCL and the WPPSI-III or the WASI were used.

However, to obtain data regarding the main focus of the study, namely the neuropsychological and psychosocial functioning of the participants, other instruments were used as well. First, the screening instruments will be discussed followed by die measuring instruments that were used to gather data regarding the hypothesis of the study.

Screening Instruments

SDH Form. The SDH form of the Behavior Assessment System for Children-2 (Reynolds & Kamphaus, 2004) consists of a form containing several structured and open-ended questions with regard to the child's background and development.

The information obtained via the SDH was used to determine if control participants met the criteria for inclusion in the study and to obtain descriptive information about the development and functioning of LiP and control participants (such as developmental milestones, educational history, school attendance, scholastic problems). The SDH begins by surveying the demographic information of the parent or caregiver, followed by a focus on family history and family relations. The history of the pregnancy, birth, and developmental milestones of the child are then explored. The SDH includes questions about the child's medical history (including hospitalisation and operations) and provides information on his or her current health status. Information on right- or left-handedness, speech, hearing, and vision are also obtained via the SDH. The SDH includes questions requiring information on any history of medical and psychological care the individual has

received. The family health history explores genetic and other high-risk health factors. Educational history is covered in the last part of the SDH (Reynolds & Kamphaus, 2004).

The items on the SDH were translated into Afrikaans by the researcher, who is proficient in both Afrikaans and English (Appendix C). The form was proofread and edited by a qualified language expert. The form may be completed independently by the parent or can be presented as a semi-structured interview (Reynolds & Kamphaus, 2004). When parents did not understand the questions, they had the opportunity to ask for clarity and the questions were explained to them.

Owing to the low educational level and consequent reading difficulties of the Afrikaans parents and caregivers, the form was presented to them as an interview. The English parents completed the SDH form independently. However, they had the opportunity to clarify any uncertainties with regard to the questions. All instances where parents were unable to provide information were indicated on the SDH.

CBCL/1.5-5 and CBCL/6-18 DSM-oriented scales. One of the criteria used to exclude potential control participants was the presence of psychiatric or developmental disorders. The DSM-oriented scales (Achenbach & Rescorla, 2000; 2001) of these checklists were used to screen the participants for the presence of psychiatric and developmental problems. The CBCL/1.5-5 and CBCL/6-18 are similar behaviour-rating scales measuring the presence of behaviour problems in younger and school-age children and adolescents and generally can be completed by a parent or caregiver in approximately 15 minutes. Achenbach and Rescorla (2000; 2001) constructed the DSM-oriented scales of the ASEBA instruments by grouping items considered by psychiatrists and psychologists to be consistent with the diagnostic categories of the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994). They found significant correlations between the ASEBA scale scores and the total number of symptoms on *DSM-IV* checklists, as well as between the presence or absence of diagnoses and the raw scores on the corresponding CBCL/6-18 scales. Other studies indicated accuracy of the CBCL/6-18 in predicting clinical diagnoses based on the criteria in the *DSM-IV*, although accuracy in the prediction of these diagnoses varied (Ferdinand, 2008; Krol, De Bruyn, Coolen, & Van Aarle, 2006).

For the purpose of this study, the CBCL/1.5-5 and CBCL/6-18 forms were completed by parents and guardians and were scored using the hand-scoring profiles. The raw scores on these scales/subscales can be transformed into transformed scores (T-scores) using the relevant norms. A distinction is made between normal (T-score below 65), borderline (T-score of 65 to 69), and clinical ranges (T-score above 70) based on the same national normative samples as that of the empirically based scales. A particular score on a DSM-oriented scale is not directly equivalent to a *DSM-IV* diagnosis, but a high score suggests that a diagnosis should be considered. Potential control participants were excluded if scores on any of the DSM-oriented scales were in the clinical range (T-score above 70). Achenbach and Rescorla (2000; 2001) reported good test-retest reliability for the CBCL/6-18 DSM-oriented scales (r_{tt} = .88) and CBCL/1.5-5 DSM-oriented scales (r_{tt} = .85), according to the criteria of Cichetti (1994).

Intelligence tests. Another criterion according to which the participants were matched was intelligence. This was necessary because intelligence levels affect children's performance on neuropsychological measures (Korkman et al., 2001; Toga & Thompson, 2005). Owing to the differences in age groups, two different IQ tests were used and will be discussed next.

WPPSI-III. The WPPSI-III is a standardised, individually administered measure of intelligence for children aged from two years six months to seven years three months (The Psychological Corporation, 2002). The following seven core subtests have to be administered to calculate an FSIQ Block Design, Information, Matrix Reasoning, Vocabulary, Picture Concepts, Word Reasoning, and Coding. The WPPSI-III yields the traditional main composite scores: Verbal IQ (VIQ), Performance IQ (PIQ) and Full Scale IQ (FSIQ).

The WPPSI-III was administered to 4- and 6-year-old LiP children and their matched controls according to the instructions set out in the *Administration and Scoring Manual for the WPPSI-III* (The Psychological Corporation, 2002). The seven core subtests were administered in the following appropriate administration order: Block Design, Information, Matrix Reasoning, Vocabulary, Picture Concepts, Word Reasoning, and Coding.

Each subtest was scored according to the procedures set out in the manual, and the total raw score for each subtest was converted to a scaled score, using the appropriate norm tables for the specific age group.

The overall average internal split-half reliability coefficient for the WPPSI-III FSIQ is .96 (The Psychological Corporation, 2002). Internal consistency is viewed as excellent or high when the coefficient is above .90 (Brooks, Sherman, & Strauss, 2010); therefore, the WPPSI-III FSIQ can be viewed as a reliable measure of intelligence.

WASI. Thornton et al. (2008) used the WASI (The Psychological Corporation, 1999), in a study on individuals with LiP living in the same community as the current research participants. Therefore, it was decided to employ the same instrument in this study to possibly compare and integrate the results of the two research projects in the future. The WASI is a brief and reliable measure of general intelligence for individuals between the ages of 6 and 89 years (The Psychological Corporation, 1999) and yields the three traditional VIQ, PIQ and FSIQ scores.

The WASI was administered to the 8-, 15- and 17-year-old research participants in the current study. All participants (LiP and controls) in the current study between the ages of 6 and 18 years were Afrikaans-speaking. Consequently, the English Vocabulary subtest of the WASI could not be administered. In the case of the 17-year-old LiP participant and his two control participants, it was possible to substitute the English WASI Vocabulary subtest with Afrikaans translation and adaptation of the Vocabulary subtest of the Wechsler Adult Intelligence Scale (3rd ed.; WAIS-III; Claassen, Krynauw, Holzhausen, & Mathe, 2001) of the Human Sciences Research Council (HSRC) of South Africa. The Afrikaans Vocabulary subtest of the WASI has a correlation coefficient of 0.88 with the English Vocabulary subtest of the WAIS-III (The Psychological Corporation, 1997). As the Afrikaans version is a translation of this subtest, the Afrikaans Vocabulary subtest of the WAIS-III was viewed as an appropriate substitute for the English Vocabulary subtest of the WASI. For Afrikaans-speaking children younger than 16 years, no Afrikaans translation of the Vocabulary subtest was available; therefore, only the Block Design, Matrix Reasoning, and Similarities subtests were administered in this age group. Consequently, it was not possible to calculate the VIQ and the FSIQ for the 8- and 15-year-old LiP and control participants. Therefore, only PIQ scores were used to match

control and LiP participants in this age range. Intercorrelation between the WASI PIQ and WASI FSIQ-4 scores (r = .89) for the sample of individuals on whom the instrument was normed is good (The Psychological Corporation, 1999), indicating concurrent validity of the WASI PIQ as a measure of general intelligence. Therefore, matching the LiP and control participants according to the PIQ was deemed to be an acceptable alternative to matching them according to the FSIQ. However, significant differences between the VIQs and PIQs of LiP participants and their matched controls may still have been present and could have affected the results of the study.

The Block Design, Similarities, and Matrix Reasoning subtests were scored as indicated in the *WASI Manual* (The Psychological Corporation, 1999). The WAIS-III Afrikaans Vocabulary test was administered according to the *WAIS-III Manual* and the supplement providing Afrikaans alternatives (Claassen et al., 2001). The test was then scored according to the original English *WAIS-III Manual* (The Psychological Corporation, 1997). The raw score for the Afrikaans Vocabulary test (WAIS-III) obtained in this way was transformed to a scaled score according to relevant tables in the original English manual (The Psychological Corporation, 1999). The scaled score was converted to its corresponding WASI T-score by using the relevant scaled score to T-score conversion table in the *WASI Manual* (The Psychological Corporation, 1999, p. 183, Table A.2) to be able to determine the FSIQ for the 17-year-old participants. This conversion method was used in a previous South African study on individuals with LiP where the Afrikaans WAIS-III Vocabulary test was used similarly as a substitute for the WASI English Vocabulary test (Thornton, 2006).

The Psychological Corporation (1999) reported very high internal consistency coefficients for PIQ in the 8- and 15-year-old age groups (r_{tt} = .93 and r_{tt} = .94 respectively), and 0.96 for FSIQ in the 17- to 19-year-old age group. According to Brooks et al. (2010), an internal consistency coefficient above .90 indicates high or excellent reliability. Therefore, the WASI PIQ and FSIQ are reliable measures of performance intelligence (used to match participants in the 8- and 15-year-old age groups) and general intelligence (used to match participants in the 17-year-old age group).

A discussion of the measuring instruments that were used to obtain information regarding the participants' neuropsychological and psychosocial functioning follows.

Instruments Measuring Neuropsychological Functioning

In order to explore the areas of neurocognitive functioning affected by LiP in children and adolescents, the neuropsychological measures utilised had to meet two criteria. First, the measures were required to sample a broad range of neurocognitive functions, as identified by a review of the LiP literature. Second, where possible, the measuring instruments had to be applicable to the range of ages included in the sample. Therefore, measures should ideally sample specific neurocognitive functions of all ages (4 to 17 years of age) included in the current sample. The NEPSY-II (Korkman, Kirk, & Kemp, 2007a) is an instrument measuring a broad range of neuropsychological functions across all ages in the current sample; therefore, it was decided to use this instrument. To measure neurocognitive functions over a wide range of ages, subtests of the NEPSY-II were included only if it could be completed by children in two or more of the age groups. The upper age limit of the NEPSY-II is 16 years and 11 months; therefore, norms are not available for 17-year-olds. Therefore, to be able to include the 17-year-old in the study, it was decided to use the norms for 16-year-olds to interpret the NEPSY-II results of the 17-year-old participant. As development of cognitive functions mature during late adolescence, it can be expected that there would not be a noticeable difference in performance between an individual who is 16 years, 11 months old and an individual who is 17 years and 9 months old.

Practical aspects of administration were taken into account when selecting subtests of the NEPSY-II, such as weighing up the validity of using standardised English audio recordings of spoken words or numbers in a sample that included rural Afrikaans-speaking children. It was decided not to use the Auditory Attention subtest of the NEPSY-II to measure attention, as the use of the English audio recording would have disadvantaged the Afrikaans-speaking participants in this task. Instead, it was decided to use the Attention Problems scales of the CBCL and C-TRF to measure attention.

From the literature study, specific neuropsychological constructs were identified as relevant to LiP, namely memory and learning, social perception and attention, and executive functioning. These constructs are represented by different dimensions, and to obtain a measurement of the participants' performance on these dimensions, different subscales had to be used. Owing to big age differences between the participants, it was

sometimes necessary to use different subscales of the same instrument to test the same construct in different age groups. The neuropsychological constructs, dimensions and subscales of the NEPSY-II, CBCL and C-TRF relevant to the different age groups are reported in Table 4.4.

Table 4.4

Neuropsychological constructs, dimensions and subscales relevant to the age groups

Neuropsychological functioning								
Construct	**Dimension**	**Subscale**	**Age**				
			4	**6**	**8**	**15**	**17**
Memory and learning	Verbal memory	NM Recognition	*	*	*		
		NM Free and Cued	*	*	*	*	*
		NM Free		*	*	*	*
	Visual memory	MD Content	*	*	*	*	*
		MD Spatial	*	*	*	*	*
		MD Total	*	*	*	*	*
		MDD Content		*	*	*	*
		MDD Spatial		*	*	*	*
		MDD Total		*	*	*	*
	Visual-verbal associative learning	MN Total				*	*
Social perception	Facial emotional recognition	Happy errors	*	*	*	*	*
		Sad errors	*	*	*	*	*
		Neutral errors	*	*	*	*	*
		Fear errors	*	*	*	*	*
		Angry errors	*	*	*	*	*
		Disgust errors	*	*	*	*	*
		AR Total	*	*	*	*	*
	Theory of mind	TM Verbal	*	*	*	*	*
		TM Total			*	*	*
	Face recognition	MF Total		*	*	*	*
Attention and executive functioning	Attention	Attention C-TRF	*	*	*	*	
		Attention CBCL	*	*	*	*	*
	Executive functioning	ST Total	*	*			
		ST Body Movement	*	*			
		ST Eye opening	*	*			
		ST Vocalization	*	*			
		INN Total errors		*	*	*	*
		INI Total errors		*	*	*	*
		INS Total errors			*	*	*
		AS Total errors			*	*	*

* The subtest can be administered in the relevant age group

In Table 4.4, it is indicated which subtests in each dimension could be administered in each age group. As the developmental rates of different neurocognitive abilities/functions in childhood vary, certain abilities are evident from relatively early in childhood, while others emerge as the child develops and continues to develop through adolescence (Anderson, et al., 2001; Annaz, Karmiloff-Smith, & Thomas, 2008). Certain neurocognitive functions, such as cognitive flexibility, are either so rudimentarily developed or perhaps absent at certain stages of early development that there is currently no feasible way of measuring such constructs in some of the younger participants (Waber et al., 2007). These variations in typical neuropsychological development are evident in the instruments designed to measure neurocognitive functions in children (Anderson et al., 2001; Baron, 2004). Consequently, the subtests of the NEPSY-II do not provide a measure for all the neurocognitive abilities at every age. The discussion of the subtests of the NEPSY-II (under the heading of each construct) will reflect the age progression of the measured functions. The different neuropsychological constructs and the instruments used to measure them will now be discussed in more detail.

Memory and learning. Thornton et al. (2008) and others (Emsley & Paster, 1985; Ghika-Schmid et al., 1997) suggest that research participants with LiP perform significantly worse than age-matched controls did in certain declarative memory tests. Deficits in immediate verbal memory, verbal learning, recognition memory, as well as percentage retention of visual material, are apparent in the Thornton et al. (2008) study; immediate visual memory deficits were observed by Emsley and Paster (1985). It is suggested that the medial temporal lobe and its connections facilitate several aspects and forms of memory and learning (Alvarado & Bachevalier, 2000; Brasted, Bussey, Murray, & Wise, 2003; Mayes, Montaldi, & Migo, 2007; Squire, 2004; Squire, Wixted, & Clark, 2007). Thus, injury to different structures of the medial temporal lobe (including the amygdala and hippocampus) may lead to memory and learning deficits (Manns & Squire, 2002; Markowitsch, 2000). The current study focused on declarative memory (specifically episodic memory) and visual-verbal associative learning, as these functions were generally found to be affected by medial temporal lesions and LiP in adults (Ghika-Scmid et al., 1997; Thornton et al., 2008; Tranel & Hyman, 1990).

Declarative memory or explicit memory can be described as the ability to recall facts or events consciously (Piguet & Corkin, 2005; Squire et al., 2007; Zola-Morgan & Squire,

1993). Episodic memory refers to memories of specific past events or episodes and provides context-rich information from all sensory modalities as opposed to semantic memory that is context poor and involves only one modality (Eichenbaum & Cohen, 2001). The processes involved in episodic memory include encoding processes (engaged when an event is experienced and leading to the formation of a new memory representation) consolidation processes (visible in delayed memory, percentage retention and associative learning), as well as retrieval processes (recognition and recall) that support the recollection or re-experiencing of the event at a later stage (Baron, 2004; Rugg, Otten, & Henson, 2002; Tulving, 2002).

Evidence from both cognitive psychology and neuropsychology shows that, although there is also a strong connection between the domain-specific processes, short-term and long-term memory is material-specific (Alloway, Gathercole, & Pickering, 2006; Pickering, Gathercole, & Peaker, 1998). Therefore, visual and verbal memory can be viewed as distinct concepts. In this study, episodic memory processes have been measured with regard to both verbal (immediate verbal and verbal recognition) and visual (immediate and long-term visual) modalities, while associative learning processes have been measured by a visual-verbal paired associative learning task.

Verbal memory. The involvement of the medial temporal lobe in verbal memory functions and the fact that adults with LiP were reported to have verbal memory and recognition deficits (Thornton et al., 2008) provided the primary motivation for suspecting that children and adolescents with LiP might exhibit deficits in this regard. This necessitated the measurement of these functions. Measures used to evaluate immediate or short-term verbal memory and verbal recognition memory will be discussed next.

Immediate verbal memory. A distinction can be made between primary (immediate), secondary (short-term) and long-term memory. Short-term memory has a relatively larger capacity and much slower decay compared to primary memory. Only short-term verbal memory was measured in the current study because the NEPSY-II does not include a long-term verbal memory measure. *Short-term* or *immediate verbal memory* (secondary memory) refers to a process in which verbal information is stored in such a way that the person will still be able to recall the information after an intrusion (Horton & Nardini,

2008). Short-term memory is different from memory span measured by digit span or similar tests where there is no intrusion before recall.

The NEPSY-II Narrative Memory (NM) subtest was used to measure immediate verbal memory for meaningful material under free recall and cued recall conditions (NM Free and Cued Recall [NM Fc Recall] and NM Free Recall). A story is read to the child. After free recall of the story (repeating the story), the child is asked questions (cued recall) to elicit missing details from his or her rendition of the story or passage (Korkman, Kirk, & Kemp, 2007b).

The NM subtest was administered to all participants. The stories and passages (verbal material) were translated into Afrikaans for the Afrikaans-speaking participants (8-, 15- and 17-year-old); the translation is discussed in more detail in the section titled *Translation and Adaptation of Measuring Instruments*.

An NM Fc Recall and an NM Free Recall score can be calculated. The NM Free Recall score can be calculated only for children of six years and older, as younger children are not expected to be able to recall structured verbal material easily without cues. The NM Free Recall Total raw score is calculated by adding the scores on free recall of the story administered. A high NM Free Recall total score indicates the ability to express and access organised verbal information without cues, while a low score indicates a poor ability to express and access organised verbal information. The NM Fc Recall total raw score is calculated by adding the scores on free recall and cued recall of the story administered. A high NM Fc Recall score indicates efficient free and cued recall of organised verbal material.

Test-retest coefficients above .70 were reported for all the age groups, except for the 9- to 10-year-olds (.65), for NM Fc Recall and for the NM Free Recall total in a sample of 1200 typically developing 3- to 16-year-olds in the United States of America (Korkman et al., 2007b). Therefore, generally, test-retest reliability can be viewed as acceptable according to the criteria of Brooks et al. (2010).

An example of evidence that seems to support the validity of the NM subtest is the large correlations (r = .61 and .63 respectively) between Free Recall and NM Fc Recall scores on the NEPSY and their NEPSY-II counterparts (Korkman et al., 2007b). Brooks et

al. (2010) view correlations between .30 and .49 as medium and correlations between .50 and 1.0 as large.

Verbal recognition memory. Yonelinas and colleagues (Yonelinas, 2001; Rugg & Yonelinas, 2003) propose that two separate processes (recall and recognition) underlie episodic memory and that people can have poor recall but excellent recognition, i.e. they cannot retrieve the memory but are able to recognise a stimulus as familiar. Recognition memory can be defined as the capacity to judge a previously encountered stimulus as familiar (Wais, Wixted, Hopkins & Squire, 2006). It involves two processes: simply knowing that the item was encountered (familiarity) and an episodic component referring to remembering the specific details of the context in which the item was encountered after presentation of a cue (Wais et al., 2006). Some researchers suggest that the hippocampus plays an important role specifically in recognition memory, although there are different views with regard to the nature of its role in recognition and familiarity (Brown & Aggleton, 2001; Fortin, Wrigth, & Eichenbaum, 2004). Nevertheless, it was found that both recognition and recall were affected negatively by temporal lobe lesions, also in people with LiP (Thornton et al., 2008). Therefore, it was deemed necessary to include a measure of verbal recognition (in addition to a measure of verbal recall) in the current study.

Recognition memory was measured by using the Narrative Memory Recognition (NM Recognition) task of the NEPSY-II. The NM Recognition task of the NEPSY-II is administered only to children between the ages of 3 and 10 years, as this function is considered to mature early (Sowell, Delis, Stiles, & Jernigan, 2001). The procedure is as follows: A story is read to the child. After free recall of the story (repeating the story), the child is asked questions (cued recall) to elicit missing details from their rendition of the story or passage (Korkman et al., 2007a). In the NM Recognition task, the child is asked questions about the story and is then provided with two possible answers. The child has to decide which one of the two responses is the correct answer. Choosing the correct answer indicates that the child recognises the verbal material.

The NM Recognition task was administered to the 3-, 6- and 8-year-old participants in the current study. As mentioned before, the Afrikaans translation of the NM subtest of the

NEPSY-II is discussed under a separate section dealing with the translation and adaptation of measuring instruments.

The NM Recognition Total raw score is calculated by adding up all the correct items in the recognition test. A high score indicates efficient verbal recognition, while a lower score indicates poor verbal recognition.

Decision consistency (percent agreement) provides a measure of reliability. Korkman et al. (2007b) reported high decision consistency (ranging from .94 to .96) for the NM Recognition subtest for a sample of 165 typically developing children (whose ages ranged from 3 to 10 years) in the United States of America. Therefore, the NM Recognition test appears to be a reliable measure of verbal recognition memory. No information on validity is provided for this subtest of the NEPSY-II.

Visual memory. It was already mentioned in the previous section that visual and verbal memory are distinct concepts. It is also suggested in the literature that memory is not only modality-specific (such as visual, auditory or olfactory), but also feature-specific (Slotnick, 2004). In support of this view, empirical evidence suggests that visual content and episodic and spatial memory may involve discrete processes and brain structures (Klauer & Zengmei, 2004; Slotnick, 2004). In the previous section, reference was made to the distinction between immediate (short-term) and long-term memory. The same distinction applies to visual memory. The distinction between short-term and long-term visual memory (similar to long-term verbal memory) lies in the degree of consolidation and quality of storage of the information, which depends on a rehearsal process (Baron, 2004).

The involvement of the medial temporal lobe in visual memory functions and the fact that adults with LiP are reported to have short-term and long-term visual memory deficits (Thornton et al., 2008) provide the primary motivation for suspecting that children and adolescents with LiP may exhibit deficits in this regard, thus necessitating the measurement of this function. The measures used to test immediate and long-term visual memory for detail and location will be discussed next.

Immediate visual content and spatial memory. The NEPSY–II Memory for Design (MD) subtest was used to measure immediate visual memory. This subtest provides a

measure of immediate content and spatial memory among children aged 3 to 16 years (Korkman et al., 2007a). Testees are shown a series of grids with four to ten designs per page for 10 seconds. The stimulus grid is then removed and the testee is required to identify the designs from a set of cards and place them on a grid in the same location as they had appeared on the stimulus grid (Korkman et al., 2007b). Certain age-related starting points and stop rules are recommended, and these rules were applied during the administration of the test.

The MD Total raw score is calculated by adding up the total of the Content, Spatial, and Bonus scores for each trial. The MD Spatial raw score and MD Content raw score are calculated by adding up the total correct items for placement or content. Poor performance in the MD subtest is said to indicate difficulties with visual-spatial memory (Korkman et al., 2007a). A low MD Total score indicates difficulty with rote memorisation of the detail and location of visual stimuli. A low MD Spatial score indicates compromised learning of the location of objects, while a low MD Content score suggests difficulty in learning visual detail (Korkman et al., 2007a).

Korkman et al. (2007b) reported poor to good test-retest reliability coefficients for the MD subtest of the NEPSY-II in a sample of 1200 typically developing 3- to 16-year-olds in the United States of America. Test-retest reliability coefficients ranged from .82 to .92 for the MD Total subtest, from .71 to .90 for the MD Spatial subtest and from .41 to .87 for the MD Content subtest (Korkman et al., 2007a). The relatively lower test-retest reliability coefficients for the MD subtests (compared to other NEPSY-II subtests) were reported being consistent with practice effects (Korkman et al., 2007a).

The intercorrelation (r = .79) of immediate and long-term visual memory scores provides evidence of the validity of the visual memory subtest of the NEPSY-II. The NEPSY-II MD subtest is also reported to have moderate correlations (.46 and .50 respectively) with both Dot Locations (immediate spatial memory) and the Learning composite of the Children's Memory Scale (Korkman et al., 2007a).

Long-term visual content and spatial memory. The NEPSY –II Memory for Design Delayed (MDD) subtest was used to measure long-term visual memory. Storage and retrieval of information from long-term memory depends on the interaction between the pre-frontal and medial temporal lobes (Simons & Spiers, 2003). Executive function (such

as the ability to organise information) is important for storage and retrieval of information and explains why younger children have difficulty in retrieving information from long-term memory (Horton & Nardini, 2008). Therefore, this subtest can be administered only from six years onwards.

The same procedures as described for the NEPSY-II MD subtest is followed. In the long-term recall condition (MDD subtest), the testee is required to recall the designs and their location on the grid following a 15- to 25-minute delay from exposure to the initial stimuli. The stimuli are not shown again, but instead the testee is expected to recall the designs and locations from memory (Korkman et al., 2007b). The various age-related starting points and stop rules were implemented in the manner recommended in the *NEPSY-II Administration Manual* (Korkman et al., 2007b).

The MDD Spatial raw scores and MDD Content raw scores are calculated by adding the total correct items for placement and the total correct items for content. The MDD Total raw score is calculated by adding the total of the Delayed Content, Delayed Spatial, and Bonus scores. Higher scores indicate better long-term memory for detail and/or location, (Korkman et al., 2007a).

Poor to good test-retest reliability was reported for MDD Total (r = .51 to .76), MDD Content (r_{tt} = .60 to .82) and MDD Spatial (r_{rr} = .58 to .74) scores (Korkman et al., 2007a) in a 1000 five- to sixteen-year-old typically developing children in the United States of America.

The correlation between the MDD and Dot Location 2 subtest (r = .36) is reported being small (Korkman et al., 2007a). This specific finding indicates that the MDD subtest of the NEPSY-II and the Dot Location 2 subtest may not measure the same construct (spatial delayed memory). It has to be kept in mind that MDD Total includes both spatial memory and memory for visual content, while Dot Location 2 measures only spatial memory. MDD Total scores correlate highly with Dot Locations (r = .55) and Learning (r = .55) scores of the Children's Memory Scale. Other types of evidence supporting the validity of the MDD subtest as a measure of memory have been reported and have been mentioned in the previous section (high correlations between MD and MDD scores).

Visual-verbal paired associative learning. Thornton et al. (2008) found that individuals with LiP presented with deficits in verbal learning. According to Ashby and O'Brien (2005), learning is a process of establishing or strengthening a new memory trace. The distinction between memory and learning is not clear, and concepts of learning and memory are intertwined (Baron, 2004). In line with this view, (Mayes et al., 2007) suggest that essentially an associative learning process forms declarative memory. Associative learning occurs when new information is acquired via a process of repetitive association (Baron 2004; Korkman et al., 2007a). Visual-verbal associative learning involves associating a verbal label with a picture or face (Korkman et al., 2007a). It is suggested that the hippocampus particularly is involved in establishing declarative, as opposed to conditioned, associations and, therefore, associative learning (Henke, Buck, Weber, & Wieser, 1998; Mayes et al., 2007). Some individuals with LiP have been reported to present with hippocampal lesions that might have explained their memory problems (Ghika-Schmid et al., 1997), although not all individuals presenting with both LiP and memory deficits had hippocampal lesions (Emsley & Paster, 1985). Thornton et al. (2008) established that learning (specifically verbal learning) was worse in a group of adults with LiP compared to controls, thereby highlighting the importance of measuring this construct (learning) when studying the neuropsychological function of individuals with LiP.

The Memory for Names (MN) subtest of the NEPSY-II was used to measure visual-verbal paired associative learning. The test measures the ability to learn by associating faces with verbal labels (Korkman et al., 2007a). Korkman et al. (2007a) indicate that the task was suited for administration to children between the ages of 5 and 16 years and 11 months.

The individual is expected to learn the names of children over three trials. Six to eight cards with a drawing of a face of a child on each are presented to the individual while the name assigned to the child is read aloud. The cards are then presented again and the child is asked to recall the names associated with each card. If the child responds incorrectly, the name he or she was unable to recall is provided (Korkman et al., 2007b). The names used in the NEPSY-II MN subtest were adapted to suit the specific cultural context of the present study, as described under the relevant section dealing with the translation and adaptation of measuring instruments later in the chapter. The scores for each trial are

calculated to obtain the MN Total raw score (maximum = 24). A high score indicates better visual-verbal associative learning.

Good reliability (average $r \geq .80$ across all the age groups) as calculated by Fisher's z transformation is reported for the MN subtest of the NEPSY-II in a sample of 1000 typically developing 5- to 16-year-old American children (Korkman et al., 2007a). Therefore, the NEPSY-II MN subtest appears to be a reliable measure of visual-verbal associative learning.

Only one validity study could be found in which reference is made to the MN subtest (Korkman et al., 2007a). The MN subtest does not correlate significantly with any of the Delis-Kaplan Executive Function System subtests. This indicates that the MN subtest measures a construct different from executive function (discriminant validity).

The second neuropsychological construct (social perception) will be discussed next. Three dimensions (facial emotional recognition, theory of mind and facial recognition) were measured to provide an indication of the participants' performance on social perception.

Social perception. Deficits in recognition of facial emotion have been found in adults, children, and adolescents with LiP (Calder et al., 1996; Thornton et al., 2008; Tranel & Hyman, 1990), while ToM deficits have been suggested in adults with LiP (Adolphs et al., 1998), as well as among adults who acquired amygdala lesions during early childhood (Shaw et al., 2004). These findings provide the motivation for measuring these functions (recognition of facial emotion and ToM) in the current study. Face recognition and memory for faces have been found to be intact in individuals with LiP (Thornton et al., 2008), but because of its essential role in social perception (Haxby, Hoffman, & Gobbini, 2002; Nelson, 2001), a measure of face recognition was included in this study. The social perception constructs and the instruments used to measure them will be discussed next.

Recognition of facial emotion. Literature suggests that adults with LiP frequently present with deficits in recognition of facial emotion (Adolphs et al., 2002; Brand et al., 2007; Thornton et al., 2008). There is some degree of variability in the literature regarding the extent and severity of deficits in the recognition of the facial expression of at least

certain emotions (Adolphs et al, 1999; Terburg et al., 2012; Thornton et al., 2008). Generally, deficits in recognition of facial emotion in LiP are thought to be the consequence of bilateral amygdala calcification (Becker et al., 2012; Tranel & Hyman, 1990). Thornton et al. (2008) reported an age-related deterioration in the ability of individuals with LiP to identify happy facial expressions accurately. However, to date, these findings have not been replicated among children and adolescents with LiP. Consequently, as this study aims to gain insight into the progression of LiP-related neuropsychological deficits across childhood and adolescence, it was necessary to administer a measure of recognition of facial emotion.

Recognition of facial emotion was measured by the NEPSY-II Affect Recognition subtest (AR). This subtest was designed to assess the ability to recognise emotional expressions (happiness, sadness, neutral, fear, anger, disgust) on photographs of children's faces (Korkman et al., 2007a). The subtest can be administered to children from 4 to 16 years and 11 months and comprises four tasks. In the first task, the child simply states whether two photographs show faces with the same affect or not. In the subsequent task, the child selects two photographs of faces with the same affect from three or four photographs. The third task requires him or her to select a face (from four presented faces) depicting the same affect as the stimulus face. Finally, the child is shown a face briefly and then selects, from memory, two out of a possible five photographs of faces that illustrate the same affect as the face shown previously (Korkman et al., 2007b).

The AR Total score comprises the sum of all the correct responses. Error scores (determined by adding the number of wrong answers for every emotion separately) for each emotion were used to identify difficulties in recognising specific facial expressions. The maximum error scores for each age differ with regard to each different facial expression. A high AR Total score indicates more efficient recognition of facial emotion. A high error score indicates poor identification of a specific emotion in facial expressions (sadness, happiness, neutral, disgust, fear or anger).

Alpha coefficients ranging from .64 to .89 (low to high) are reported for the AR Total subtest of the NEPSY-II in a sample of 1200 3- to 16-year-old typically developing children in the United States of America (Korkman et al., 2007a). Alpha coefficients ranging from .67 to .75 (low to fairly high) are reported for the AR Total of 3- to 3-year-

olds in the same sample. However, values expressing decision consistency for the error scores are all above .80 (good to excellent) for the different emotions and across the different age ranges; except for a decision consistency score of .72 (fair) for Sad Errors in the age range of 7 to 8 years and 11 months (Korkman et al., 2007a). Acceptable to excellent decision consistency suggests that the error scores of the NEPSY-II AR subtest are generally reliable measures of recognition deficits with regard to specific facial expressions of emotion.

The AR subtest is reported to have very low correlations (ranging from .15 to .30) with the WISC-IV subtests and composites, suggesting that it measures a skill not related to intellectual functioning (Korkman et al., 2007a). This provides evidence of validity (discriminant validity).

ToM. ToM is defined as the ability to present the full range of mental states (beliefs, desires, intentions, imagination and emotions) to reflect on the contents of the minds of the self and others, and to understand and predict behaviour in terms of these states (Baron-Cohen, 2001b; Happé, Brownell, & Winner, 1999). ToM deficits have been suggested in at least one study of an adult with LiP (Adolphs et al., 1998) and have been associated with amygdala lesions acquired during early childhood (Shaw et al., 2004). However, to date, no research has been conducted to explore ToM among children and adolescents with LiP. Consequently, as this study aimed to gain insight into the neuropsychological and psychosocial functioning of children and adolescents with LiP, it was necessary to administer a measure of ToM.

ToM was measured by the NEPSY-II Theory of Mind (TM) subtest (Korkman et al., 2007a). The NEPSY-II TM subtest comprises a verbal and a contextual task. In the verbal task, the child is shown pictures of scenarios and then asked questions requiring him or her to take another person's perspective in order to answer. The child's comprehension of abstract phrases is also tested. The contextual task involves showing the child a picture of a social situation in which the face of the main figure is not visible. The child is then asked to choose the appropriate emotional expression for the situation from a set of four photographs of faces. The TM subtest can be administered to children and adolescents from 4 to 16 years and 11 months of age (Brooks et al., 2010). The TM subtest was administered according to the instructions in the *NEPSY-II Administration Manual*

(Korkman et al., 2007b), but the items and passages were translated into Afrikaans for the Afrikaans-speaking participants. Names used in this subtest were changed to locally familiar names. The process of translation and adaptation will be discussed later in the chapter. The TM Total raw score comprises the sum of the scores on each item, while the TM Verbal raw score comprises the sum of the scores for the verbal section of the TM subtest. A high TM Total score indicates effective comprehension of others' perspectives and mental states. The TM Verbal score may provide insight into the role of language in the child's performance on the TM measures, as this subsection uses language as opposed to visual stimuli to measure the child's ToM abilities.

Alpha coefficients ranging from .76 to .84 (fairly high to high) for TM Total are reported for the 3- to 6-year-olds in a sample of 1200 typically developing children in the United States of America (Korkman et al., 2007a). Excellent decision consistency coefficients (all above .90) for TM Total are reported for the 7- to 16-year-old children in a sample of 1200 typically developing children in the United States of America (Korkman et al., 2007a). Therefore, the TM subtest of the NEPSY-II is a reliable measure of ToM.

Korkman et al. (2007b) reported evidence of a large test-criterion correlation between the NEPSY-II TM subtest and a diagnosis of Autistic Disorder in a sample of 23 children and matched controls with a clinical diagnosis of Autistic Disorder based on the Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.; *DSM-IV-TR*). The TM subtest of the NEPSY-II accurately classified 70% of children as being autistic. Only 9% of the children in the control group received a low score on the TM subtest (Korkman et al., 2007a). These findings suggest that some evidence exists that the TM subtest of the NEPSY-II is a valid measure of ToM.

Face recognition. Although memory for faces is viewed as a form of non-verbal memory (Korkman et al., 2007a), remembering faces also requires an intact ability to distinguish between and recognise different faces (Wada & Yamamoto, 2001). *Face recognition* involves a holistic, face-specific system that processes faces as undifferentiated wholes (Marotta, Genovese, & Behrmann, 2001). Furthermore, it refers to an individual's ability to distinguish one face from other faces despite wide variations in changes of viewpoint, lighting, emotional expression and other contexts (McKone, Crookes & Kanwisher, 2009).

Research has consistently indicated deficits in face recognition in children with developmental disorders associated with social impairment (Baron-Cohen, 2001b; Castelli, 2005; Jemel, Motron, & Dawson, 2006; Pelphrey, Adolphs, & Morris, 2004). Individuals with face recognition deficits have been found to present with social-emotional difficulties, such as social withdrawal, anxiety and feelings of embarrassment in situations where they are required to recognise people (Duchaine, 2003; Yardley et al., 2008). For these reasons, Korkman et al. (2007a) suggest that the NEPSY-II Memory for Faces (MF) subtest (measuring memory for faces and face recognition) may be included in the social perception domain, along with the NEPSY-II measures of recognition of facial emotion (AR subtest) and ToM (TM subtest).

The ability to recognise faces and facial expressions was suggested to rely on interconnected cognitive processes and brain areas and deficits in face recognition may therefore affect recognition of facial emotion (Calder & Young, 2005; Duchaine & Weidenfeld, 2003; Yardley et al., 2008). For this reason, face recognition measures have been included in research on the neuropsychological functioning of individuals with LiP (Thornton et al., 2008). Generally, intact face recognition has been reported (Siebert et al., 2003; Thornton et al., 2008; Tranel & Hyman, 1990). Up to date, the face recognition of a group of children and adolescents with LiP has not been explored; therefore, a measure of facial recognition was included.

The Memory for Faces (MF) subtest was used to measure face recognition. The subtest is administered to children from 5 to 16 years. Photos of unfamiliar faces are shown to the child, who has to select the faces he was shown previously from a series of photos. Correct responses are added up to derive the total raw score, with a maximum score of 16 (Korkman et al., 2007b). A high score indicates intact face recognition.

Test-retest reliability coefficients of .50 to .78 were reported for the MF subtest of the NEPSY-II in a sample of 1200 typically developing children (5 to 16 years old) in the United States of America (Korkman et al., 2007a). Therefore, test-retest reliability for this test is marginal in some age groups (5- to 8-year-olds and 11- to 12- -year-olds) and acceptable in others (Brooks et al., 2010). Similar to all the other memory tests, the relative lower reliability coefficients were interpreted as reflecting practice effects (Korkman et al., 2007a).

A medium correlation (r_{tt} = .44) between the NEPSY-II MF subtest and the Faces test of the Children's Memory Scale was reported. From perusal of the literature it is assumed that a correlation below .50 does not indicate acceptable validity. However, the NEPSY-II MF correlates highly (r_{tt} = .55) with the MF Total score of the NEPSY, providing evidence of the concurrent validity of the subtest. Thus, the results of validity studies with regard to the validity of the subtest are variable and inconclusive.

The third neuropsychological construct (attention and executive functioning) will now be discussed under two separate headings, namely *Attention* and *Executive Function*.

Attention. Attention is often divided into different dimensions, such as selective attention, sustained attention and supervisory attention or executive attention (Baron, 2004; Kelly, 2000; Mirsky et al., 1991; Stuss, 2006), but it has been suggested that a collaborating attention system underlies the different attention functions (Chica et al., 2012; Mesulam, 1999). Attention processes also overlap with the components of executive function and memory (Barkley, 1996). In Barkley's (1997) theoretical model of ADHD, inattention is viewed as the manifestation of difficulties with sustained attention. Inability to sustain attention was suggested to be the consequence of the breakdown of a complex system maintained by the main function of inhibition.

Thornton (2006) notes a tendency for adults with LiP to present with attention deficit, while one child with LiP was reported to present with ADHD. Individuals with LiP often have bilateral amygdala lesions suggested to affect vigilance, selective attention, and shifting attention negatively (Gallagher & Holland, 1994; Gallagher & Schoenbaum, 1999; Sinclair & Taylor, 2008). The amygdala is involved in modulating attention by directing or shifting attention to emotionally significant stimuli (involuntary attention); therefore, attention can be either enhanced or impaired by the allocation of resources towards emotionally significant stimuli (Pessoa, et al., 2009). For example, the tendency of a highly anxious person to attend to threatening stimuli might distract the person from a task that needs to be finished. Attention is fundamental to almost all cognitive tasks and therefore plays an important role in children's learning and everyday functioning (Gomes et al., 2012; Posner & Rothbart, 2007; Stevens & Bavelier, 2012). As the amygdala, which is often affected by LiP, was suggested to be involved in modulating attention, the CBCL

and C-TRF Attention Problems scales were used to measure inattentive behaviour and impulsivity in the current study.

The CBCL/1.5-5 (completed by parents) and C-TRF (completed by teachers) are rating scales for preschool children's problem behaviour (Achenbach & Rescorla, 2000). The CBCL/6-18 (completed by parents) and TRF (completed by teachers) are similar scales for children and adolescents between the ages of 6 and 18 years (Achenbach & Rescorla, 2001). The Attention Problems scales of these instruments are similar and contain descriptions of a number of inattentive, hyperactive, and impulsive behaviour (Achenbach & Rescorla, 2000; 2001).

The Attention Problems scale of the CBCL/1.5-5 contains five statements of inattentive, hyperactive and impulsive behaviour (Achenbach & Rescorla, 2000), while the C-TRF Attention Problems scale contains nine statements of such behaviour. Caregivers or teachers are required to rate the behaviour described in the items as either *never present* (0), *sometimes present* (1) or *always present* (2). The ratings are added up to obtain a total raw score (range: 0-18). The rating for each statement on the CBCL/1.5-5 Attention Problem scale (0, 1 or 2) is added to obtain a total raw score (range: 0-10), while the ratings on the C-TRF are added up to obtain a total raw score ranging from 0 to 18.

The Attention Problems scale of the CBCL/6-18 contains 11 statements of inattentive, hyperactive and impulsive behaviour (Achenbach & Rescorla, 2000), while the TRF Attention Problems scale contains 26 statements of such behaviour. Teachers and parents rate the intensity or absence of behaviour such as inability to concentrate, not finishing tasks, not following directions, and inattention (Achenbach & Rescorla, 2001). The ratings (0, 1 or 2) for the different statements on the Attention Problems scale of the TRF are added up in a similar fashion as the ratings for the CBCL/1.5-5 and the C-TRF to obtain a total raw score (Achenbach & Rescorla, 2001).

High scores on the Attention Problems scales indicate a high frequency and intensity of inattentive, impulsive, and hyperactive behaviour, while a low score indicates of the absence of these types of behaviour.

All the research participants above the age of six were Afrikaans-speaking; therefore, the Afrikaans version of the CBCL/6-18 was administered. Owing to the lower education

and literacy levels of the rural parents, the questionnaire was administered to four of them as a structured interview in accordance with the procedures specified in the manual (Achenbach & Rescorla, 2001). As there was not an Afrikaans translation of the TRF, the researcher obtained permission from the publishers to translate the instrument and to reproduce it for the Afrikaans-speaking teachers participating in this study. The translation procedures will be discussed under a separate heading.

Acceptable test-retest reliability (Pearson correlations) was reported for the Attention Problems scale of the CBCL/1.5 (r = .78) in a sample of 68 non-referred children in the United States of America (Achenbach & Rescorla, 2000). Good test-retest reliability (r = .84) was reported for the Attention Problems scale of the C-TRF in a sample of 59 non-referred children in the United States of America. Therefore, the Attention Problems scales of the CBCL/1.5-5 and C-TRF appears to be reliable measures of inattentive, hyperactive, and impulsive behaviour.

A Cronbach's alpha coefficient of .86 was reported for the Attention Problems scale of the CBCL/6-18 in samples of 1605 referred and 1605 matched non-referred children in the United States of America (Achenbach & Rescorla, 2001). The reported test-retest reliability coefficients for the Attention Problems scale *(r* = .92) of the CBCL/6-18 are very high. The correlation coefficient between the CBCL Attention Problems Scale and the ADHD Index of the Conners' Parent Rating Scale is reported to be .77 (Achenbach & Rescorla, 2001), indicating fair concurrent validity for the Attention Problems scale of the CBCL/6-18.

A high Cronbach's alpha coefficient (r_{tt} = .95) was reported for the Attention Problems scale of the TRF in a sample of 1543 referred and 1543 non-referred children in the United States of America (Achenbach & Rescorla, 2001). A high correlation (r = .89) between the TRF Attention Problems syndrome scale and the Conners' Teacher Rating Scale ADHD Index was reported, also indicating good concurrent validity of the Attention Problems scale of the TRF (Achenbach & Rescorla, 2001).

Although behavioural ratings should not be assumed to be an alternative for performance on attention measures, significant correlations (ranging from r = .23 to r = .35) between the Attention Problems scales of the school-aged ASEBA instruments (TRF and CBCL/6-18) and multiple measures of attention (Conners' Continuous Performance

Test, NEPSY Auditory Attention) have been reported (Fahey, 2006). These results give some evidence of the validity of the Attention Problem scales of the CBCL/6-18 and TRF.

Executive function. Executive function includes the ability to plan, initiate, and execute behaviour, as well as to inhibit inappropriate or irrelevant responses and behaviour (Baron, 2004; Garavan et al., 2002; Miyake et al., 2000). Executive function includes monitoring or keeping track of stimuli and facilitating flexible shifting of the mind in order to adapt to changing situations (Lezak et al., 2012). Working memory, inhibition and shifting are key executive function concepts and were suggested to be separate but correlated functions (Barkley, 1997; Huizinga et al., 2006; Miyake et al., 2000).

Variable and sometimes contradictory findings have been reported with regard to executive function in LiP (Brand et al., 2007; Tranel & Hyman, 1990; Morgan et al., 2012). Some adults with LiP were reported to perform poorly on selective executive function tasks measuring working memory, design fluency and switching (Thornton, 2008; Tranel & Hyman, 1990) while others obtained scores within the normal limits on similar measures (Siebert et al., 2003; Talmi et al., 2010). In a group of adults with LiP presenting with specific calcification of the basolateral amygdala, paradoxical facilitation of working memory was reported (Morgan et al., 2012). Executive skills play a progressively more important role in the cognitive and social functioning of developing children and adolescents (Anderson et al., 2001). Therefore, measures of executive function (especially inhibition and cognitive flexibility) were included.

Inhibition. Barkley (1997) describes behavioural inhibition (executive function) in detail and identifies three components of behavioural inhibition: inhibition of prepotent or automatic responses, the ability to interrupt ineffective, continuing responses, and the ability to resist distraction from current thoughts, plans, and behaviour. The inhibition of behaviour is an important skill that influences children's ability to adjust socially, learn in a social environment and concentrate on or disengage from a task to respond to different task requirements in different situations (Blair & Diamond, 2008; Mikami, Huang-Pollock, Pfiffner, McBurnett, & Hangai, 2007; Rhoades, Greenberg, & Domitrovich, 2009). The literature suggests the possibility that children and adolescents with LiP may have difficulty with psychosocial adjustment and present with attention deficit and impulsivity

(Steenkamp, 1997; Thornton, 2006). Therefore, it was decided to include measures of inhibition in the current study.

Statue Subtest of the NEPSY-II. The ST subtest of the NEPSY-II was used to measure behavioural inhibition and motor persistence in the 4- and 6-year-old LiP and control participants. The child is instructed to maintain a certain body position while ignoring the examiner's sound distractions (Brooks et al., 2010; Korkman et al., 2007b). Body movement, eye opening or vocalisation in response to distractions is considered errors. The raw error score for each of the three types of errors is determined by adding up the frequency for each error type (Korkman et al., 2007b). Separate error scores (ST Body Movement Total, ST Eye Opening Total and ST Vocalisation Total) as well as an ST Total raw score (maximum = 30) can be computed. The ST Total raw score is derived by adding the frequencies for each type of error score. The ST Total raw score is then transformed to a scaled score according to the norm table. A higher Statue Total score indicates that the child is able to inhibit responses well, while a high error score indicates that the child is unable to inhibit automatic responses well.

Test-retest reliability coefficients ranging from .82 to .88 (high) for the Statue Total score were reported in a sample of 300 typically developing North American children between the ages of 4 and 6 years (Korkman et al., 2007a). Decision consistency scores above 0.89 (high) for all error scores (ST Body Movement, ST Eye Opening and ST Vocalisation) across the 3- to 7-year-old age range were also reported in a sample of 165 typically developing North American children (Korkman et al., 2007a). Therefore, the ST subtest seems to be a reliable measure of behavioural inhibition.

The large corrected correlation (r = .70) between the ST score of the NEPSY-II and ST score on the NEPSY provides evidence that the NEPSY-II ST subtest measures a construct (behavioural inhibition) similar to what the original NEPSY ST subtest measures and therefore implies that the ST subtest appears to be a valid measure of behavioural inhibition.

Inhibition Subtest of the NEPSY-II. The Inhibition (IN) subtest of the NEPSY-II was used to measure inhibition in children from the age of 7 to 17 years. As a whole, the IN subtest is a visual task and involves three different conditions, each measuring a different component (Korkman et al., 2007b). The three components measured by the IN subtest

include processing speed (IN Naming), inhibition (IN Inhibition), and cognitive flexibility (IN Switching). The naming component of the task involves rapid and sequential naming of black and white shapes or the direction of arrows (Brooks et al., 2010; Korkman et al, 2007b). The inhibition component (INI) of the task involves giving an alternate response (saying the opposite) depending on the direction or colour (black or white) of the shape or arrow depicted (Korkman et al., 2007b). A maximum time of 360 seconds is allowed to complete each of the naming and inhibition components.

As inhibitory control is not fully matured in young children, this function is generally considered difficult to assess validly in individuals younger than six years of age (Davidson, Amso, Anderson, & Diamond, 2006). Korkman et al. (2007a) did not include this test in the NEPSY-II for children under the age of five years. Therefore, the subtest was administered only to the 6-, 8-, 15- and 17-year-old participants in the current study.

The raw error scores (maximum = 80) for each of the naming and inhibition conditions is determined by adding up all the corrected errors and uncorrected errors for that particular condition (Korkman et al., 2007b). High INN Total scores indicate slow processing speed. Although processing speed is not one of the constructs directly measured in this study, the INN Total score is essential for the interpretation of the INI Total Errors score. Slow processing speed may affect the individual's performance on the inhibition component (INI) of the measure negatively (Korkman et al., 2007a). Therefore, if both the INN Total Errors score and the INI Total Errors score are high, this might indicate slow processing speed rather than difficulty with inhibition. When the INI Total Errors score is high and the INN Total Errors score is average or low, it is assumed that processing speed did not affect on the individuals' performance in the inhibition component of the test negatively. Therefore, disinhibition is more likely when the INI Total score is high and the INN Total Errors score is low or average.

Decision consistency of classification was reported for 165 typically developing North American children from the age of 3 to 16 years (Korkman et al., 2007a). Decision consistency scores for INN Total Errors are reported to be between .72 and .90 (fairly high to very high) while coefficients from .83 to .96 were reported for the INI Total Errors scale. Overall, the reliability of the INN and INI components of the Inhibition subtest of

the NEPSY-II seems to be moderate to good; therefore, these scales may be viewed as reliable measures of processing speed and inhibition.

Korkman et al. (2007a) reported that the NEPSY-II IN Total Errors score shows a large correlation (r = .54) with the Total Errors score of the Color-Word Interference Test on the Delis-Kaplan Executive Function System. This provides some evidence of the concurrent validity of the NEPSY-II IN Inhibition subtest.

Cognitive flexibility. Cognitive flexibility requires an individual to be able to shift flexibly from one mindset to another (Davidson et al., 2006). The IN Switching (INS) and Animal Sorting subtests of the NEPSY-II (Korkman et al., 2007a) were used to measure cognitive flexibility in the 8- to 17-year-old age group.

Inhibition Subtest of the NEPSY-II. The IN subtest of the NEPSY-II is discussed in detail in the previous section; therefore, only details regarding the IN Switching (INS) condition of the task will be described here.

The switching component of the IN subtest of the NEPSY-II was used to measure cognitive flexibility in the current study and can be administered to children from 7 to 16 years old. As mentioned in the previous section, the whole IN subtest is a visual task and involves three different components, namely speed, inhibition, and cognitive flexibility (Korkman et al., 2007b). The child is required to look at a series of shapes (squares and circles) or arrows pointing up or down. The switching (INS) component of the Inhibition subtest of the NEPSY-II involves naming either the correct shape or arrow direction if the object is white, or naming the opposite shape or direction if the shape or arrow is black.

Because young children have difficulty with switching, Korkman et al. (2007a) did not include the switching component of the test for children younger than seven. Therefore, the subtest was administered only to the 8-, 15- and 17-year-old participants in the current study.

The raw INS Total Errors score (maximum = 80) for the switching condition is determined by adding up the corrected and uncorrected error scores of the INS subtest (Korkman et al., 2007b). A high INS Total Errors score indicates difficulty with inhibition and switching.

Decision consistency coefficients from .72 to .90 for the INS Total Errors scale were reported for 165 typically developing North American children from the age of 3 to 16 years (Korkman et al., 2007a). The results on the INS Total Errors subtest can be viewed as a reliable reflection of cognitive flexibility.

Korkman et al. (2007a) report that the NEPSY-II IN scores (including the INS Total Errors score) show consistent medium to large relationships (r = .43-.57) with the Color Word Interference Test scores of Delis-Kaplan Executive Function System. Therefore, variable results are reported with regard to validity studies of the INS Total Errors component of the NEPSY-II. Evidence of the concurrent validity of the IN subtest – therefore, also the inhibition (INI) and switching components (INS) of the subtest – as a measure of cognitive flexibility is not conclusive.

Animal Sorting Subtest of the NEPSY-II. The Animal Sorting (AS) subtest is a card-sorting task designed to evaluate concept formation, initiation, and cognitive flexibility (Korkman et al., 2007a; Brooks et al., 2010). The child is required to sort cards into two groups of four cards by generating different categories for sorting (Korkman et al., 2007a). Because young children have difficulty with concept formation and cognitive flexibility, Korkman et al. (2007a) determined that the test should be administered only to children above the age of six years. Consequently, the subtest was administered only to the 8-, 15- and 17-year-old participants in the current study.

The AS Total Errors raw score is determined by adding up the number of incorrect sorts separately. A high AS Total Errors score indicates poor cognitive flexibility and concept formation.

High decision consistency of classification scores (.89 to .96) were reported for the AS Total Errors score of the NEPSY-II in a sample of 165 typically developing children in the United States of America (Korkman et al., 2007a). Therefore, the AS Total Errors score can be viewed as a reliable measure of cognitive flexibility, initiation, and concept formation.

Korkman et al. (2007a) do not report evidence of construct validity for the AS subtest, but medium correlations between the AS subtest of the NEPSY-II and the WISC-IV Similarities subtest (r = .41) and between the AS subtest and the WISC-IV Matrix

Reasoning subtest (r = .49) are evident. These WISC-IV subtests measure verbal and visual abstract reasoning respectively. The AS subtest of the NEPSY-II intended to measure not only abstract thinking, but also initiation and switching. Therefore, the reported correlation coefficients suggest that the AS subtest is not a valid test of abstract reasoning alone. This shows that the concepts measured by the AS subtest and the WISC-IV measures (tests of verbal and visual abstract reasoning) are related only moderately.

The measuring instruments that were used to measure the different dimensions of the psychosocial functioning of the participants will be discussed next.

Instruments Measuring Psychosocial Functioning

According to the literature discussed in the previous chapter of the thesis, the psychosocial development of children and adolescents with LiP may be affected negatively by their condition. Deficits in social perception, executive function, and emotional memory associated with LiP may lead to poor social adjustment (Fuster, 2002). Symptoms and signs of LiP, such as hoarseness and disfiguring skin lesions, may cause further difficulties with psychosocial adjustment (Steenkamp, 1997). LiP is also associated with certain psychiatric problems such as mood disorders and psychosis (Thornton et al., 2008). To explore the psychosocial functioning of children and adolescents with LiP, it was necessary to obtain information about the participants' current adaptive functioning and emotional or social difficulties. It was decided to use instruments that provide an understanding of a wide range of adaptive and maladaptive behaviour, as very little is known about the psychosocial functioning of children and adolescents with LiP (Thornton et al., 2008). It was also important that the instruments had to cover a wide age range. Consequently, to obtain data with regard to psychosocial adjustment and adaptive functioning, relevant scales of the ASEBA forms (CBCL/1.5-5, CBCL/6-18, C-TRF, and TRF) and subdomains of the Vineland-II were used (Achenbach & Rescorla, 2001).

The psychosocial functioning constructs (adaptive and maladaptive behaviour), dimensions, and subscales relevant to the different age groups are reported in Table 4.5.

Table 4.5

Psychosocial Constructs, Dimensions and Subscales Relevant to the Age Groups

Psychosocial functioning								
Construct	**Dimension/test**	**Subscale**	**Age**				
			4	**6**	**8**	**15**	**17**
Adaptive behaviour	Vineland II Adaptive Behavior	Interpersonal Relationships	*	*	*	*	*
		Play and Leisure Time	*	*	*	*	*
		Coping Skills	*	*	*	*	*
	Teacher Report Form	Adaptive functioning			*	*	
Maladaptive behaviour	CBCL 1.5-5/6-18 Syndrome scales	Total Problems	*	*	*	*	*
		Internalising Problems	*	*	*	*	*
		Externalising Problems	*	*	*	*	*
		Social Problems			*	*	*
	C-TRF Syndrome scales	Total Problems	*	*	*	*	
		Internalising Problems	*	*	*	*	
		Externalising Problems	*	*	*	*	
		Social Problems			*	*	

* The subtest can be administered in the relevant age group

Table 4.5 indicates which test or subtest could be administered or used in each age group. The C-TRF does not have a scale that measures social problems; therefore, social problems were not measured in the 4- and 6-year-old age groups. Although the TRF scale can be administered to the parents of 17-year-olds, the 17-year-old LiP participant who participated in this study did not attend school; therefore, it was not used in this age group. Next, the instruments used to measure adaptive and maladaptive behaviour will be discussed under two separate headings.

Adaptive behaviour. Adaptive behaviour is viewed as a broad and multi-dimensional concept that includes the ability to apply intelligence to everyday settings and situations in order to be personally and socially competent (Sparrow, Balla, & Cicchetti, 2005).

Bierman and Welsh (2000, pp. 536-537) conceptualise *social competence* as a construct that reflects the child's capacity to integrate behavioural, cognitive, and affective skills to adapt flexibly to diverse social contexts and demands. Deficits in social-emotional processing affect social competence; therefore, by implication, adaptive behaviour (Leppännen & Hietanen, 2001). Because the amygdala is viewed as a key brain structure with regard to the processing of emotionally and socially significant information, this structure plays an important role in social behaviour (Adolphs, 2004, 2009; Buchanan, Tranel, & Adolphs, 2009). Socially inappropriate behaviour has been described in individuals with LiP and amygdala damage (Kennedy, Glascher, Tyszka, & Adolphs, 2009; Tranel & Hyman, 1990). For this reason, it is important to evaluate the adaptive behaviour of children and adolescents with LiP.

Vineland-II socialisation domain. The Vineland-II Socialisation domain consists of three subdomains, namely Interpersonal Relationships, Play and Leisure Time, and Coping Skills (Sparrow et al., 2005). The Interpersonal Skills subdomain comprises items referring to skills such as initiation of conversations, co-operating with others, having friends, and belonging to clubs and other groups. Items in the Play and Leisure Time subdomain refer to skills such as pretend play, playing games, having hobbies, engaging in group activities and going places independently. Coping skills (in the Coping Skills subdomain) include skills such as exhibiting table manners, controlling emotions, apologising, borrowing, and returning, and keeping appointments (Sparrow et al., 2005).

Parents rated their children's developmental skills for every item (0, 1, or 2) in each section of the Vineland-II Adaptive Behaviour checklist. A "2" indicates that the individual usually performs the behaviour without help or reminders, while a "1" indicates that the individual sometimes performs the behaviour or performs behaviour with help or reminders. A "0" indicates that the individual never or very seldom performs the behaviour or never performs it without help or reminders. The *NEPSY-II Administration Manual* (Korkman et al., 2007b) prescribes using different starting points for children of different ages; therefore, the guardians in the current study were instructed to complete the Vineland-II survey forms from a starting point recommended for their child's specific age group.

English-speaking urban parents were capable of completing the standardised English version of the instrument independently. The possibility of the interference of a language barrier when administering the Vineland-II Adaptive Behaviour Scales to the rural Afrikaans-speaking parents (three LiP and six control participants) was considered. Permission could not be obtained to translate the Vineland-II formally into Afrikaans. However, the publishers consented to an informal Afrikaans translation of the instrument (by the researcher), presented as a structured interview by a bilingual (English/Afrikaans) research assistant (a registered educational psychologist). Parents were given an English Parent/Caregiver Rating Form booklet, whereafter the items were read to them in Afrikaans. The parents then recorded their responses on an English Parent/Caregiver Rating Form. The translation and adaptation of the Vineland-II and other instruments is discussed in more detail under a separate heading later in the chapter.

The scale was scored according to the instructions in the manual (Sparrow et al., 2005). Raw scores on the Interpersonal Relationships (range = 0-62), Play and Leisure Time (range = 0-62) and Coping Skills (range = 0-60) subdomains are calculated by adding the scores within each subdomain. The raw scores for these subdomains are converted to v-scale scores (Sparrow et al., 2005). A higher score is interpreted as indicating better social skills, play and leisure skills, and coping skills, while a lower score is interpreted as indicating poorer social skills, play and leisure skills, and coping skills.

Good to excellent split-half reliability (coefficients ranging from .86 to .95) was reported for the Socialisation subdomain of the Vineland-II in a sample of 2290 typically developing children, adolescents and young adults from birth to 21 years of age in the United States of America. Fair to good Split-half reliability coefficients were reported for the Interpersonal Relationships (.81 to .87), Play and Leisure Time (.73 to .83) and Coping Skills (.80 to .88) domains in the same sample. The Vineland-II Adaptive Behaviour Scale, particularly the Socialisation subdomain of this scale, appears to be a reliable measure of adaptive behaviour.

Several lines of evidence supporting the validity of the Vineland-II, specifically the Vineland-II Socialisation domain, are reported in the Survey Forms Manual (Sparrow et al., 2005), but the information is too much to repeat here. The adjusted correlations between the Social Composite Domain of ABAS-II and the Socialisation subdomains of

the Vineland-II are .59 for the 0- to 5-year-olds and .72 for the 5- to 20-year-olds. These correlation coefficients can be described as moderately high and high respectively (Sparrow et al., 2005). Therefore, the Vineland-II and ABAS-II Socialisation domains seem to measure similar constructs (social adaptation), especially in the 5- to 20-year-old age group. This is just one example of a validity study on the Vineland-II, but overall, there are several lines of evidence supporting the validity of the Socialisation domain of the Vineland-II (Sparrow et al., 2005).

TRF Adaptive Functioning Scale. The TRF Adaptive Functioning Scale can be used to obtain ratings of competencies as they manifest in the school situation (Achenbach & Rescorla, 2001). Neuropsychological deficits such as memory and executive dysfunction have been shown to affect scholastic achievement and adjustment negatively (Fasteneau et al., 2004; Schouten, Oostrom, Pestman, Peters, & Jennekens-Schinkel, 2002; Willoughby, Kupersmidt, & Voegler-Lee, 2012). Children and adolescents with LiP are very likely to have such difficulties (Emsley & Paster, 1985; Savage et al., 1988; Thornton et al., 2008). Consequently, the current state of the scholastic adjustment of the children and adolescents with LiP is an area of interest that warrants exploration in the current study. Therefore, the competence scales of the TRF were used to assess adaptive functioning in the school setting. Only two of the LiP research participants (8- and 15-year-olds) were attending school at the time the data were collected. Consequently, ratings on the adaptive functioning scale of the TRF were obtained only for these two participants and their controls. The fact that the TRF form was translated into Afrikaans was mentioned before, and the translation process is discussed in detail in the section dealing with the translation and adaptation of the measures that were used in the study.

The manual for the CBCL/6-18 (Achenbach & Rescorla, 2001) stipulates that teachers have to rate academic progress by allocating a level of performance (1 = *far below grade*; 2 = *somewhat below grade*; 3 = *at grade level*; 4 = *somewhat above grade level*; and 5 = *far above grade*) to each of the specific learning areas in which the child participates. Adaptive characteristics (working hard, behaving appropriately, learning, and happiness) are rated similarly (1 = *much less*; 2 = *somewhat less*; 3 = *slightly less*; 4 = *about average*; 5 = *slightly more*; 6 = *somewhat more*; and 7 = *much more*). The average of the ratings on the Academic Performance scale and the scores for each of the adaptive items (working hard, behaving appropriately, learning and happiness) form the total raw score (range: 4 to

28) for the TRF Adaptive Functioning scale (Achenbach & Rescorla, 2001). A high score on the TRF Adaptive Functioning Scale is interpreted as an indication of good adjustment, while a low score is interpreted as an indication of poor adjustment in the school situation.

A Cronbach's alpha coefficient of .90 (very high) was reported for the Adaptive Functioning scale of the TRF in a sample of 1543 referred and 1543 non-referred children in the United States of America (Achenbach & Rescorla, 2001). A test-retest reliability coefficient of .93 (very high) was reported for the TRF Adaptive Functioning scale of the TRF in the same sample (Achenbach & Rescorla, 2001). Overall, the Problem scales of the Adaptive Functioning scale of the TRF seem to be reliable measures of adaptive behaviour.

No studies on the construct validity of the TRF Adaptive Functioning scale have been reported, but Achenbach and Rescorla (2001) indicate that the probability that a score was from a referred sample decreased when the TRF Academic and Adaptive scores increased. This indicates that ratings of children's adaptive behaviour on the TRF (in the sample used by Achenbach and Rescorla – 2001) distinguished between children who adapted well and those who did not.

Maladaptive behaviour. Behaviour problems refer to maladaptive forms of behaviour consisting of behaviour that can be challenging for others or that can compromise the internal stability or adjustment of the individual (Achenbach & Rescorla, 2001). Externalising behaviour problems, such as oppositional, aggressive, and antisocial behaviour, manifest in children's outward behaviour and indicate that the child is reacting negatively to the external environment (Campbell, Shaw, & Gilliom, 2000). Internalising behaviour problems, such as withdrawn, anxious, inhibited, and depressed behaviours, affect the child's internal psychological environment rather than the external world (Campbell et al., 2000).

Behaviour problems in children and adolescents with LiP have been suggested (Steenkamp, 1997) and may be related to brain structure and function, psychosocial factors or other unknown factors. Steenkamp (1997) notes internalising behaviour problems (such as depression), externalising behaviour problems (temper outbursts), and social problems (such as being teased by peers) among children with LiP. Steenkamp (1997) is of the opinion that these problems are strongly related to the disfiguring skin lesions and

hoarseness associated with LiP. Psychiatric disorders, such as anxiety and depression, linked to temporal lobe pathology were reported in adults with LiP and were suggested to be evident among children and adolescents with this condition, too (Steenkamp, 1997; Thornton, 2006). Behaviour problems may be unrelated to psychiatric disorders but can also be a primary or secondary manifestation of such disorders (Xeniditis, et al., 2001). Therefore, it was necessary to include an instrument evaluating behaviour problems in the current study. The ASEBA forms (CBCL/1.5-5, C-TRF, CBCL/6-18, and TRF) were used to measure internalising behaviour problems, externalising behaviour problems, social problems, and severity of behaviour problems in general.

CBCL/1.5-5. The CBCL/1.5-5 is a 100-item parent-rated questionnaire yielding a scale reflecting the overall severity of the child's problems (Total Problems), an Internalising Problems scale, Externalising Problems scale and six empirical scales (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Sleep Problems, Attention Problems and Aggressive Behaviour), as well as a scale reflecting problem behaviour not included in the other empirical scales (Other Problems). Parents rate the child's behaviour along a scale with responses ranging from *never present* (0), *sometimes present* (1) or *always present* (2).

In the current study, the CBCL 1.5-5 was administered to the parents of 4- and 6-year-old research participants (n = 6) even though the instrument was designed for children between the ages of one-and-a-half to five years. This was done because these children were still attending preschool at the time when data were gathered. The questions on the CBCL/1.5-5 are more appropriate to the preschool environment compared to those of the CBCL/6-18, where reference is made to school performance and behaviour in the school setting. As the parents of the 4 and 6-year-old children with LiP and control children were English speaking and had a high level of education (Grade 12 and higher), they completed the instruments independently (Achenbach & Rescorla, 2000).

Hand-scoring profiles were used for scoring the CBCL/1.5-5 questionnaires. The totality of the child's behaviour problems is reflected by the sum of the scores (range: 0-200) on all the empirical scales (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Sleep Problems, Attention Problems and Aggressive Behaviour scales), plus the score on the Other Problems scale (Achenbach & Rescorla, 2000). The

score on the Internalising scale (range: 0-72) consists of the sum of raw scores on the Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn scales. The total score on the Externalising scales of the CBCL/1.5-5 (range: 0-48) is calculated by adding up raw scores on the Attention Problems and Aggressive Behaviour scales. Higher scores on the scales of the CBCL/1.5-5 (Total Problems, Internalising Problems and Externalising Problems) indicate internalising or externalising problems that are more severe.

Good to excellent test-retest reliability was reported for the scales of the CBCL/1.5 (r_{tt} scores above .80) in a sample of 68 non-referred children in the United States of America (Achenbach & Rescorla, 2000). The reported test-retest reliability coefficient for the Total Problems scale (r_{tt} = .90) of the CBCL/1.5 is excellent (Achenbach & Rescorla, 2000; Cichetti, 1994). Across all scales of the CBCL/1.5-5, the mean correlation (Fisher's *z* transformation) indicates good reliability (r = .85). Overall, the empirical scales of the CBCL/1.5-5 seem to be reliable measures of maladaptive behaviour.

The construct validity of the problem scales (Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Attention Problems and Aggressive Behaviour scales) of the CBCL/2-3 (the instrument preceding the CBCL/1.5-5) is supported by concurrent and predictive associations with a variety of instruments, such as the Infant-Toddler Social and Emotional Assessment (Briggs-Gowan & Carter, 1998). According to Achenbach and Rescorla (2000), all the items on the CBCL/2-3 and CBCL/1.5-5, except for two, are the same; therefore, the authors concluded that concurrent validity of the CBCL/1-5 would be very similar to that of the CBCL/2-3. Thus, evidence from the mentioned validity studies suggests that the CBCL/1.5-5 is a valid measure of behaviour problems in children.

C-TRF. The C-TRF is equivalent to the CBCL/1.5 but completed by teachers. It yields the same scales as the CBCL/1.5 (Total Problems, Internalising Problems scale, Externalising Problems scale). It is completed in a manner similar to the completion of the CBCL/1.5. Teachers and other staff members who had known a child for at least two months completed the C-TRF.

The C-TRF is scored similarly to the CBCL/1.5. The totality of the child's behaviour problems is reflected by the sum of the scores (range: 0-166) on all the empirical scales

(Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Attention Problems and Aggressive Behaviour scales) plus the scores on the Other Problems scale (Achenbach & Rescorla, 2000). The total score (range: 0-64) on the Internalising scales of the C-TRF consists of the sum of raw scores on the Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn scales for each instrument. The total score (range: 0-68) on the Externalising scales of the C-TRF- is calculated by adding raw scores on the Attention Problems and Aggressive Behavior scales. Scores on the scales of the C-TRF are interpreted in the same way as scores on the CBCL/1.5-5 are interpreted.

Achenbach and Rescorla (2000) reported good test-retest reliability for the Total Problems scale of the C-TRF (r = .88) in a sample of 59 non-referred children in the USA. In addition, the mean correlation across all the C-TRF scales (Fisher's z transformation) is reported to be .81. Thus, apparently, the empirical scales of the C-TRF provide a reliable measure of maladaptive behaviour. No studies in which the validity of the C-TRF had been investigated could be found.

CBCL/6-18. The CBCL/6-18 is a 113-item, parent-rated measure (similar to the CBCL/1.5-5) of behaviour problems in 6- to 18-year-old children and adolescents (Achenbach & Rescorla, 2000). The questionnaire yields a scale reflecting the overall severity of the child's problems (Total Problems), an Internalising Problems scale, Externalising Problems scale and empirical scales (Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-breaking Behaviour and Aggressive Behaviour), as well as a scale reflecting problem behaviour not included in the empirical scales (Other Problems). In the current study, the CBCL/6-18 (Achenbach & Rescorla, 2001) was administered to the parents and guardians of 6- to 18-year-old participants.

As all the rural participants were Afrikaans-speaking, the Afrikaans version of the CBCL/6-18 was used. The lower education level of the rural parents was taken into consideration by verbally presenting the items to parents with an education level below Grade 5 or to those who expressed a need for assistance in completing the forms (four parents in total). An Afrikaans version of the CBCL/6-18 form was given to these parents, and the research assistant then recorded their responses on an exact copy of the Afrikaans

CBCL/6-18 form. The remaining six participants did not find it difficult to complete the forms (having at least completed Grade 5). The reliability of the results could have been affected by differences in administration, but Achenbach and Rescorla (2001) reported excellent inter-interviewer reliability coefficients obtained by interviewer-rated CBCL/6-18 forms (.96) in the specific sample they had used.

The CBCL/6-18 behaviour checklist is scored similarly to the CBCL/1.5 and C-TRF scales. The score (range: 0-200) on the Total Problems scale of the CBCL/6-18 consist of the sum of raw scores on all the empirical scales (Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints scales, Rule-breaking Behaviour, Aggressive Behaviour, Social Problems, Thought Problems) and the Other Problems scale (Achenbach & Rescorla, 2001). The score on the Internalising Problems scale of the CBCL/6-18 (range = 0-64) consists of the sum of raw scores on the Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints scales (Achenbach & Rescorla, 2001). The total score (range: 0-70) on the Externalising Problems scale of the CBCL/6-18 is calculated by adding up the raw scores on the Rule-breaking Behaviour and Aggressive Behaviour scales. The Social Problems scale of the CBCL/6-18 consists of 11 statements requiring parents to rate the presence and intensity of social behaviour problems such as overly dependent behaviour, complaints of loneliness, not getting along with other children, not being liked by other children and being teased (Achenbach & Rescorla, 2001). Raw scores on the Social Problems scale of the CBCL/6-18 range from 0 to 22. Higher scores on the Total Problems, Internalising Problems, and Externalising Problems scales indicate total, internalising, externalising or social problems that are more severe.

Cronbach's alpha coefficients above .80 (good to excellent) were reported for the empirical scales of the CBCL/6-18 in samples of 1605 referred and 1605 matched non-referred children in the United States of America (Achenbach & Rescorla, 2001). The reported Cronbach's alpha coefficients for the Total Problems scale, as well as the test-retest reliability (r_{tt} = .94), are excellent (Achenbach & Rescorla, 2001; Cichetti, 1994). Overall, the empirical scales of the CBCL/6-18 seem to be a reliable measure of general maladaptive behaviour, internalising problems, externalising problems and social problems.

TRF. The TRF is an equivalent to the CBCL/6-18 but completed by teachers. The questionnaire yields the same scales as the CBCL/6-18: Total Problems scale, Internalising Problems scale, Externalising Problems scale and empirical scales (Anxious/Depressed, Withdrawn/Depressed, Rule-breaking Behaviour, Somatic Problems, Social Problems, Thought Problems, Attention Problems, Aggressive Behaviour), as well as a scale reflecting problem behaviour not included in the empirical scales (Other Problems). Rating is done in a similar fashion as with the CBCL/6-18.

No Afrikaans version of the TRF was available. As all the participants above the age of seven years attended an Afrikaans-medium school, a translation of the instrument was required. The researcher obtained permission from the publishers to translate and reproduce the instrument. The translation procedures are discussed under a separate heading (4.4.4).

Scoring is done via hand-scoring profiles. The Total Problems score (range: 0-226) reflects the totality of the child's scores on all the empirical scales plus the Other Problems scale (Achenbach & Rescorla, 2001). The total raw score (range: 0-66) on the Internalising scale of the TRF consists of the sum of raw scores on the Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints scales (Achenbach & Rescorla, 2001). The total score (range: 0-64) of the Externalising Problems scale of the TRF is calculated by adding up the raw scores on the Rule-breaking Behaviour and Aggressive Behaviour scales. The Social Problems subscale of the TRF is similar to the CBCL/6-18 and consists of 11 statements requiring teachers to rate the presence and intensity of social behaviour problems (Achenbach & Rescorla, 2001). Raw scores on the Social Problems scale of the TRF range from 0-22. Higher scores on the mentioned scales of the TRF (Total Problems, Externalising Problems, Internalising Problems and Social Problems) are interpreted in the same way as higher scores on the CBCL/6-18.

Good to excellent reliability (Cronbach's alpha coefficients above .8) was reported for the empirical scales of the TRF in a sample of 1543 referred and 1543 non-referred children in the United States of America (Achenbach & Rescorla, 2001). The reported Cronbach's alpha coefficient for the Total Problems scale of TRF (r_{tt} = .94 to .97), as well as the test-retest reliability coefficient for the Total Problems scale of the TRF (r_{tt} = .95), is very high (Achenbach & Rescorla, 2001; Cichetti, 1994). Overall, the TRF seems to be a

reliable measure of overall behaviour problems, internalising behaviour problems, externalising behaviour problems and social problems.

In terms of reliability and validity of the ASEBA instruments within and across different cultural groups, Achenbach et al. (2008) concluded that comparable results on the ASEBA instruments are found in many populations. Scaled scores vary more within than between populations, and distributions of scores overlap greatly among different populations (Achenbach & Rescorla, 2007). Overall, the ASEBA instruments seem to test a similar construct (maladaptive behaviour) as the Behaviour Assessment System for Children. The ASEBA instruments also seem to test the same construct across different cultural groups; therefore, they may be viewed as valid measures of behaviour problems.

Three of the LiP participants were Afrikaans speaking; therefore, before any of the measuring instruments could be administered, it was important to attend to the translation and adaptation of the instruments. This will be discussed next.

Translation and Adaptation of Measuring Instruments

The following measures were translated and adapted:

- NEPSY-II: Narrative Memory and Theory of Mind subtests (Korkman et al., 2007b)
- Vineland-II Behavior Scales (Sparrow et al., 2005)
- Teacher Report Form of the ASEBA instrument (Achenbach & Rescorla, 2001)

Principles of good practice recommended by Wild and colleagues (2005) were followed in the translation and cultural adaptation of the measures. The steps of the translation process included preparation, forward translation, reconciliation, back translation, back translation review, cognitive debriefing, review of cognitive debriefing results, finalisation, proofreading and final result. These steps will now be discussed in more detail.

Preparation. During this step, permission was obtained from the publisher (Appendix D) to translate the TRF into Afrikaans according to the stipulations of the publisher, but it was impossible to obtain a license from Pearson Assessment to translate

the NEPSY-II and the Vineland-II instruments. The publisher of the latter two instruments provided guidelines to translate these instruments into Afrikaans informally (Kina Thomas, Pearson Assessment, personal communication, 18 August 2008). The publishers indicated that items might be translated into Afrikaans and verbally administered as long as the answer sheets were not altered or reproduced in any way and the responses were recorded on the original booklet. The translated versions of the instruments could not be included as appendices, as the publishers of the TRF, NEPSY-II and Vineland-II stipulated that they might not be reproduced or published.

Forward translation. It was required that the forward translation be done by a native speaker or professional translator (Wild et al., 2005); therefore, a bilingual (English/Afrikaans) language expert translated the Vineland-II into Afrikaans.

To translate the NEPSY-II instructions and items, an understanding of the administration and rationale of the instrument and each subtest was necessary. Therefore, the researcher, who is bilingual (Afrikaans and English) and has a good understanding of the administration of the NEPSY-II, translated the NEPSY-II subtests into Afrikaans.

As the TRF is very similar to the previous version (TRF/5-18) of the instrument that was translated into Afrikaans, the researcher, who is familiar with the CBCL/6-18 and the TRF/5-18, was responsible for translating this instrument. Most items in the TRF/5-18 were retained in the new version (TRF), with small changes in the wording of items 51, 54, 56f, 75, 83 and 105. After the changed English items had been compared to the corresponding Afrikaans items (TRF/5-18), it was decided to retain the original Afrikaans wording. However, the three new items (items 5, 28, and 99), which had replaced rarely endorsed items in the previous version of the instrument, were translated.

Back translation and review. Three qualified and bilingual (English/Afrikaans) psychologists performed back translations of the instruments. The back translations were compared to the originals to highlight discrepancies between the original and the translated versions. Differences between the originals and the back translations were reconciled by deciding which terms/formulations were consistently viewed to be similar to the original.

Cognitive debriefing and review. The new translations of the instruments were administered to Afrikaans-speaking respondents determine if the translation was

understandable and culturally relevant, and if it was interpreted correctly by the respondents. The new Afrikaans translation of the TRF was administered to six teachers in the rural areas from where the 8-, 15- and 17-year-old participants were drawn. Following their input, terms such as “special class”, “special education”, “remedial teacher” and “pupils” were substituted with terms used locally, such as "learners" and “special needs education”.

With regard to the names used in the NEPSY-II Verbal Memory, Memory for Names and TM subtests, children that did not participate in the study were recruited from the rural and urban areas to determine which names were familiar to children from the different environments. Ten children (two children of ages similar to each of the 4-, 6-, 8-, 15- and 17-year-old LiP participants) were recruited by word of mouth from the same municipal clinics (rural) and schools (urban) as the control participants and asked for the names of their friends. The names were written down and those repeatedly mentioned or similar to the original names in the NEPSY-II were used to substitute the relevant names in the Memory for Names subtest (an example is Anna instead of Ann). After consultation with the Afrikaans-speaking children and adolescents (8-, 15- and 17-year-olds) in the same sample described above and the parents of the children recruited, expressions used in the ToM subtest were changed to locally familiar Afrikaans expressions (e.g. "hulle is soos vinkel en koljander" rather than "they are like two peas in a pod"). Children and adolescents and their parents were asked if they understood the expressions used in the Afrikaans translation. Most of these children, adolescents, and parents were able to explain the meaning of these expressions.

Some of the items of the Vineland-II were changed to make the instrument relevant to South African children/adolescents. Changes were made with regard to monetary values (such as "rand" instead of "dollar"), distances ("kilometres" instead of "miles") and examples of games played by children. With regard to the games children played in the different communities, ten children in the urban and rural areas were recruited (the same children and adolescents mentioned in the discussion of the adaptation of the names and expressions in the NEPSY-II). They were asked what sport, board games, and card games they often played. Their answers were used to adapt the relevant items.

Proofreading. The last step in the translation and adaptation process was to proofread the final translation of the instruments. The qualified translator, who was responsible for the original forward translation of the Vineland-II, proofread the final translations of all the instruments and commented on spelling mistakes, typing errors and Afrikaans grammar. These comments were then used to improve the accuracy and presentation of the translation.

Ethical Considerations. The current study is an extension of a wider, interdisciplinary research project on LiP approved by the Committee for Human Research (Health Research Ethics Committee 1 and 2) at Stellenbosch University (Faculty of Health Sciences). The ethical approval granted to the wider research project (project number 2002/C103) was extended to include approval for the current study. Furthermore, the Research Committee in the Department of Psychology at the University of the Free State, as well as by the Committee for Title Registration at the same institution approved a research proposal outlining the current study.

Written informed consent was obtained from the legal guardians of all the children and adolescents involved in the initial screening and all the children and adolescents involved in the study. Consent was obtained in the guardian's language of preference (English or Afrikaans) once he or she had read an information sheet written in his or her home language detailing the objectives and procedures of the wider research project (see Appendix A). To obtain information about the children from their respective schools, parents were asked to sign a release form (Appendix B). Guardians of the participants were informed that their children would incur no risks by participating in the screening or research and that no costs would be involved. Neither the guardians nor their children would be disadvantaged should they decline to consent or exercise their right to withdraw from the study at any stage. Guardians who signed consent forms gave permission to either partake in structured interviews or complete a form regarding their children's developmental histories, their psychiatric status, health, and psychosocial functioning. They also consented to their children completing a number of neuropsychological measures. In the context of the wider research project, guardians of children and adolescents with LiP were requested to consent to an EEG and a number of neuroimaging procedures. Controls were not included in the part of the wider study requiring

neuroimaging and EEGs; consequently, it was not necessary to obtain consent for these procedures from the guardians of the controls.

All the guardians who were approached for screening consented to the participation of their children in the study. None of these individuals withdrew from the study. All the children and adolescents recruited or screened gave their consent to participate in the study. Given the small sample size and the geographical proximity of some of the LiP participants to one another, it was not possible to provide the participants with a guarantee of anonymity. However, all information was treated in the strictest confidence, and particular care was taken to protect the identities of the individuals involved in the study when interviewing other participants or dealing with members of the wider community. Participants were informed that the research was being conducted for study purposes and that the findings might be published in professional journals or presented at conferences. In addition, it was clearly communicated that taking part in the research would not benefit the participants directly, but that the findings from the study could increase the knowledge base regarding LiP and thus be of future benefit to individuals with LiP and their families.

Guardians and children were not compensated for their participation in the study, but their transport costs were covered. Food and refreshments were also provided during the testing and interviews. Guardians of participants (as well as the guardians of children who were screened) were informed of their rights with regard to access to their children's test results. All guardians of children chose to receive feedback. This information was provided verbally or in writing, depending on the specific guardian's preference. Participants were also referred to appropriate professional services (such as speech therapy and occupational therapy) where necessary.

Data Analysis

The first goal of the study was to compare the neuropsychological and psychosocial functioning of children and adolescents with LiP to that of typically developing children. The LiP group represented the entire known population of individuals with this illness in South Africa. The matched control group (described earlier in this chapter) consisted of two controls for every LiP child/adolescent and thus added up to 10 children and adolescents. The demographic characteristics of the LiP participants (especially the rural participants) differed substantially from the U.S. standardisation samples on which the

normative data for the different measures were based (Achenbach & Rescorla, 2000, 2001; Korkman et al., 2007a; Sparrow et al., 2005). Therefore, it was decided to compare the test results of each LiP child and the controls matched to them to mean scores reported for samples with similar demographics as the standardisation sample (Korkman et al., 2007a). These control groups (samples), reflected the demographics of the United States of America and consisted of typically developing children from ages 3 to 16 or 3 to 17 years old, depending on the different measures (Korkman et al., 2007a). The published norm groups were employed to determine whether the LiP group had been biased or disadvantaged during the assessment and therefore represented additional control groups (additional to the two controls matched to each LiP child or adolescent). A comparison between the performance of the LiP participants and that of the published norm group on each specific measure was employed as an additional means of ensuring the validity of the findings. This was necessary because the language and geographic environment – urban (4- and 6-year-old) and rural (8-, 15- and 17-year-old) – LiP participants differed.

However, matching each LiP child and adolescent to two controls would contextualise cultural and socioeconomic differences between the LiP and norm group. To summarise, the scores of the LiP children and adolescents obtained on measures of neuropsychological and psychosocial functioning were compared to the mean scores of the matched controls and to the mean scores reported for the samples on which the instruments were normed.

When raw mean scores for a certain test or subtest were not available, LiP and control group raw scores had to be transformed into scaled scores or standard scores to be able to compare the groups. Therefore, while raw scores were used in data analysis for most of the tests, the following NEPSY-II subtest raw scores were converted to scaled scores: MD and MDD Total, MD and MDD Content, MD and MDD Spatial, Memory for Names, Sentence Repetition, AR Total, ST Total, INN Combined, INI Combined, INS Combined and Animal Sorting Combined. Scaled score or raw means for the norm group were obtained from the results reported for reliability studies in the respective test manuals for the NEPSY-II, Vineland-II and CBCL instruments (Achenbach & Rescorla, 2000; 2001; Korkman et al., 2007a; Sparrow et al., 2005). Scores for the 17-year-old research participants were converted by using the NEPSY-II data reported for 16-year-olds, as the upper age limit of the test is 16 years and 11 months.

In the case of a complete population (as is the case with the LiP participants), testing of the statistical hypothesis is not relevant, and effect sizes can be used to determine the significance of differences between mean scores (Steyn, 2000). Therefore, in this study, the significance of differences between mean scores was determined by calculating effect sizes, using the following formula:

$$|\mu_1 - \mu_2| / \sigma = d$$

Where:

μ_1 = score of the LiP participant

μ_2 = mean score of the two control participants/norm group

σ = pooled (estimated) standard deviation

The population mean score (μ_1) of the LiP participant was compared to the mean scores of the control group and the mean scores of the norm group. Effect size d_1 (LiP compared to control group) and effect size d_2 (LiP compared to norm group) were calculated. The standard deviation of the norm group was used to calculate d for each of the control and sample groups, as the size of the control group was too small to determine a standard deviation for this group. The two effect sizes (d_1 and d_2) were interpreted by using Cohen's (1988, 1992) criteria: very small ($d < 0.1$), small ($d = 0.2$), medium ($d = 0.5$), large (≥ 0.8), and very large ($d > 1.0$).

Serlin and Lapsley (1985) suggest that, where effect sizes are employed to compare mean scores, the null and alternative hypotheses for each research question should be represented as follows:

$H_0 : |\mu_1 - \mu_2| / \sigma < 0.8$, as opposed to

$H_1: |\mu_1 - \mu_2| / \sigma \geq 0.8$

In the current study, the null hypothesis was rejected only where *both* d_1 and d_2 were equal to or above 0.8.

Conclusion

In this chapter, the aims, hypotheses, methods, participants, measures and data analysis were described. Non-experimental research was completed by way of a cross-sectional cohort design based on age. Five LiP participants who represented the entire known population of children and adolescents with LiP in South Africa, were included in the study. Two controls were matched to each LiP participant according to IQ, home language, right- or left-handedness, sex, race and type of environment.

An outline of the constructs and measuring instruments followed. The WPPSI-III, WASI, NEPSY-II, Vineland-II, CBCL and C-TRF forms were used to measure constructs related to the neuropsychological and psychosocial functioning of children with LiP. Formal translation of the CBCL and C-TRF forms into Afrikaans was described, and the adaptation or verbal translation of the NEPSY-II and Vineland-II items into Afrikaans was discussed.

A description of the data analysis indicates that, in order to reach the goals of the study, effect size was used to determine meaningful differences between the mean scores obtained by the LiP and control participants, as well as differences between the scores of the LiP participants and norm groups. The results of the study are reported in the next chapter.

Chapter 5

Results

In this chapter, the results of the research are reported. The primary aim of the study was to determine whether the mean neuropsychological and psychosocial functioning scores of children and adolescents with LiP were significantly different (higher or lower) compared to those in the control group as well as the average person in the age-related norm group (the groups that the tests were normed on). It is important to note that raw mean scores were compared when they were also available for the norm group. In some cases, only standardised mean scores (T-scores) were available for the norm group, and in those cases, the LiP and control participants' raw mean scores were transformed into T-scores before comparisons were made. It should be kept in mind that the null hypothesis was rejected only when both d_1 and d_2 were equal to or above 0.8. Only in these cases, the results are discussed in detail.

A secondary aim of the study was to explore whether any developmental or age-related trends were apparent in the performance of the LiP participants on neuropsychological and psychosocial measures across age and to what extent such developmental age-related trends may differ between the LiP participants and typically developing children and adolescents (matched controls and norm groups). To determine the aforementioned trends, it was necessary to compare the scores of individuals across various age groups. Given that the reported mean scores and standard deviations for the measuring instruments vary across age, it was not possible to compare raw mean scores on the various measures across age. Consequently, scores of the LiP participants, their matched controls and the norm groups were transformed into standardised scores (McCall T-scores) with an average of 50 and a standard deviation of 10. The developmental or age-related trends will be represented graphically. Significant differences between the scores of LiP participants and their matched controls and significant differences between LiP participants and the norm group will be reported. General trends among the LiP and control participants apparent in the graphs will also be highlighted. At the end of the chapter, the results will be summarised, forming the basis of the discussion in the next chapter. The results of the neuropsychological assessment will be discussed next, followed by a discussion of the results of the psychosocial assessment.

Neuropsychological Functioning

Memory and Learning

The performance of the LiP participants (aged between 4 and 17) was compared to that of the matched controls and the norm group to determine if they performed significantly different on these measures compared to the typically developing children and adolescents. The following NEPSY-II subtests were used to measure the different memory and learning constructs: Verbal recognition memory was measured by means of Narrative Memory Recognition (NM Recognition). Immediate memory for structured verbal information was measured by means of Narrative Memory Free Recall and Narrative Memory Free and Cued Recall (NM Fc Recall). Short-term visual memory for content and location was measured by means of Memory for Designs Content (MD Content), Memory for Designs Spatial (MD Spatial) and Memory for Designs Total (MD Total). Memory for Designs Delayed Content (MDD Delayed Content), Memory for Designs Delayed Spatial (MDD Delayed Spatial) and Memory for Designs Delayed Total (MDD Total) were used to measure long-term visual memory for content and location. Memory for Names (MN) was used to measure visual-verbal associative learning.

Raw mean scores and scaled mean scores ($\overline{X}$ = 10; *sd* = 3) were used to compare the performance of the LiP child with his or her controls and the average person in the norm group. The scores mentioned (scaled scores and raw scores) were converted into McCall T-scores, thus allowing them to be compared graphically.

Next, the differences in the mean scores of the 4-year old LiP participant (compared to those of the control and norm groups) on the learning and memory measures and subtests will be reported and displayed graphically.

Four-year-old LiP participant. The score of the 4-year-old LiP participant, the mean scores of the two matched controls and the norm group, the standard deviations and effect sizes on the measures of memory and learning are reported in Table 5.1.

Table 5.1

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 4-year-old LiP Participant, Matched Controls and Norm Group on Measures of Memory and Learning

Memory and Learning Measures	LP Score (μ) (n = 1)	Control Mean ($\overline{X}$) (n = 2)	Norm Group $\overline{X}$	Norm Group *sd*	d_1	d_2
Verbal Memory						
NM Recognition	6.0	11.5	9.3	2.2	**2.5***	**1.5***
NM Free and Cued#	8.0	15.5	10.5	3.7	2.0	0.7
Visual Memory						
MD Content#	8.0	11.5	10.3	2.1	**1.7***	**1.1***
MD Spatial#	8.0	14.0	11.2	2.8	**2.1***	**1.1***
MD Total#	8.0	14.0	10.2	2.9	**2.1***	**0.8***

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; NM Recognition = Narrative Memory Recognition; NM Free and Cued = Narrative Memory Free and Cued Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total.

In Table 5.1, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the mean scores (d_2) of the age-related norm sample (from here on referred to as the ARN group) with regard to the NM Recognition score ($d_1 = 2.5$; $d_2 = 1.5$), MD Content score ($d_1 = 1.7$; $d_2 = 1.1$), the MD Spatial score ($d_1 = 2.1$; $d_2 = 1.1$) and the MD Total score ($d_1 = 2.1$; $d_2 = 0.8$). Thus, the 4-year-old LiP participant performed significantly worse (significant lower μ) than the matched controls (d_1) and norm group (d_2) did in tasks that tap the ability to accurately remember the content and position (spatial relationship) of novel visual stimuli and to recognise organised verbal information. Consequently, the H_0 with regard to MD Content, MD Position, MD Total, and NM Recognition scores can be rejected.

Figure 5.1 graphically compares the McCall T scores of the LiP participant (LP) on measures of memory and learning to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.1.

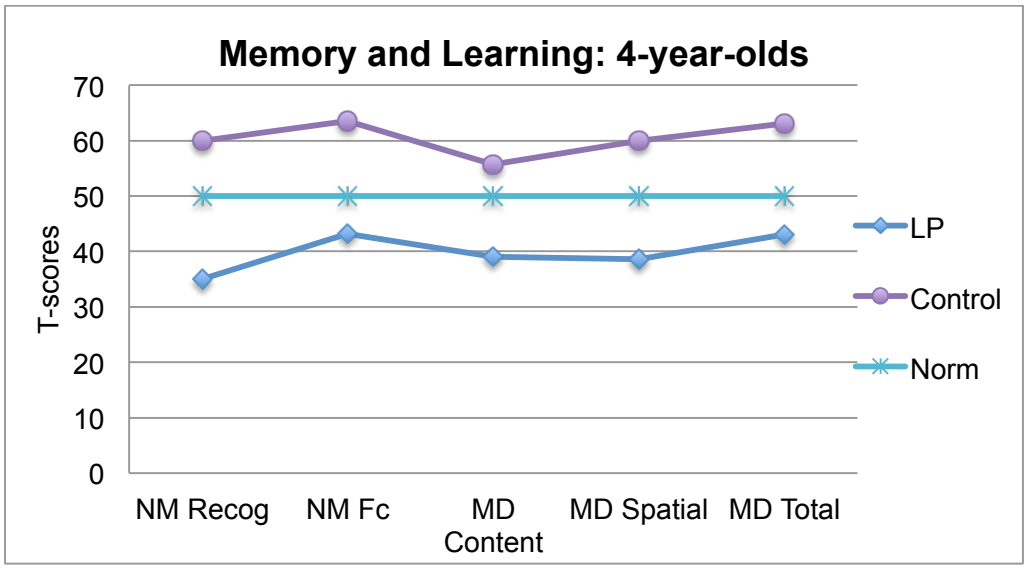

Figure 5.1. Memory and learning profiles of the 4-year-old participants.

It is evident In Figure 5.1 that the LiP individual's score is significantly below the mean score of the matched controls on all measures of memory and learning. In addition, the mean scores of the matched controls on all measures of memory and learning are higher than the corresponding mean scores of the ARN group.

Next, the differences in the mean scores of the 6-year old LiP participant (compared to those of the control and ARN groups) on the learning and memory measures/subtests will be reported and displayed graphically.

Six-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 6-year-old LiP participant, the matched controls and the ARN group on the measures of memory and learning are reported in Table 5.2.

Table 5.2

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 6-year-old LiP Participant, Matched Controls and Norm Group on Measures of Memory and Learning

Memory and Learning Measures			**Norm Group**		***d*1**	***d*2**
	LP score (*μ*) (*n* = 1)	**Control Mean ($\overline{X}$) (*n* = 2)**	$\overline{X}$	***sd***		
Verbal Memory						
NM Recognition	13.0	15.5	13.4	2.1	1.2	0.2
NM Free and Cued#	10.0	12.0	9.9	3.0	0.7	0.0
NM Free#	9.0	11.5	9.9	2.9	0.9	0.3
Visual Memory						
MD Content#	10.0	13.0	9.8	2.7	1.1	0.1
MD Spatial#	8.0	13.0	10.3	2.8	**1.8***	**0.8***
MD Total#	10.0	12.5	9.9	2.8	0.9	0.0
MDD Content#	10.0	11.5	10.6	3.0	0.5	0.2
MDD Spatial#	6.0	12.0	10.4	2.8	**2.1***	**1.6***
MDD Total#	8.0	12.0	10.2	2.9	**1.4***	**1.6***

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; NM Recognition = Narrative Memory Recognition; NM Free and Cued = Narrative Memory Free and Cued Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total; MDD Content = Memory for Design Delayed Content; MDD Spat = Memory for Design Delayed Spatial; MDD Total = Memory for Design Delayed Total.

In Table 5.2, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean score (d_2) with regard to the MD Spatial score ($d_1 = 1.8$; $d_2 = 0.8$), MDD Spatial score ($d_1 = 2.1$; $d_2 = 1.6$) and the MDD Total score ($d_1 = 1.4$; $d_2 = 1.6$). The 6-year-old LiP participant performed significantly worse (significant lower μ) than the other two groups did in tasks that tap the ability to accurately remember the position (spatial relationship) of novel visual stimuli both immediately and after a delay. The 6-year-old LiP participant also scored significantly

lower on MDD Total, a measure combining scores for spatial and content memory. Consequently, the H_0 with regard to three visual memory scales, namely MD Spatial, MDD Spatial, and MDD Total, can be rejected.

Figure 5.2 graphically compares the McCall T scores of the LiP participant (LP) on measures of memory and learning to that of the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.2.

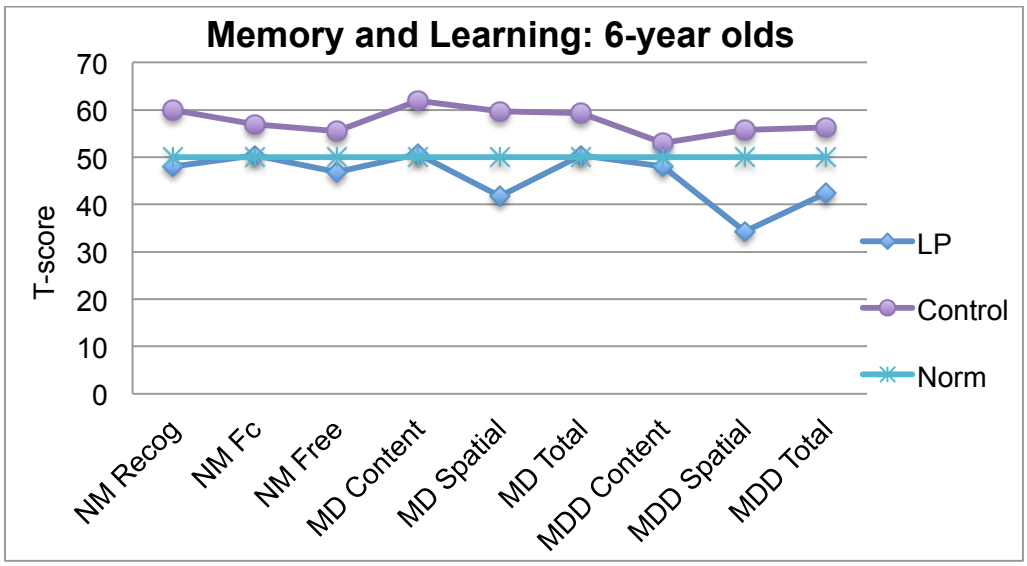

Figure 5.2. Memory and learning profiles of the 6-year-old participants.

In Figure 5.2, it is evident that the LiP individual performed worse than the matched controls did on all measures of memory and learning, although the differences for NM Free and Cued Recall and MDD Content are not significant. In addition, the mean scores of the matched controls are higher than the corresponding mean scores of the ARN group on all measures of memory and learning.

Next, the differences in the mean scores of the 8-year-old LiP participant (compared to those of the control and ARN groups) on the learning and memory measures/subtests will be reported and displayed graphically.

Eight-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 8-year-old LiP participant, the controls and the ARN group on the measures of memory and learning are reported in Table 5.3.

Table 5.3

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 8-year-old LiP Participant, Matched Controls and Norm Group on Measures of Memory and Learning

Memory and Learning Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**		d_1	d_2
			$\overline{X}$	*sd*		
Verbal Memory						
NM Recognition	12.0	14.0	14.5	1.5	**1.3***	**1.7***
NM Free and Cued#	5.0	5.5	9.8	3.2	0.2	1.5
NM Free#	6.0	5.5	9.9	3.2	0.2	1.2
Visual Memory						
MD Content#	10.0	11.0	10.1	3.2	0.3	0.0
MD Spatial#	11.0	12.5	11.1	3.0	0.5	0.2
MD Total#	11.0	11.0	10.3	3.4	0.0	0.2
MDD Content#	11.0	11.5	9.8	3.1	0.2	0.4
MDD Spatial#	14.0	11.0	10.7	2.7	**1.1***	**1.2***
MDD Total#	13.0	10.5	9.9	2.9	**0.9***	**1.1***

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; underlined = LiP score is significantly higher than both control and norm group mean scores**;** NM Recognition = Narrative Memory Recognition; NM Free and Cued = Narrative Memory Free and Cued Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total; MDD Content = Memory for Design Delayed Content; MDD Spat = Memory for Design Delayed Spatial; MDD Total = Memory for Design Delayed Total.

In Table 5.3, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to the NM Recognition score ($d_1 = 1.3$; $d_2 = 1.7$), the MDD Spatial score ($d_1 = 1.1$; $d_2 = 1.2$) and the

MDD Total score (d_1 = 0.9; d_2 = 1.1). The LiP participant obtained a score that is significantly below the control group average and norm group mean on a task that taps the accurate recognition of organised verbal information. However, the 8-year-old LiP participant obtained a score that is significantly above the mean of the controls and the ARN group mean on tasks that tap the ability to remember the position (spatial relationship) of novel visual stimuli accurately after a delay. The LiP participant also obtained a significantly higher score than the control mean and ARN group mean on a scale measuring both long-term visual-spatial memory and long-term visual memory for detail. Consequently, the H_0 with regard to NM Recognition, MDD Spatial, and MDD Total can be rejected.

Figure 5.3 graphically compares the McCall T-scores of the LiP participant (LP) on the measures of memory and learning to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.3.

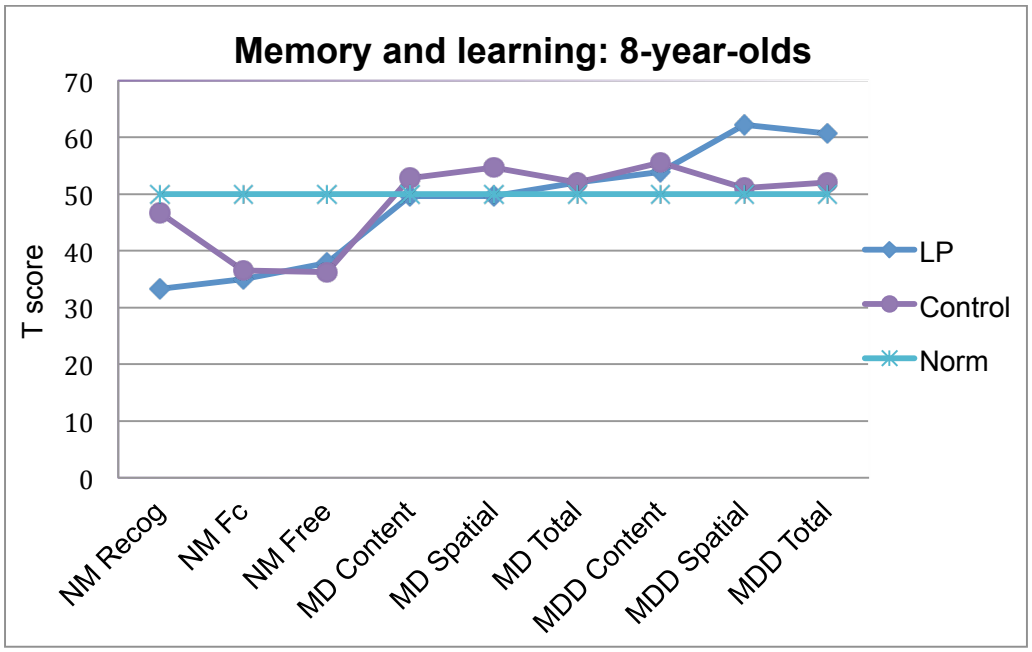

Figure 5.3. Memory and learning profiles of the 8-year-old participants.

In Figure 5.3, it is evident that the LiP participant's scores on a measure of recognition of organised verbal material and memory for spatial detail are lower than the control mean and the ARN mean, although the difference is not significant on the MD Spatial subtest. It

is also evident that the LiP individual performed significantly better than the matched controls and the ARN group did on a measure of long-term recall of location (MDD Spatial) and a combined measure of long-term memory for both visual detail and location (MDD Total). In addition, it is interesting to note that the two control participants, similar to the LiP participant, scored lower than the ARN group mean on two measures of short-term free recall of verbal information (NM Fc Recall and NM Free Recall).

Next, the differences in the mean scores of the 15-year-old LiP participant (compared to those of the control and norm groups) on the learning and memory measures/subtests will be reported and displayed graphically.

Fifteen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 15-year-old LiP participant, the matched controls and the ARN group on the measures of memory and learning utilised in the study are reported in Table 5.4.

Table 5.4

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 15-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Memory and Learning

Memory and Learning Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	**Norm Group** *sd*	d_1	d_2
Verbal Memory						
NM Free and Cued#	7.0	7.5	10.2	3.4	0.1	0.9
NM Free#	8.0	8.0	10.0	3.9	0.0	0.5
Visual Memory						
MD Content#	3.0	6.5	9.5	3.0	**1.2***	**2.2***
MD Spatial#	8.0	5.5	10.3	3.0	**0.8***	**0.8***
MD Total#	5.0	5.0	10.1	3.0	0.0	1.7
MDD Content#	4.0	9.5	10.8	3.0	**1.8***	**2.3***
MDD Spatial#	6.0	5.0	10.3	2.4	0.4	1.8
MDD Total#	5.0	6.5	10.1	2.8	0.5	1.8
Visual-verbal Associative Learning						
MN Total#	8.0	9.5	10.0	2.6	0.6	0.8

Note: # Data are presented as scaled scores (range 0-20, $\overline{X}$ = 10, *sd* = 3); * Both d_1 and $d_2 \geq 0.8$**;** NM Free and Cued = Narrative Memory and Cued Recall; NM Free = Narrative Memory Free Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total; MDD Content = Memory for Design Delayed Content; MDD Spat = Memory for Design Delayed Spatial; MDD Total = Memory for Design Delayed Total; MN Total = Memory for Names Total.

In Table 5.4, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group mean score (d_2) with regard to MD Content (d_1 = 1.2; d_2 = 2.2), MD Spatial (d_1 = 0.8; d_2 = 0.8) and the MDD Content (d_1 = 1.8; d_2 = 2.3). The 15-year-old LiP participant performed significantly worse (significant lower μ) than the other two groups did on tasks that tap the ability to accurately remember the detail of novel visual stimuli and the ability to recall the position of visual detail after a

delay. The LiP participant performed significantly better (significant higher μ) than the matched controls did in a task that measures the immediate recall of the location of visual information. Consequently, the H_0 with regard to MD Content, MD Spatial, and MDD Content can be rejected.

Figure 5.4 graphically compares the McCall T-scores of the LiP participant (LP) on measures of memory and learning to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.4.

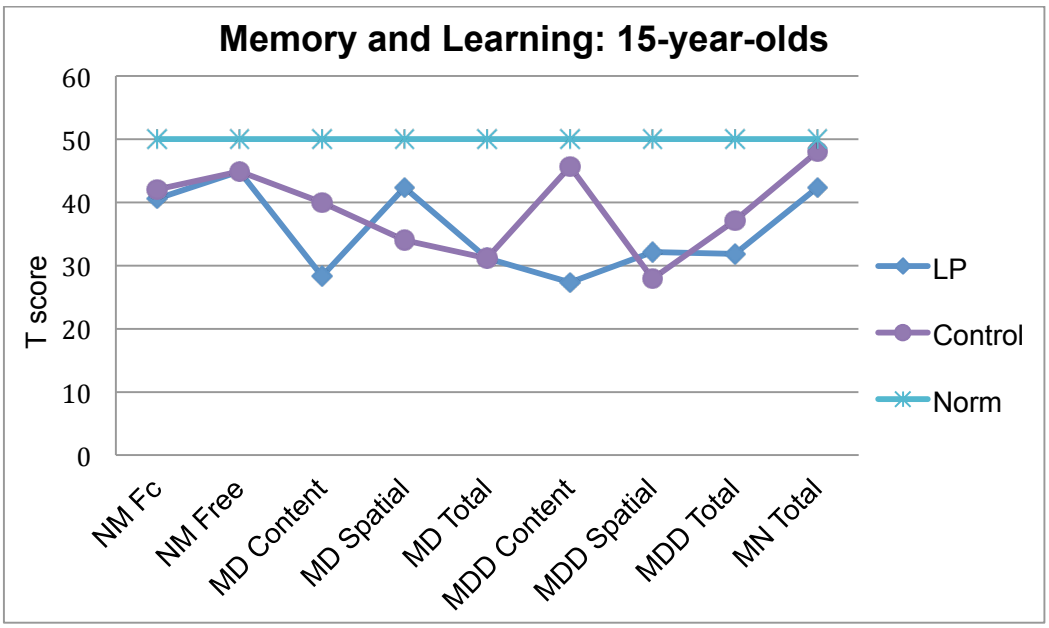

Figure 5.4. Memory and learning profiles of the 15-year-old participants.

In Figure 5.4, it is evident that the LiP individual performed worse than the matched controls did on measures of immediate recall of visual detail (MD Content), delayed recall of visual detail (MDD Content), a combined measure of delayed recall of detail and position and a measure of visual-verbal associative learning. The LiP participant's scores on tasks measuring spatial memory (MD Spatial) and delayed spatial memory (MDD Spatial) are higher than the mean scores of the matched controls, although the difference is not significant on the MDD Spatial subtest. It is noticeable that the mean scores of the two controls are clearly below the mean scores of the ARN group on all memory and learning tests, although the score on MN Total appears to be close to the mean of the ARN group.

Next, the differences in the mean scores of the 17-year-old LiP participant (compared to those of the control and norm group) on the learning and memory measures/subtests will be reported and displayed graphically.

Seventeen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 17-year-old LiP participant, the two controls and the ARN group on the measures of memory and learning utilised in the study are reported in Table 5.5.

Table 5.5

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 17-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Memory and Learning

Memory and Learning Measures	**LP Score (μ) (n = 1)**	**Control ($\overline{X}$) (n = 2)**	**Norm Group Mean $\overline{X}$**	***sd***	***d*$_1$**	***d*$_2$**
Verbal Memory						
NM Free and Cued#	5.0	8.0	10.2	3.4	**0.9***	**1.5***
NM Free#	5.0	8.5	10.0	3.9	**0.9***	**1.3***
Visual Memory						
MD Content#	10.0	8.5	9.5	3.0	0.5	0.2
MD Spatial#	9.0	8.0	10.3	3.0	0.3	0.4
MD Total#	11.0	9.0	10.1	3.0	0.7	0.3
MDD Content#	12.0	8.5	10.8	3.0	1.2	0.4
MDD Spatial#	11.0	5.0	10.3	2.4	2.5	0.3
MDD Total#	13.0	8.0	10.1	2.8	**1.8***	**1.0***
Visual-verbal Associative Learning						
MN Total#	10.0	8.5	10.0	2.6	0.6	0.0

Note: #Data are presented as scaled scores (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; NM Free and Cued = Narrative Memory and Cued Recall; NM Free = Narrative Memory Free Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total; MDD Content = Memory for Design Delayed Content; MDD Spat = Memory for Design Delayed Spatial; MDD Total = Memory for Design Delayed Total; MN Total = Memory for Names Total.

In Table 5.5, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to the NM Free Cued score ($d_1 = 0.9$; $d_2 = 1.5$), NM Free Recall score ($d_1 = 0.9$; $d_2 = 1.3$) and MDD Total score ($d_1 = 1.8$; $d_2 = 1.0$). The 17-year-old LiP participant's scores are significantly worse (significant lower μ) than the control mean and ARN group mean on tasks that tap the ability to accurately recall the content of organised verbal information (a story) freely and when provided with cues. However, the LiP participant obtained a score that is significantly better (significant higher μ) than the mean scores of the controls and the ARN group on a task that taps the ability to accurately recall detail and position of visual stimuli after a delay (MDD Total). Consequently, the H_0 with regard to NM Fc Recall, NM Free Recall, and MDD Total can be rejected.

Figure 5.5 graphically compares the McCall T-score of the LiP participant (LP) on measures of memory and learning to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) on which the instruments were normed are also depicted in Figure 5.5.

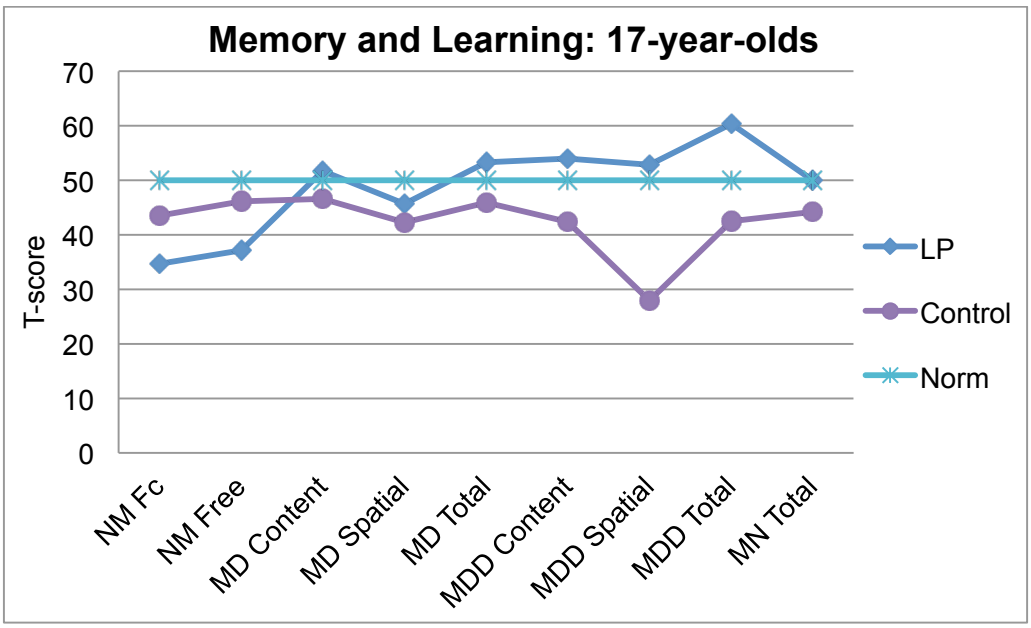

Figure 5.5. Memory and learning profiles of the 17-year-old participants.

The LiP participant's scores are higher than the average scores of the matched controls on all tests of visual memory, although the differences are significant only on tasks measuring delayed memory for position (MDD Spatial), delayed memory for detail (MDD Content), and a combined measure of delayed memory for detail and position (MDD Total). In Figure 5.5, it is evident that the LiP individual performed much lower than the matched controls did on NM Fc and NM Free Recall. It is noticeable that the mean scores of the two controls on several of the memory and learning measures (NM Fc, MD Spatial, MDD Content, MDD Spatial, MDD Total, MN Total) are below the ARN group mean, although some are close to the ARN group mean (NM Free, MD Content and MD Total).

Summary of memory and learning profiles. Table 5.6 provides a summary of the effect sizes (d_1 and d_2) of every memory and learning construct for the 4- to 17-year-old participants to identify patterns in the findings. Effect sizes are marked with an asterisk when both d_1 and $d_2 \geq 0.8$ (significant differences between the LiP participant's score and the mean scores of the control group and the ARN group). Effect sizes (d_1 and d_2) are marked with an asterisk and underlined when the LiP participant performed significantly better than the controls and the similarly aged average person in the ARN group did.

Table 5.6

Effect Sizes (d_1; d_2) of the 4-, 6-, 8-, 15- and 17-year-olds on Measures of Memory and Learning

Memory and Learning Measures	4-year-olds		6-year-olds		8-year-olds		15-year-olds		17-year-olds	
	d_1	d_2	d_1	d_2	d_1	d_2	d_1	d_2	d_1	d_2
Verbal Memory										
NM Recognition	**2.5***	**1.5***	1.2	0.2	**1.3***	**1.7***				
NM Free and Cued (Nm Fc Recall)	2.0	0.7	0.7	0.0	0.2	1.5	0.1	0.9	**0.9***	**1.5***
NM Free Recall			0.9	0.3	0.2	1.2	0.0	0.5	**0.9***	**1.3***
Visual memory										
MD Content	**1.7***	**1.1***	1.1	0.1	0.3	0.0	**1.2***	**2.2***	0.5	0.2
MD Spatial	**2.1***	**1.1***	**1.8***	**0.8***	0.5	0.2	**0.8***	**0.8***	0.3	0.4
MD Total	**2.1***	**0.8***	0.9	0.0	0.0	0.2	0.0	1.7	0.7	0.3
MDD Content			0.5	0.2	0.2	0.4	**1.8***	**2.3***	1.2	0.4
MDD Spatial			**2.1***	**1.6***	**1.1***	**1.2***	0.4	1.8	2.5	0.3
MDD Total			**1.4***	**1.6***	**0.9***	**1.1***	0.5	1.8	**1.8***	**1.0***
Visual-verbal associative learning										
MN Total							0.6	0.8	0.6	0.0

Note: * Both d_1 and $d_2 \geq 0.8$; NM Recognition = Narrative Memory Recognition; NM Free and Cued = Narrative Memory Free and Cued Recall; NM Free = Narrative Memory Free Recall; MD Content = Memory for Designs Content; MD Spatial = Memory for Designs Spatial; MD Total = Memory for Designs Total; MDD Content = Memory for Designs Delayed Content; MDD Spatial = Memory for Designs Delayed Spatial; MDD Total = Memory for Designs Delayed Total.

In Table 5.6, it is evident that significant differences ($d \geq 0.8$) exist between LiP participants' scores on memory and learning tests and the mean scores of the matched controls (d_1), as well as between LiP participants' scores and the mean scores of the ARN groups (d_2). Although a different profile is evident for each LiP participant, it is noticeable that every LiP participant's score on one or more of the visual memory and learning measures differs significantly from the control mean and the ARN group mean. Three of the LiP participants (4-, 8- and 17-year-olds) also performed significantly worse than the controls and the average individual in the ARN group did on one or more of the verbal

memory measures. Another observation is that only one LiP participant's (17-year-old) scores on the NM Fc Recall and NM Free Recall tests are significantly worse than the mean scores of the controls and the ARN group. The 4- and 8-year-old LiP participants performed significantly worse than the controls and the average individual in the ARN group did on measures of verbal recognition memory (NM Recognition).

It is interesting to note that the 8- and 17-year-old LiP participants obtained significantly better scores compared to the mean scores of the controls and the mean scores of the ARN group on some measures of long-term visual memory, while this is not the case for the two urban LiP participants (4- and 6-year-olds) and the 15-year-old LiP rural participant, who obtained significantly lower scores compared to the typically developing individuals on different measures of visual memory.

Finally, it is noticeable that none of the LiP participants' scores on a test measuring verbal-visual associative learning (NM) differs significantly from the mean scores of the matched controls (d_1) and the mean scores of the ARN group (d_2).

Memory and learning trajectories. Graphs were plotted to represent the performance of the LiP participants across the five different age groups on the memory and learning measures employed in this study. This was done to identify developmental trends. No hypothesis is tested; therefore, this aspect of the research is purely explorative. Trajectories were plotted for every learning and memory construct. T-scores ($\overline{X} = 50$; $sd = 10$) were used to represent the performance of the LiP participants, the mean scores of the controls (Control) and the mean scores of the ARN group (Norm).

NM recognition. Figure 5.6 graphically compares the NM Recognition scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also shown. As the NM Recognition subtest was constructed only for 3- to 12-year-olds, this test was not administered to 15- and 17-year-olds; therefore, no data is represented for these individuals.

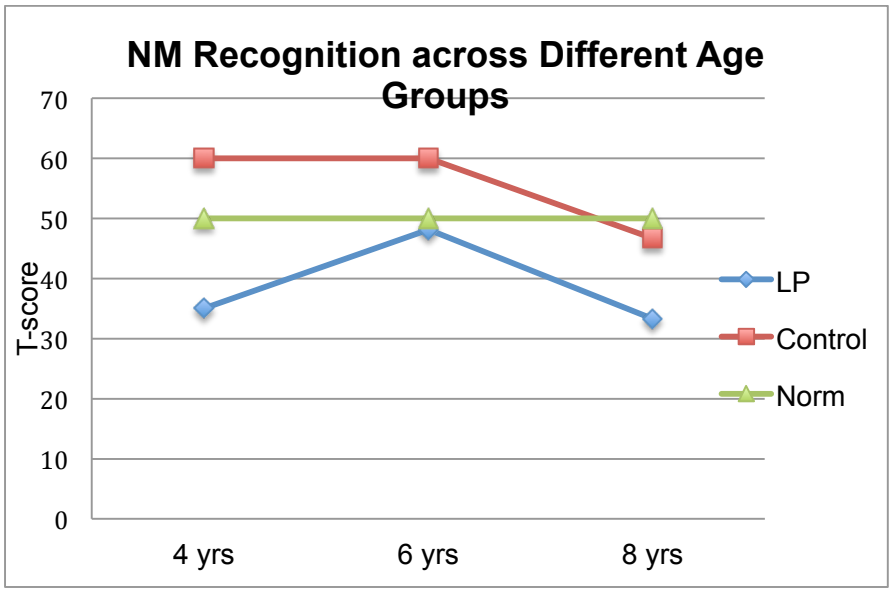

Figure 5.6. *NM Recognition across different age groups.*

Figure 5.6 indicates that the 4-, 6- and 8-year-old LiP participants' scores on the NM Recognition subtest are significantly lower than the mean scores of the matched controls (5-year-old: $d_1 = 2.5$; 6-year-old: $d_1 = 1.2$; 8-year-old: $d_1 = 1.3$). This suggests a consistent trend across all three age groups in which the LiP children appear less proficient at recognising organised verbal information than their non-LiP peers are. The 4-year-old ($d_2 = 1.5$) and 8-year-old ($d_2 = 1.7$) participants also seem to be significantly less able to recognise organised verbal information than the similarly aged average individual in the ARN group is. However, this trend is not apparent across the entire age range depicted in Figure 5.6 (6-year-old LiP participant: $d_2 = 0.2$). It is interesting to note that the mean NM Recognition scores of the urban controls are above the mean scores reported for the ARN group, while the rural control (8-year-old) mean score is below (although close to) the corresponding mean score reported for the ARN group.

Short-term verbal memory (NM Fc Recall and NM Free Recall). Figure 5.7 graphically compares the NM Fc Recall scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean score of the ARN group (Norm) are also depicted.

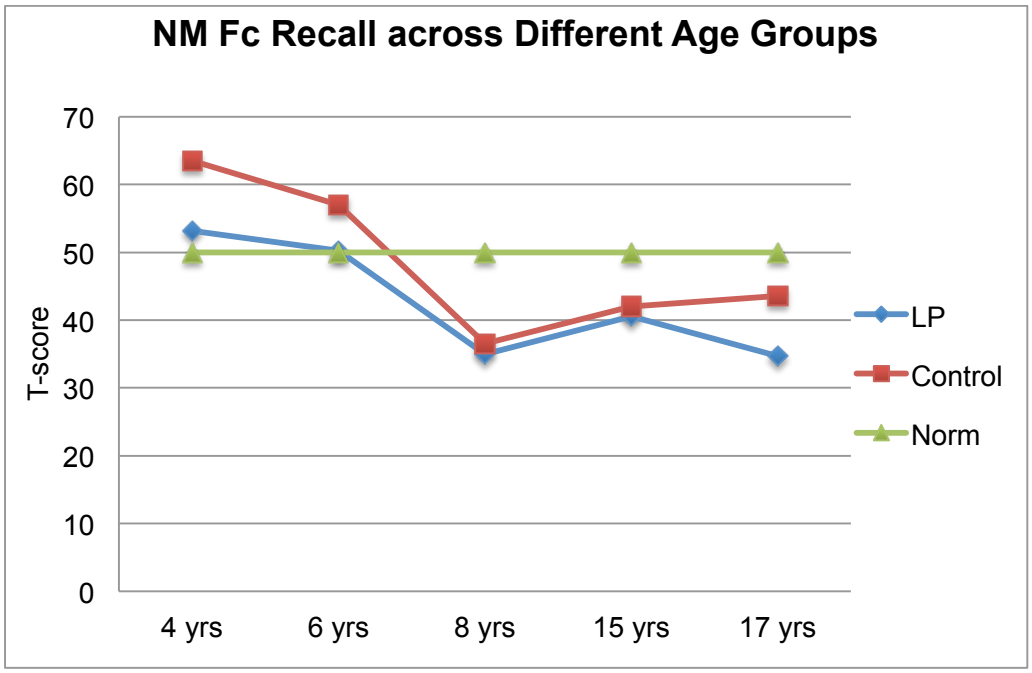

Figure 5.7. NM Fc Recall across different age groups.

In Figure 5.7, it is apparent that only the 4-year-old (d_1 = 2.0) and 17-year old (d_1 = 0.9) LiP participants performed significantly worse than their matched controls did at recalling narrative information in both free recall and cued conditions. The 8-year-old (d_2 = 1.5), 15-year-old (d_2 = 0.9) and 17-year old (d_2 = 1.5) LiP participants obtained scores significantly below the reported mean scores for the ARN group. This could possibly be interpreted as indicating an age-related deterioration in free and cued recall of narrative information (compared to the mean scores reported for the ARN group) emerging at some stage between six and eight years of age. However, the graph representing the control participants in these age groups appears to follow that of the LiP participants closely. Consequently, attributing this apparent deterioration solely to the neurocognitive effects of LiP does not seem prudent, particularly because the 4- and 6-year-old, whose NM Fc Recall scores do not fall below the mean scores of the ARN group, differ from LiP participants whose scores do fall below the mean scores of the ARN group with regard to geographical environment (urban/rural). The tendency of the scores of the rural LiP and control participants to fall below the mean scores reported for the ARN group is evident in Figure 5.7. Conversely, in keeping with the data depicted in Figure 5.6, the data for the urban controls contained in Figure 5.7 show that these individuals scored higher than their

LiP peers did and higher than the reported mean scores for the ARN group (Korkman et al., 2007b).

Figure 5.8 graphically compares the NM Free Recall scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the 6-year-old to 17-year-old age range. In addition, the mean scores of the ARN group (Norm) are also depicted. The NEPSY-II manual (Korkman et al., 2007a) provides norms only for NM Free Recall scores for children aged 6 years and older. Consequently, Figure 5.8 does not reflect data for the 4-year-old participants.

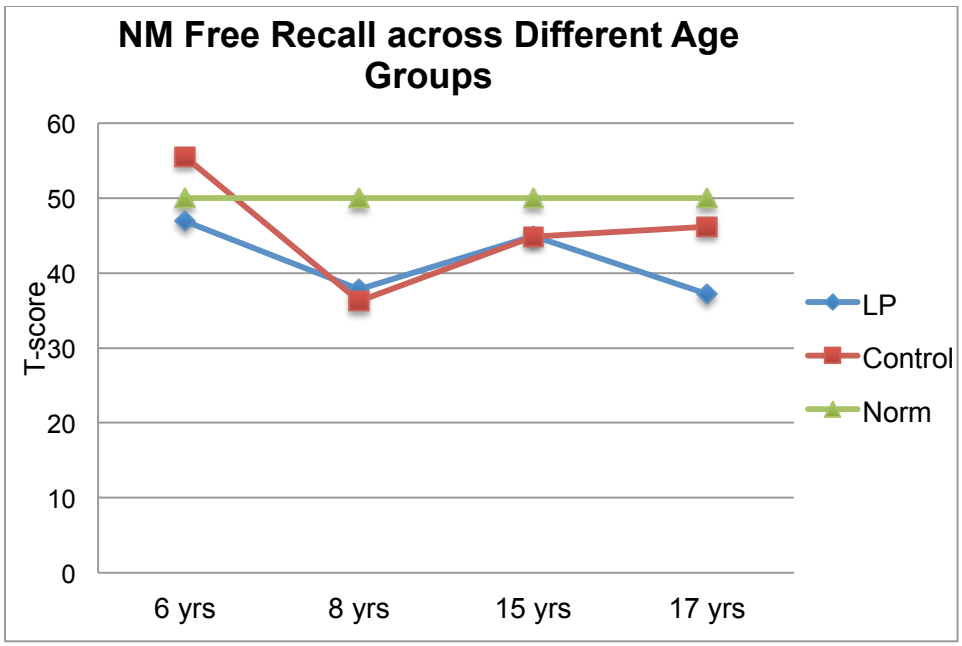

Figure 5.8. NM Free Recall across different age groups.

In Figure 5.8, It is evident that the 6-year-old (d_1 = 0.9) and 17-year old (d_1 = 0.9) LiP participants seem to perform significantly worse at freely recalling narrative information compared to their matched controls. The 8-year-old (d_2 = 1.2) and 17-year-old (d_2 = 1.3) LiP participants also obtained scores significantly below the reported mean scores for the ARN group on NM Free Recall, but their scores do not fall below the mean scores of their matched controls. Therefore, only the 17-year-old LiP participant performed significantly worse than his matched controls and the average individual in the ARN group did on this measure of verbal free recall. Thus, no specific trend is evident in this graph. With regard

to Free Recall, the reasons for the differences in performance are unclear and do not appear to be based on whether the LiP participants were in rural or urban environments.

The 6-year-old control participants performed better than was expected in relation to the mean of the established ARN group. Generally, on all the verbal memory measures, the younger (urban) control participants tended to outperform the published norms for their age group, and the 8-, 15- and 17-year-old rural participants tended to score below the published norms for their age group.

Short-term visual memory (MD Content, MD Spatial, and MD Total). Figure 5.9 graphically compares the MD Content scores of the LiP participants (LP) to the mean scores of their matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.9.

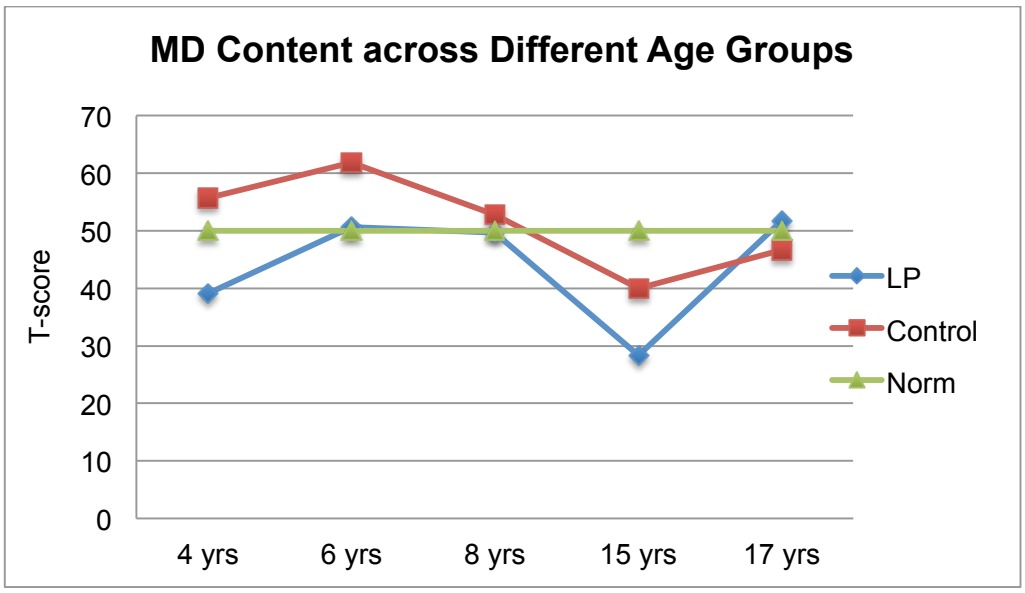

Figure 5.9. MD Content across different age groups.

In Figure 5.9, it is evident that the 4-year-old (d_1 =1.7), 6-year-old (d_1 =1.1) and 15-year-old (d_1 =1.2) LiP participants' scores on MD Content are significantly lower compared to matched controls. The 4-year-old (d_2 =1.1) and 15-year old (d_2 = 2.2) LiP participants also scored significantly below the reported mean of the ARN group on MD Content. Thus, no age-related trend is evident with regard to recall of visual details among the LiP participants whose data are reflected in Figure 5.9.

The 4- and 6-year-old control participants scored above the mean scores of the ARN group, while the 15- and 17-year-old control participants scored below the mean scores of the ARN group. Therefore, an apparent deterioration in the performance of the control participants seems evident between the ages of 6 and 15 years. This tendency is similar to the trend observed on the verbal memory scales. However, on this measure of short-term visual memory, the 8-year-old control's performance equals the mean score of the ARN group. Therefore, the tendency of the 8-year-old control participants to perform below the mean scores of the ARN group on the verbal memory measures is not apparent in this measure. This possibly suggests a neuropsychological influence of which cognitive domain (verbal versus visual memory) is assessed.

Figure 5.10 graphically compares the MD Spatial scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted.

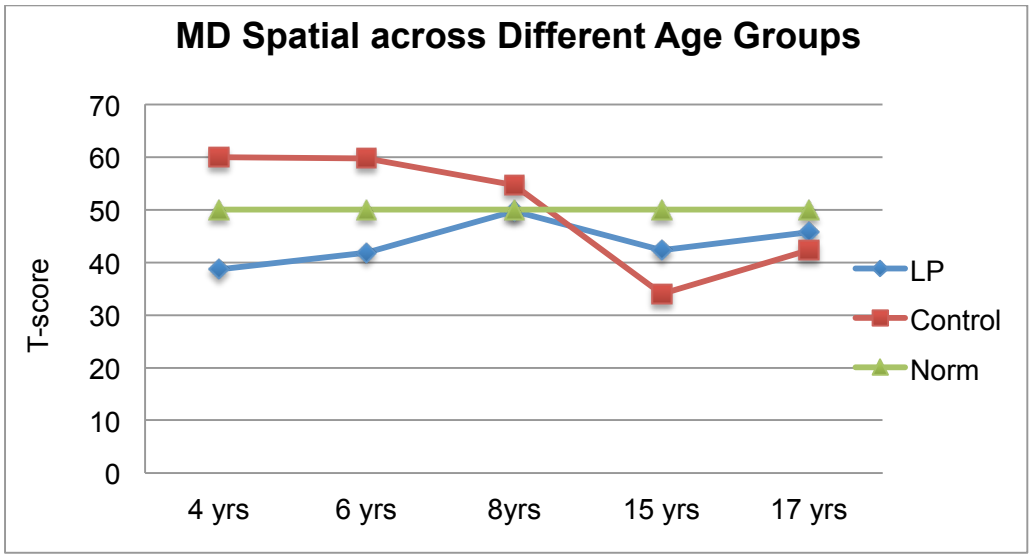

Figure 5.10. MD Spatial across different age groups.

In Figure 5.10, it is evident that the 4-year-old (d_1 = 2.1) and 6-year-old (d_1 =1.8) LiP participants' scores on MD Spatial are significantly below the mean score of the matched controls, while the 15-year-old (d_1 = 0.8) LiP participant's score is significantly above the mean score of the control participants. The 4-year-old (d_2 = 1.1) and 6-year-old (d_2 = 0.8) LiP participants also scored significantly below the reported mean for the ARN group on MD Spatial. Thus, the urban LiP participants scored below the mean scores of their

matched controls and the mean scores of the ARN group, while none of the rural LiP participants scored significantly below the mean scores of the ARN and control groups.

The graph representing the mean scores of the control participants shows almost the opposite pattern compared to the graph representing the scores of the LiP participants. The mean scores of the 4-, 6- and 8-year-old control participants are above the mean scores of the ARN group, while the mean scores of the 15- and 17-year-old control participants are below the reported mean scores of this group. Therefore, deterioration in the performance of the controls between ages 8 and 15 years is evident. This deterioration is not evident among the LiP participants.

Figure 5.11 graphically compares the MD Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.11.

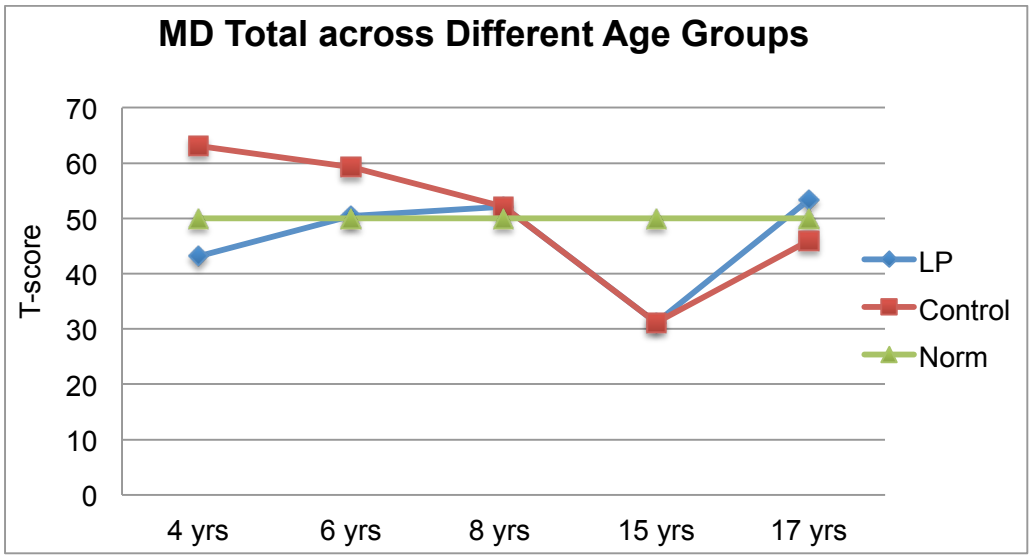

Figure 5.11. MD Total across the different age groups.

In Figure 5.11, it is apparent that the 4-year-old (d_1 = 2.1) and 6-year-old (d_1 = 0.9) LiP participants' scores on MD Total are significantly lower compared to the mean scores of the matched controls, while the 8-year-old (d_1 = 0.0), 15-year-old (d_1 = 0.0) and 17-year-old (d_1 = 0.7) LiP participants' scores are similar to those of the controls. A tendency for the urban LiP participants to score significantly below the mean scores of their matched

controls and for the rural LiP participants to score equal to the matched controls on MD Total is apparent in Figure 5.10 (MD Spatial) and Figure 5.11 (MD Total).

The 4-year-old (d_2 = 0.8) LiP participant's score is also significantly below the reported mean score of the ARN group on MD Total. Similarly, the 15-year old (d_2 = 1.7) LiP participant obtained a score that is significantly below the mean score of the ARN group on MD Total, but this participant obtained the same score as the mean score of his matched controls, who also scored below the mean of the ARN group. Thus, none of the LiP participants, except for the youngest urban LiP participant (4-year-old) scored below the mean score of the matched controls and the mean score of the ARN group. Therefore, no age-related trend is evident with regard to recall of visual details among the LiP participants whose data are reflected in Figure 5.9. Deterioration in the performance of the controls between the ages of 6 and 15 years seems evident.

Long-term visual memory (MDD Content, MDD Delayed Spatial and MDD Total). Figure 5.12 graphically compares the MDD Content scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.12. The MDD Content subtest of the NEPSY-II is not administered to 4-year-olds. Therefore, no data is presented for the 4-year-old LiP participant and her matched controls.

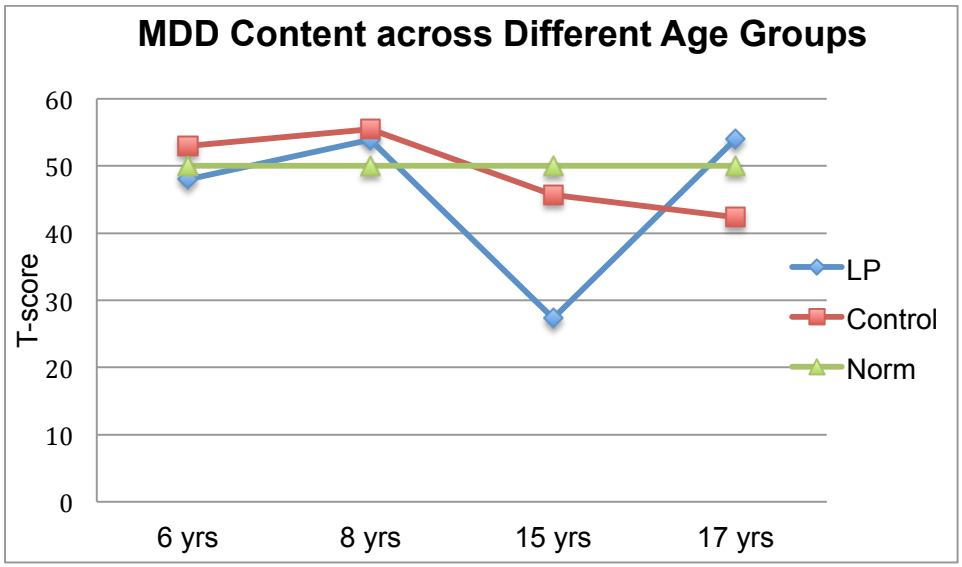

Figure 5.12. MDD Content across the different age groups.

In Figure 5.12, it is evident that the 15-year-old (d_1 = 1.8) LiP participant's score on MDD Content is significantly lower than the score of the matched controls, while the 17-year old (d_1 = 1.2) LiP participant's score is significantly higher than the mean score of the controls. The 15-year-old (d_2 = 2.3) LiP participant's score is also significantly below the reported mean score of the ARN group on MDD Content. Therefore, only the 15-year-old LiP participant's performance differs significantly from the mean score of the controls and the mean score of the ARN group. Thus, no age-related trend is evident with regard to delayed recall of visual content among the LiP participants.

The mean scores of the 6- and 8-year-old controls on MDD Content are higher than the mean scores of the ARN group, while the scores of the 15- and 17-year-old controls are below these mean scores. Therefore, deterioration in the performance of the controls on MDD Content is evident between the ages of 8 and 15 years. This trend is similar to the trend observed on the short-term visual memory scales that have been discussed so far (MD Content, MD Spatial, and MD Total).

Figure 5.13 graphically compares the MDD Spatial scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN Group (Norm) are also depicted in Figure 5.13.

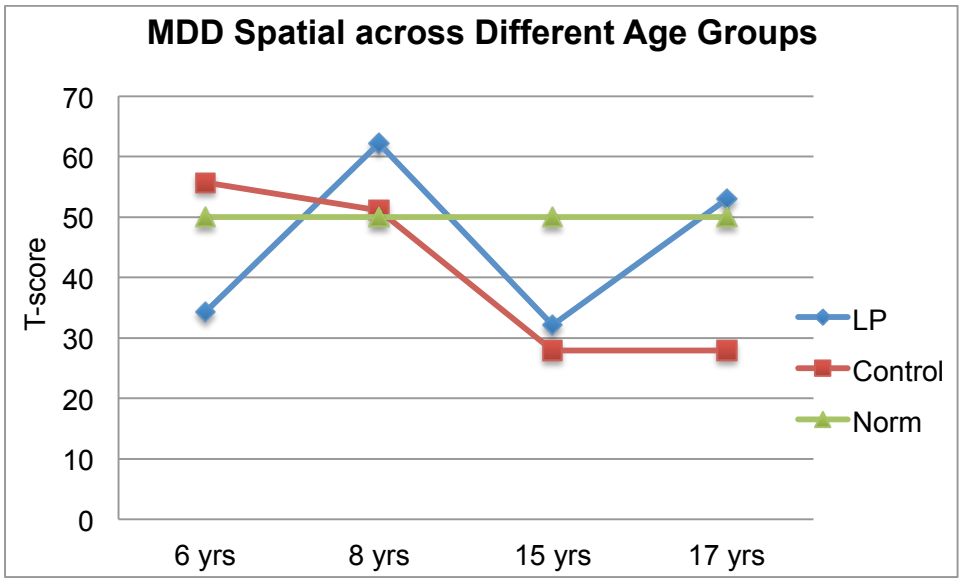

Figure 5.13. MDD Spatial across the different age groups.

In Figure 5.13, it is evident that the 6-year-old (d_1 = 2.1) LiP participant's score on MDD Spatial is significantly lower than the score of the matched controls, while the scores of the 8-year-old (d_1 = 1.1) and 17-year old (d_1 = 2.5) LiP participants are significantly higher than the scores of their matched controls on this measure. The 6-year-old (d_2 = 1.6) LiP participant's score is also significantly below the reported mean score of the ARN group, while the 8-year-old (d_2 = 1.2) LiP participant's score is also significantly above the reported mean score of the ARN group. Although the 15-year-old (d_2 = 1.8) LiP participant scored significantly below the mean score of the ARN group, the participant's score did not differ significantly from the mean score of the controls. Thus, no age-related trend is evident with regard to delayed recall of location among the LiP participants whose data are reflected in Figure 5.13.

Similar to the trend found with regard to all the other visual memory measures discussed so far, the 6- and 8-year-old control participants' mean scores on MD Spatial are higher than the mean scores of the ARN groups, while the 15- and 17-year old controls scored below the mean scores of this group. Deterioration in the performance of the controls between the ages of 8 and 15 years seems evident.

Figure 5.14 graphically compares the MDD Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.14.

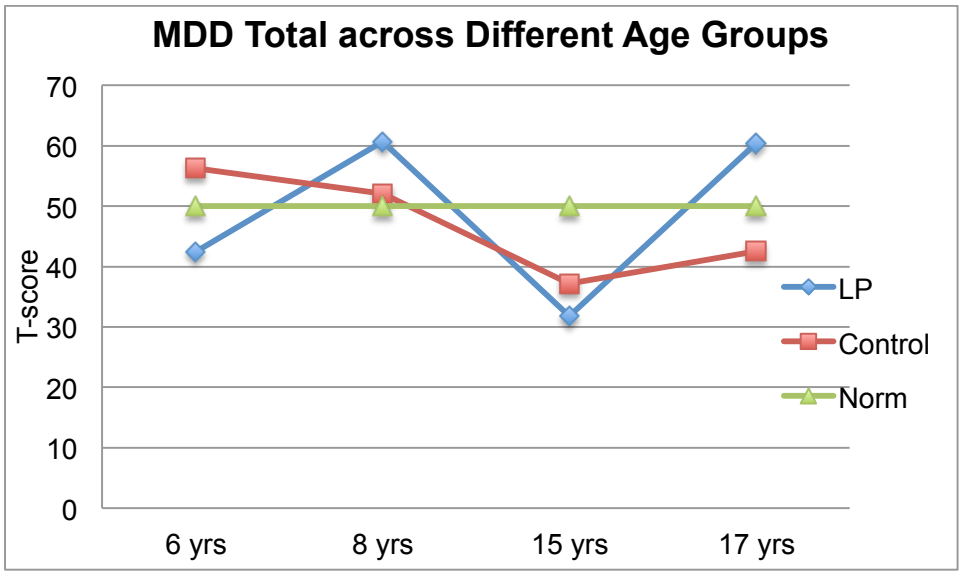

Figure 5.14. MDD Total across the different age groups.

In Figure 5.14, it is evident that the 6-year-old (d_1 = 2.1) LiP participant's score on MDD Total is significantly lower compared to the scores of matched controls, while the scores of the 8-year-old (d_1 = 1.1) and 17-year old (d_1 = 2.5) LiP participants are significantly higher than those of the controls on this measure are. The 6-year-old (d_2 = 1.6) LiP participant's score is also significantly below the reported mean score of the ARN group, while the scores of the 8-year-old (d_2 = 1.2) and 17-year-old (d_2 = 1.0) LiP participants are also significantly above the reported mean scores of the ARN groups. Although the 15-year-old (d_2 = 1.8) LiP participant scored significantly below the reported mean score of the ARN group, the participant's score is not significantly below the mean score of the matched controls.

Similar to the tendency observed on the other short- and long-term visual memory scales, the mean scores of the 6- and 8-year-old controls on MDD Total are higher than the mean scores reported for the ARN groups. The 15- and 17-year-old controls achieved scores that are lower than the mean scores reported for the ARN groups on this measure. Therefore, deterioration in the performance of the controls on MDD Total between the ages of 8 and 15 years seems evident.

Visual-verbal associative learning (MN Total). Figure 5.15 graphically compares the MN Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across two age groups (15- and 17-year-old). In addition, the mean scores of the

ARN group (Norm) are also depicted in Figure 5.15. MN Total mean scores were reported only for 15- and 17-year-olds in the *NEPSY-II Clinical and Interpretive Manual* (Korkman et al., 2007a); therefore, no data for the younger age groups are represented.

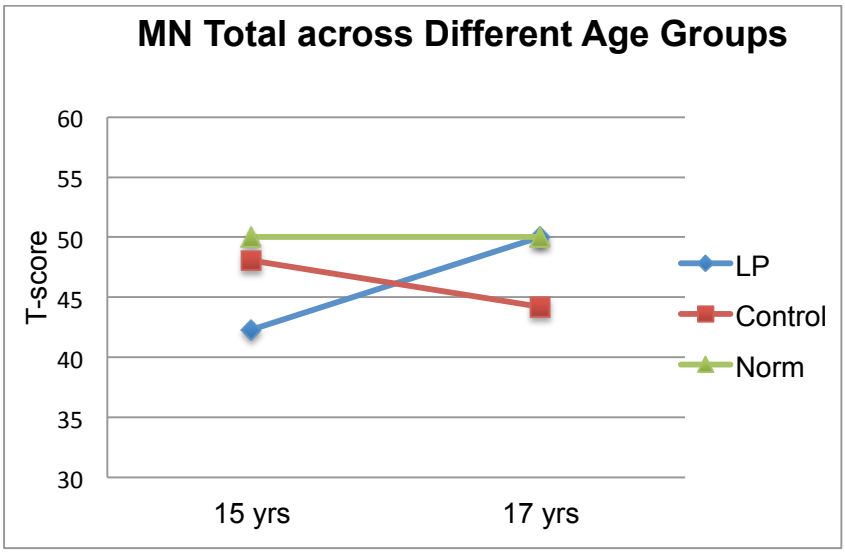

Figure 5.15. MN Total across the different age groups.

In Figure 5.15, it is evident that none of the LiP participants (15-year old: $d_1 = 0.6$; 17-year old: $d_1 = 0.6$) scored significantly below the mean scores of the controls on MN Total. The 15-year-old ($d_2 = 1.8$) LiP participant scored significantly below the mean score reported for the ARN group, but not significantly below the mean score of the controls. Therefore, none of the LiP participants scored below both the mean scores of the controls and the mean scores reported for the ARN groups. Both the 15- and 17-year-old controls obtained lower scores than the average individual in the ARN group did. This trend is similar to the tendency noted on all the other visual memory scales. However, in the absence of scores for the 4-, 6- and 8-year-olds, no conclusions can be drawn with regard to trends on this graph.

Summary of memory and learning trajectories.

Verbal memory. Relative to the mean scores of the controls, there is a trend across all the age groups in which the LiP children appear less proficient at recognising organised verbal information than the control group. However, this trend is not apparent across the

entire age range when the LiP scores are compared to the mean scores of the ARN group. Such a trend was also not evident for the free recall conditions.

Relative to the mean scores of the ARN group on a measure of verbal free and cued recall, deterioration in performance of the LiP participants between the ages of 6 and 8 years is evident. This pattern of performance is similar to the trajectory of the control participants' scores on this (free and cued recall) and other verbal memory measures: The mean scores of the urban controls (four- and 6-year-olds) on verbal memory measures are higher than the corresponding mean scores of the ARN groups. In contrast, the rural control participants (eight-, 15- and 17-year-olds) obtained scores that are below the mean scores reported for the ARN groups. This trend is most likely attributable to differences between the urban and rural participants. Therefore, the deterioration in the performance of the LiP participants between the ages of 6 and 8 years on the measure of Free Recall can most likely not be attributed solely to the effect of LiP on their functioning, but may also be due to differences between the urban and rural LiP participants (such as socio-economic and cultural differences).

Visual memory. The graph depicting scores and mean scores across the age groups obtained on a measure of short-term spatial memory indicates that both the 4- and 6-year-old LiP participants performed significantly worse than their matched controls and the average individual in the ARN groups did. The 4- and 6-year-old matched controls scored above the mean score of the ARN group. Contrary to the urban LiP participants, none of the rural LiP participants scored significantly below the mean scores of the ARN group and the means of the controls on this measure. This may indicate that the effect of LiP on spatial memory functioning may be different in the urban and rural LiP participants. LiP appears to have affected the spatial memory of the urban LiP participants negatively, but it did not have a negative effect on the rural participants.

No specific age-related trends are evident with regard to delayed recall of visual details and location.

When considering the LiP participants' performance on all the visual memory measures (short term and long term), no specific age-related trends are evident. Therefore, individual characteristics may have influenced the outcome of these individuals' visual memory abilities.

A certain tendency is noted among the controls, relative to the reported mean scores of the ARN groups on measures of visual memory: The urban control participants (4- and 6-year-olds) obtained higher scores on measures of visual memory than the ARN group did. The 8-year-old rural control participants generally obtained scores that are higher or equivalent to the mean scores of the ARN group on measures of visual memory, while the 15- and 17-year-old rural control participants generally obtained scores that are lower than the mean scores of the relevant norm groups (MD Content, MD Spatial, MD Total, MDD Spatial) on these measures. Thus, deterioration in scores on the short- and long-term visual memory measures between 8 and 15 years is consistently evident. This trend differs from the trend that has been observed on the verbal memory measures among the controls. On the verbal memory measures, deterioration in the mean scores of the controls between the ages of 6 and 8 years has been observed. Differences between the urban and the rural controls may explain the deterioration of scores on the verbal memory measures. However, differences between the urban and rural participants do not explain the deterioration in scores of the controls on the visual memory measures, as the 8-year-old rural control participant did not perform below the reported ARN group mean. Therefore, a neuropsychological influence, of which the domain was assessed (verbal versus visual memory), is evident.

Visual-verbal associative learning. In comparison to the matched controls, there were no significant differences in the performance of the 15- and 17-year-old LiP participants on a measure of visual-verbal associative learning. Control participants consistently obtained scores lower than the ARN group mean on this measure. This pattern of performance of the 15- and 17-year-old control participants is similar to the trajectories on the other memory measures, but cannot be interpreted in the absence of mean scores for the 4-, 6- and 8-year-old ARN groups.

Conclusion: Memory and learning.

Significant differences. Compared to the mean scores of the controls and the mean scores of the ARN group, the LiP participants performed significantly worse on different measures of verbal and visual memory.

Three individuals (4, 8- and 17-year-olds) scored significantly lower on measures of verbal memory. The 4- and 8-year-olds scored significantly worse on a verbal recognition

measure, while the 17-year-old scored significantly below the mean score of the norm group on a measure of verbal free recall and verbal free and cued recall. Therefore, it seems that not all the LiP participants performed worse than their healthy peers did on any specific verbal measure.

Not all the LiP participants performed worse than their healthy peers did on any specific visual measure. Compared to their matched controls and the typically developing individuals in the relevant norm groups, the 4- and 6-year-olds (4-year-olds: short-term visual memory measures; 6-year-olds: short-term and long-term spatial memory and long-term memory for location and content) performed significantly worse, the 8- and 17-year-olds performed significantly better (long-term visual memory measures), and the 15-year-old had inconsistent results. Compared to matched controls and the average individual in the ARN group, the 15-year-old performed significantly worse on measures of short-term and long-term visual memory for content, but significantly better than the controls did on a measure of short-term spatial memory.

No significant differences between the performance of the LiP participants and those of the control participants and between the performance of the LiP participants and that of the similarly aged average individual in the ARN group on a measure of visual-verbal associative learning are evident.

Trends. Deterioration in the performance of the LiP participants between the ages of 6 and 8 years on a measure of verbal free and cued recall is noticeable. Regression in the performance of the control participants between the ages of 6 and 8 years on this verbal memory measure is also evident and could be explained by differences between the urban (4- and 6-year-old) versus rural (8-, 15- and 17-year-old) participants. Therefore, the regression of LiP participants' scores on verbal short-term memory (free recall) measures may not be attributed to LiP alone, but has to be interpreted in the context of the mean scores of peers with similar characteristics and a similar socioeconomic background. The effects of these differences on the performance of the urban participants versus the performance of rural control participants are evident on all verbal memory measures: verbal recognition memory, verbal free and cued recall, and verbal free recall.

Compared to the LiP participants' performance on the verbal memory measures, trends in the performance of the LiP participants on the visual memory measures are

different. In most cases, no specific trend with regard to visual memory among the LiP participants is observed. A regression in control mean scores on all the visual memory measures between the ages of 8 and 15 years is observed. As the 8-year-old control participant obtained scores that are equal to or above the mean scores of the ARN group, the regression in scores is evidently not due to differences between the urban and rural participants. As the observed trends on the visual memory measures among the LiP and control participants differ, it is evident that the factors that caused the regression of control scores between the ages of 8 and 15 years among the control participants, cannot explain the significantly worse or better performance of the LiP participants on the visual memory measures.

There is one instance (MD Spatial) where the differences between rural and urban LiP participants evidently determine whether or not LiP would affect their visuospatial memory functioning. Opposite trends are observed for the LiP versus control participants on a measure of short-term spatial memory: The 4- and 6-year-old LiP participants performed significantly below the mean score of the ARN group, while the 4- and 6-year-old controls performed above the mean score of the ARN group. The scores of the 8-, 15- and 17-year-old LiP participants on the short-term visual-spatial memory measure do not differ significantly from the mean score of the ARN group. Therefore, LiP appears to have affected the visual memory functioning of the rural LiP differently from that of the urban LiP participants.

Overall, there is a difference between the trends noted with regard to verbal memory compared to the trends noted for visual memory among the LiP participants. This possibly suggests a neuropsychological influence of the cognitive domain that was assessed (verbal versus visual memory).

Social Perception

The performance of the LiP children and adolescents on the social perception scales was compared to that of controls and a norm group (the ARN group). The various social perception constructs were measured by means of subtests of the NEPSY-II (Korkman et al., 2007a). Recognition of facial emotion was measured by means of AR Total, Happy Errors, Sad Errors, Neutral Errors, Fear Errors, Angry Errors, and Disgust Errors subtests. ToM was measured by means of TM Verbal and TM Total. Face recognition was

measured by means of the MF subtest. Mean raw scores were reported for most social perception measures (Korkman et al., 2007a). However, no raw scores were reported for AR Total (Korkman et al., 2007a). Raw scores and scaled scores ($\overline{X}$ = 10, *sd* = 3) were used to compare the performance of the LiP participants and the controls and the LiP participants and the typically developing individuals in the ARN groups on AR Total. Scores on all the measures were converted into McCall T-scores ($\overline{X}$ = 50; *sd* = 10) to be compared graphically. Next, the differences in mean scores on the social perception measures will be reported by age group in ascending order.

Four-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 4-year-old LiP participant, the two matched controls and the ARN group on the measures of social perception are reported in Table 5.7.

Table 5.7

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 4-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Social Perception

Social Perception Measures	LP Score (μ) (n = 1)	Control Mean ($\overline{X}$) (n = 2)	Norm Group $\overline{X}$	Norm Group *sd*	d_1	d_2
Recognition of Facial Emotion						
Happy Errors	1.0	0.0	0.9	1.1	0.9	0.1
Sad Errors	1.0	1.5	1.1	0.7	0.7	0.1
Neutral Errors	1.0	0.0	0.3	0.6	**1.7***	**1.2***
Fear Errors	2.0	0.0	0.3	0.6	**3.3***	**2.8***
Angry Errors	0.0	0.0	0.2	0.4	0.0	0.5
Disgust Errors	0.0	0.0	0.1	0.3	0.0	0.3
AR Total#	7.0	12.0	9.9	3.1	**1.6***	**0.9***
Theory of Mind						
TM Verbal	6.0	14.5	5.9	2.9	2.9	0.0

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; AR Total = Affect Recognition Total; TM Verbal = Theory of Mind Verbal.

In Table 5.7, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to Neutral Errors ($d_1 = 1.7$; $d_2 = 1.2$), Fear Errors ($d_1 = 3.3$; $d_2 = 2.8$) and AR Total ($d_1 = 1.6$; $d_2 = 0.9$). The 4-year-old LiP participant performed significantly worse (significant lower μ) than the matched controls and ARN group did in a task that taps the ability to recognise facial emotion expressions accurately. Additionally, the LiP participant made significantly more errors (significant higher μ) than controls and the ARN group made in tasks requiring the ability to identify neutral and fearful facial expressions accurately. Consequently, the H_0 hypothesis with regard to Neutral Errors, Fear Errors, and AR Total can be rejected.

Figure 5.16 graphically compares the McCall T-scores of the LiP participant (LP) to the mean scores of the matched controls (Control) on the AR Error scales of the NEPSY-II. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.16. The TM Verbal and AR Total scores are not error scores; therefore, a high score on these scales is interpreted differently from scores on the error scales. Therefore, to avoid confusion, these scores are plotted in a separate graph (Figure 5.17).

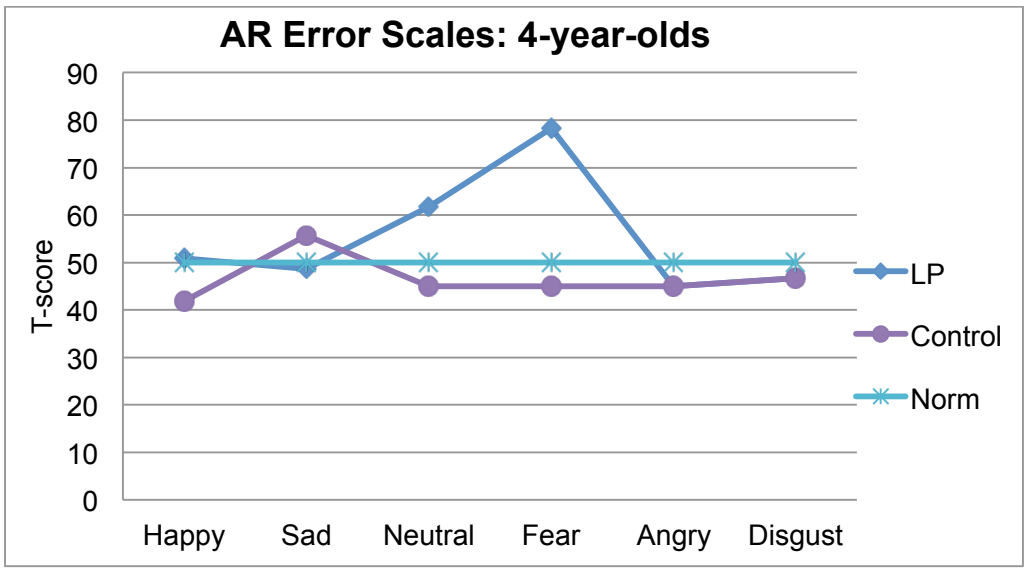

Figure 5.16. AR Error profiles of the 4-year-old participants.

In Figure 5.16, it is evident that the LiP participant's error scores on tasks measuring accuracy in identifying happy, neutral and fearful faces are higher than the scores of the

matched controls are. However, only the scores on the Neutral and Fear Errors scales are significantly elevated compared to the mean score reported for the ARN group. It is noticeable that the scores of the two controls are above (more errors) the reported mean score of the ARN group on the Sad Errors scale and below the mean score of the ARN group (fewer errors) on the other error scales.

Figure 5.17 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) on TM Verbal and AR Total. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.17. As mentioned before, the TM Verbal and AR Total scores are not error scores; therefore, high scores indicate better performance.

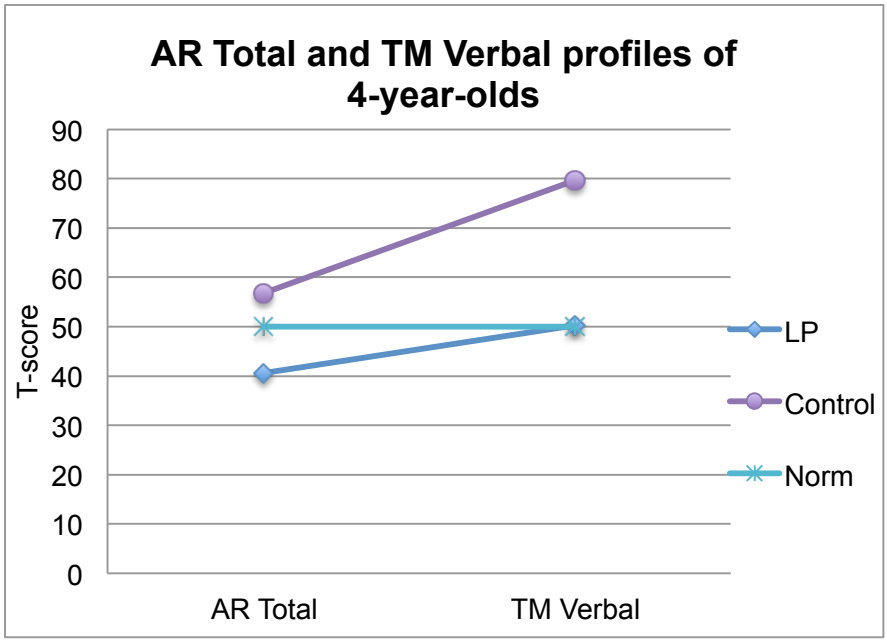

Figure 5.17. AR Total and TM Verbal profiles of the 4-year-old participants.

In Figure 5.17, it is evident that the LiP individual performed worse than the matched controls did on the AR Total and TM Verbal scales. However, only the AR Total LiP score is significantly below the mean score of the ARN group. It is noticeable that the mean scores of the two controls are above the reported mean score of the ARN group (indicating better performance) on the measures of recognition of facial emotion and ToM.

Next, the differences in the mean scores of the 6-year old LiP participant (compared to the mean scores of the control and ARN groups) on the social perception measures/subtests will be reported and displayed graphically.

Six-year-old LiP participant. The mean scores, standard deviations, and effect sizes of the 6-year-old LiP participant, the two matched controls, and the ARN group on the measures of social perception utilised in the study are reported in Table 5.8.

Table 5.8

Scores, Mean Scores, Standard Deviations, and Effect Sizes of the 6-Year-Old LiP Participant, Matched Controls, and Norm Group on Measures of Social Perception

Social Perception Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	***d_1***	***d_2***
Recognition of Facial Emotion						
Happy Errors	0.0	0.0	0.4	0.7	0.0	0.6
Sad Errors	3.0	2.0	1.8	1.0	**1.0***	**1.2***
Neutral Errors	0.0	2.0	0.9	0.6	**3.3***	**2.2***
Fear Errors	0.0	1.0	0.3	0.6	1.7	0.5
Angry Errors	1.0	2.0	1.0	0.9	1.1	0
Disgust Errors	0.0	1.0	0.7	0.8	**1.3***	**0.9***
AR Total#	14.0	8.5	9.0	3.4	**1.6***	**1.5***
Theory of Mind						
TM Verbal	12.0	13.5	11.5	3.9	0.4	0.1
Face Recognition						
MF Total#	9.0	9.0	9.9	2.9	0.0	0.3

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq$ 0.8; AR Total = Affect Recognition Total; TM Verbal = Theory of Mind Verbal; MF Total = Memory for Faces Total.

In Table 5.8, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between

the LiP participant's scores and the ARN group's mean scores (d_2) with regard to Sad Errors (d_1 = 1.0; d_2 = 1.2), Neutral Errors (d_1 = 3.3; d_2 = 2.2), Disgust Errors (d_1 = 1.3; d_2 = 0.9) and AR Total (d_1 = 1.6; d_2 = 1.5). The 6-year-old LiP participant performed significantly better (significant higher μ) than the matched controls and the average individual in the ARN group did in a task that taps the general ability to recognise facial expressions accurately. The LiP participant also performed better (fewer errors – significantly lower μ) than the typically developing individuals did when required to recognise neutral and disgusted facial expressions. The LiP participant obtained a significantly higher score (more errors – significantly higher μ) than the mean score of the matched controls and the mean score of the ARN group when required to recognise sad facial expressions. Consequently, the H_0 hypothesis with regard to Sad Errors, Neutral Errors, Disgust Errors, and AR Total can be rejected.

Figure 5.18 graphically compares the McCall T-scores of the LiP participant (LP) on the measures of social perception to that of each of the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.18. The AR Total, TM Verbal, and MF Total scores are not included in Figure 5.18, but are plotted in a separate graph (Figure 5.19).

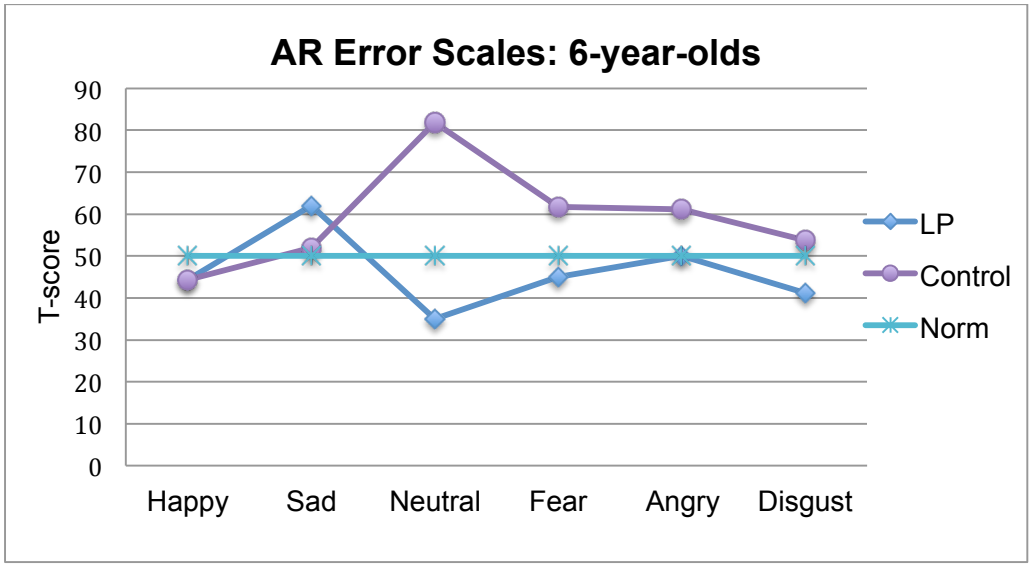

Figure 5.18. AR Error profiles of the 6-year-old participants.

In Figure 5.18, it is evident that the LiP individual made significantly more errors than the matched controls did on the Sad Errors scale, but made fewer errors than the controls did on Neutral Errors, Fear Errors, Angry Errors and Disgust Errors. However, the LiP mean score on the Fear and Disgust Errors scale is not significantly different from the mean score of the ARN group. It is noticeable that controls made more errors compared to the similarly aged average individual in the ARN group on tasks measuring accurate recognition of neutral, fearful, and angry facial expressions.

Figure 5.19 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) on the AR Total, TM Verbal, and MF subtests of the NEPSY-II. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.19.

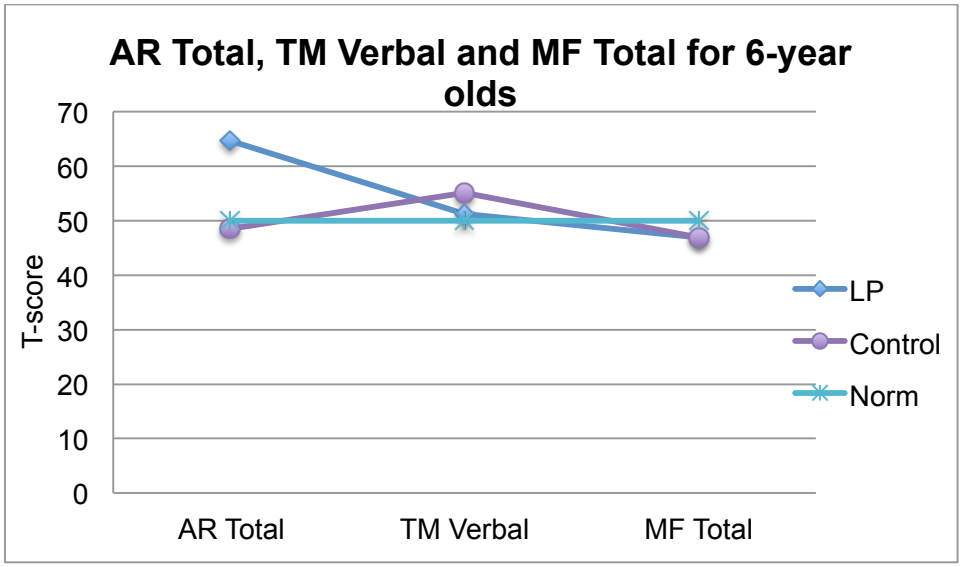

Figure 5.19. AR Total, TM Verbal, and MF Total profiles of the 6-year-old participants.

In Figure 5.19, it is evident that the LiP individual performed better than the matched controls did on the AR Total. The LiP participant's score on this task, measuring accuracy in identifying facial expressions, is significantly higher than the mean score of the matched controls and the mean score reported for the ARN group. The controls scored above the reported mean score of the ARN group on TM Verbal, but below the mean score of the norm group on MF Total.

Next, the differences in the mean scores of the 8-year old LiP participant (compared to the control and ARN groups) on the social perception measures/subtests will now be reported and displayed graphically.

Eight-year-old LiP participant. The score, mean scores, standard deviations and effect sizes of the 8-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of social perception are reported in Table 5.9.

Table 5.9

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 8-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Social Perception

Social Perception Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	***d_1***	***d_2***
Recognition of Facial Emotion						
Happy Errors	0.0	0.5	0.2	0.4	1.3	0.5
Sad Errors	4.0	4.0	2.6	1.7	0.0	0.8
Neutral Errors	6.0	2.0	1.5	1.2	**3.3***	**3.8***
Fear Errors	1.0	1.0	0.9	1.0	0.0	0.1
Angry Errors	2.0	1.0	2.6	1.8	0.6	0.3
Disgust Errors	2.0	2.5	1.8	1.4	0.4	0.1
AR Total#	8.0	10.0	10.7	2.7	0.7	1.0
Theory of Mind						
TM Verbal	14.0	13.5	15.7	3.5	0.1	0.5
TM Total	19.0	18.5	20.3	4.2	0.1	0.3
Face Recognition						
MF Total#	7.0	6.5	9.9	2.8	0.2	1.0

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq$ 0.8; AR Total = Affect Recognition Total; TM Verbal = Theory of Mind Verbal; MF Total = Memory for Faces Total.

In Table 5.9, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2) with regard to Neutral Errors ($d_1 = 3.3$; $d_2 = 3.8$). Thus, the 8-year-old LiP participant obtained an error score that is significantly above (worse performance) the mean score of the matched controls and mean score of the ARN group on a task that taps the ability to recognise neutral facial expressions. Consequently, the H_0 hypothesis can be rejected only with regard to Neutral Errors.

Figure 5.20 graphically compares the McCall T-scores of the LiP participant (LP) on measures of social perception error scales to that of the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.20.

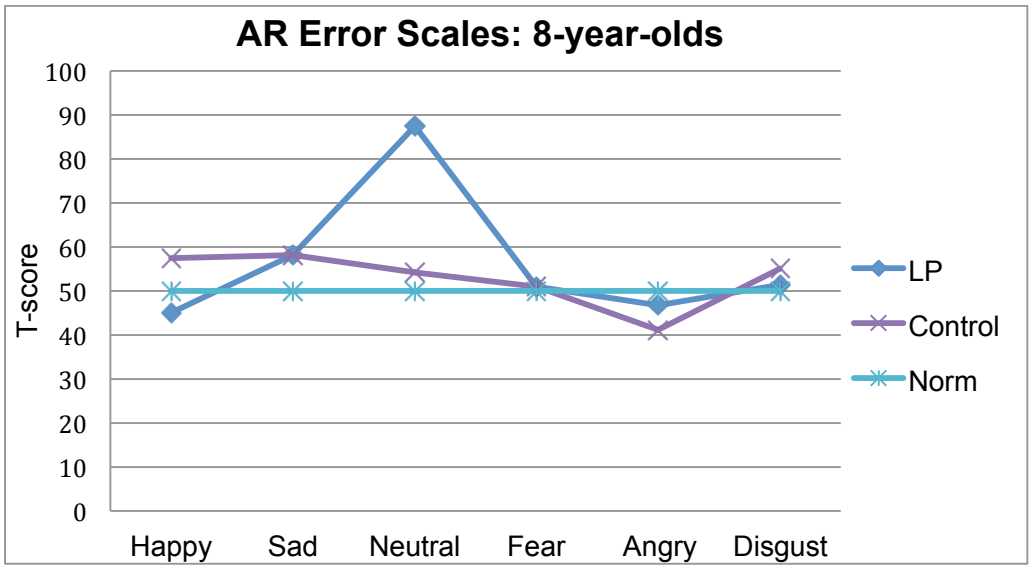

Figure 5.20. AR Error profiles of the 8-year-old participants.

In Figure 5.20, it is evident that the LiP individual's scores are higher than the average score of the matched controls on Neutral Errors and Angry Errors and lower than the score of the matched controls on Happy Errors. However, only the score on the Neutral Errors scale is significantly different (more errors) from the mean score of the ARN group. Further, it is noticeable that the two controls obtained a higher score than the mean score of the ARN group (more errors) when required to identify happy, sad, neutral and disgusted

facial expressions accurately, but obtained a lower score when required to identify angry facial expressions.

Figure 5.21 graphically compares the performance of the LiP participant (LP) to that of the mean scores of the matched controls (Control) on these measures. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.21. As mentioned before, the AR Total, TM Verbal, TM Total, and MF scores are not error scores; therefore, a higher score indicates a better performance.

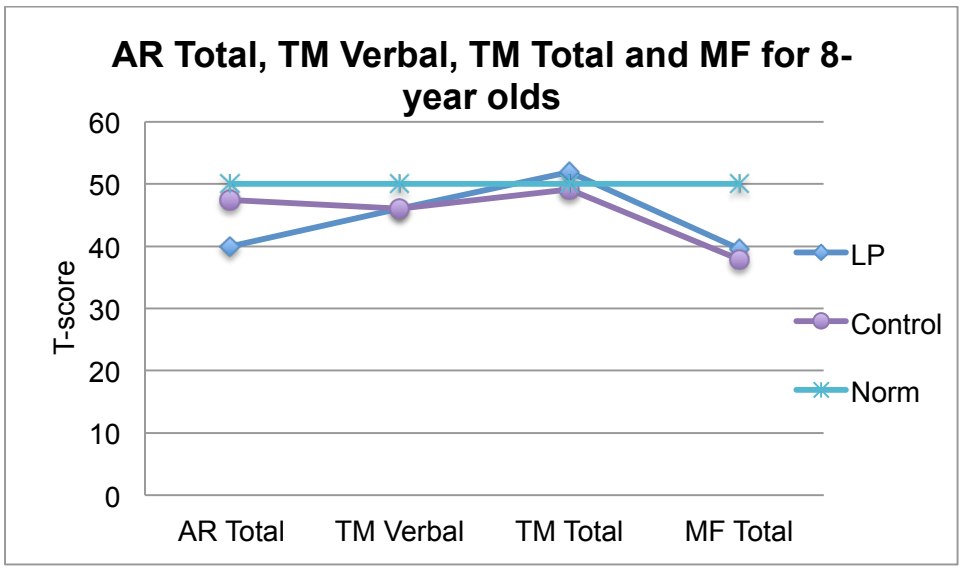

Figure 5.21. AR Total, TM Total, and MF Total profiles of the 8-year-old participants.

In Figure 5.21, it is evident that the LiP individual's score is lower than the mean score of the controls on AR Total, although not significantly. The LiP participant did not perform significantly worse than the controls did on any of the other social perception scales depicted in Figure 5.21. It is noticeable that the mean scores of the controls are below the reported mean score of the ARN group on MF Total, while their mean scores on AR Total, TM Verbal, and TM Total are also lower, but closer, to the mean score reported for this group.

Next, the differences in the mean scores of the 15-year old LiP participant (compared to the mean scores of the control and ARN groups) on the social perception measures/subtests will be reported and displayed graphically.

Fifteen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 15-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of social perception are reported in Table 5.10.

Table 5.10

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 15-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Social Perception

Social Perception Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**		d_1	d_2
			$\overline{X}$	*sd*		
Recognition of Facial Emotion						
Happy Errors	0.0	0.0	0.0	0.2	0.0	0.0
Sad Errors	2.0	3.5	1.8	1.1	1.4	0.2
Neutral Errors	1.0	1.0	1.0	1.1	0.0	0.0
Fear Errors	0.0	1.0	0.3	0.6	1.7	0.5
Angry Errors	5.0	2.0	1.7	1.8	**1.7***	**1.8***
Disgust Errors	3.0	2.0	1.5	1.4	**0.8***	**1.1***
AR Total#	8.0	8.5	9.3	3.3	0.2	0.4
Theory of Mind						
TM Verbal	21.0	21.0	19.8	3.0	0.0	0.4
TM Total	26.0	25.0	25.3	3.6	0.3	0.2
Face Recognition						
MF Total#	12.0	10.0	10.3	3.1	0.7	0.6

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq$ 0.8; AR Total = Affect Recognition Total; TM Total = Theory of Mind Total; TM Verbal = Theory of Mind Verbal; MF Total = Memory for Faces Total.

In Table 5.10, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the mean scores of the ARN group (d_2) with regard to Angry Errors ($d_1 = 1.7$; $d_2 = 1.8$) and Disgust Errors ($d_1 = 0.8$; $d_2 = 1.1$). Consequently, the 15-year-old LiP participant performed significantly worse (made more errors – significant

higher μ) than the matched controls and the average individual in the ARN group did on tasks that tap the ability to accurately recognise angry and disgusted facial expressions. Consequently, the H_0 hypothesis with regard to Angry Errors and Disgust Errors can be rejected.

Figure 5.22 graphically compares the McCall T-scores of the LiP participant (LP) on the measures of social perception to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.22.

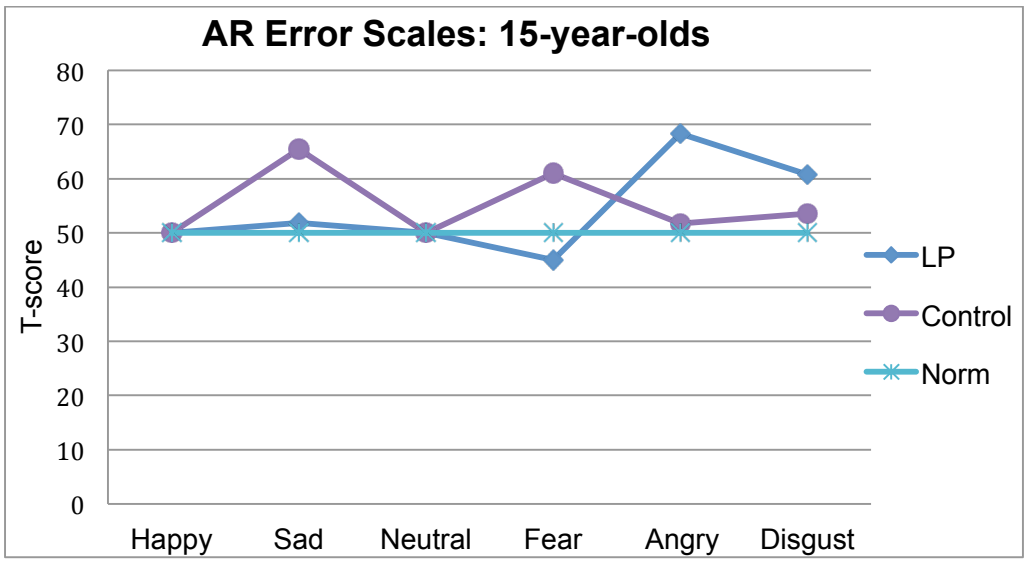

Figure 5.22. AR Error profiles of the 15-year-old participants.

In Figure 5.22, it is evident that the LiP participant made significantly more errors in recognising angry and disgusted facial expressions than the matched controls and the average individual in the ARN group did on the AR Error scales. However, the LiP participant's error scores on scales measuring the accurate perception of fearful and sad facial expressions are lower (indicating better performance) than the scores of the matched controls (but not significantly lower than the mean score of the ARN group). It is noticeable that the mean scores of the control participants on Sad Errors and Fear Errors are higher than the mean scores reported for the ARN group, while the scores on the other error scales are close to the mean scores of the ARN group.

Figure 5.23 graphically compares the performance of the LiP participant (LP) on AR Total, TM Verbal, TM Total, and MF Total to the mean scores of the matched controls

(Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.23.

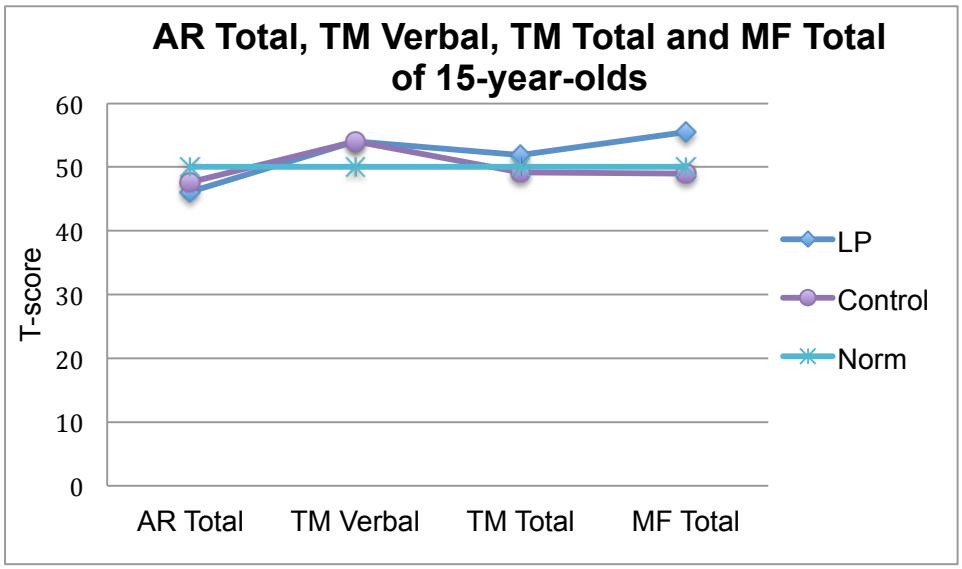

Figure 5.23. AR Total, TM Verbal, TM Total, and MF Total profiles of the 15-year-old participants.

In Figure 5.23, it is evident that the LiP participant's scores are not significantly different from the mean scores of the matched controls or the ARN group on any of the measures. It is noticeable that the mean scores of the controls are equal to or close to the mean scores of the ARN group on AR Total, TM Verbal, TM Total, and MF Total.

Next, the differences in the mean scores of the 17-year old LiP participant (compared to the mean scores of the control and ARN groups) on the social perception measures/subtests will be reported and displayed graphically.

Seventeen-year-old LiP Participant. The social perception scores of the 17-year-old LiP participant and the mean scores, standard deviations and effect sizes of the two matched controls and the ARN group (Norm Group) are reported in Table 5.11.

Table 5.11

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 17-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Social Perception

Social Perception Measures	LP Score (μ) (n = 1)	Control Mean ($\overline{X}$) (n = 2)	Norm Group $\overline{X}$	Norm Group *sd*	d_1	d_2
Recognition of Facial Emotion						
Happy Errors	0.0	0.0	0.0	0.2	0.0	0.0
Sad Errors	6.0	0.0	1.8	1.1	**5.5***	**3.8***
Neutral Errors	3.0	2.5	1.0	1.1	0.5	1.8
Fear Errors	1.0	1.5	0.3	0.6	**0.8***	**1.2***
Angry Errors	3.0	2.5	1.7	1.8	0.3	0.7
Disgust Errors	3.0	2.0	1.5	1.4	**0.8***	**1.1***
AR Total#	6.0	8.0	9.3	3.3	0.6	1.0
Theory of Mind						
TM Verbal	21.0	18.0	19.8	3.0	1.0	0.4
TM Total	23.0	23.5	25.3	3.6	0.1	0.6
Face Recognition						
MF Total#	7.0	7.0	10.3	3.1	0.0	1.1

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; AR Total = Affect Recognition Total; TM Total = Theory of Mind Total; TM Verbal = Theory of Mind Verbal; MF Total = Memory for Faces Total.

In Table 5.11, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to Sad Errors ($d_1 = 5.5$; $d_2 = 3.8$), Fear Errors ($d_1 = 0.8$; $d_2 = 1.2$) and Disgust Errors ($d_1 = 0.8$; $d_2 = 1.1$). The 17-year-old LiP participant obtained significantly higher error scores (poorer performance) than the mean error scores of matched controls and those of the ARN group on tasks that tap the ability to recognise sad and disgusted facial expressions accurately. The LiP participant obtained a significantly lower error score than the mean error score of the matched controls, but a significantly higher mean error score than the mean score of

the ARN group on a task that taps the ability to recognise fearful facial expressions accurately. Consequently, the H_0 hypothesis with regard to Sad Errors, Fear Errors, and Disgust Errors can be rejected.

Figure 5.24 graphically compares the McCall T-scores of the 17-year-old LiP participant (LP) on measures of social perception to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.24. The AR Total, TM Verbal, TM Total, and MF Total scores are not included in Figure 5.24, but are plotted in a separate graph (Figure 5.25).

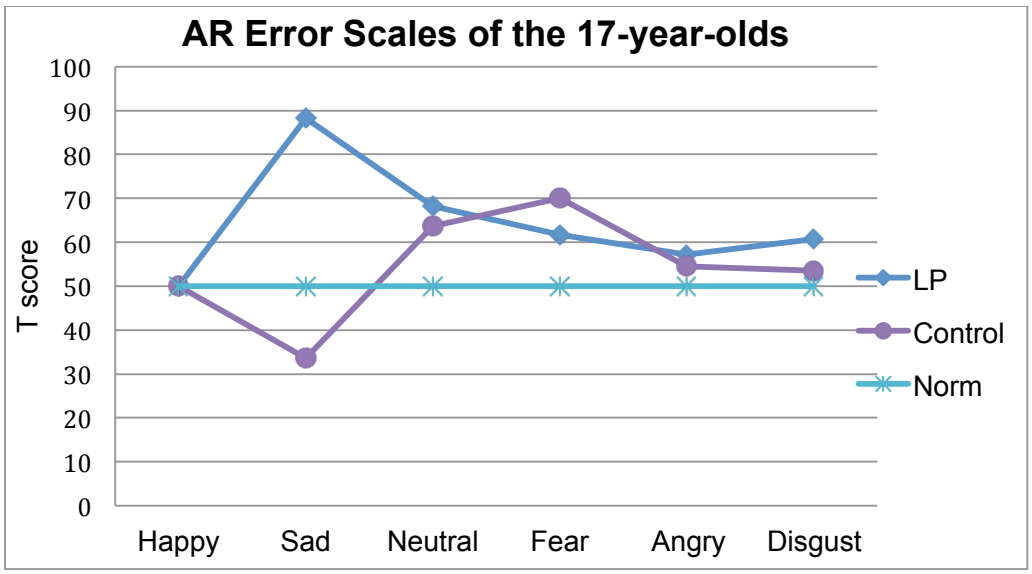

Figure 5.24. AR Error profiles of the 17-year-old participants.

In Figure 5.24, it is evident that the LiP individual made significantly more errors compared to the matched controls when required to recognise sad and disgusted facial expressions. The LiP participant's scores on these two scales were also significantly higher (more errors) compared to the mean score of the ARN group. Further, it is evident that the LiP participant made fewer errors compared to the matched controls when required to identify fearful facial expressions, but obtained a higher error score than the mean score of the ARN group on this task.

It is noticeable that the scores of the two controls are above the mean score of the ARN group (indicating more errors) on the Neutral Errors, Fear Errors, Angry Errors, and

Disgust Errors scales. The mean scores of the control participants on the Sad Errors scale are below the mean score of the ARN group.

Figure 5.25 graphically compares the performance of the LiP participant (LP) on the measures of social perception (AR Total, TM Verbal, TM Total, and MF Total) to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.25. A higher score on AR Total, TM Verbal, TM Total, and MF Total indicates a better performance.

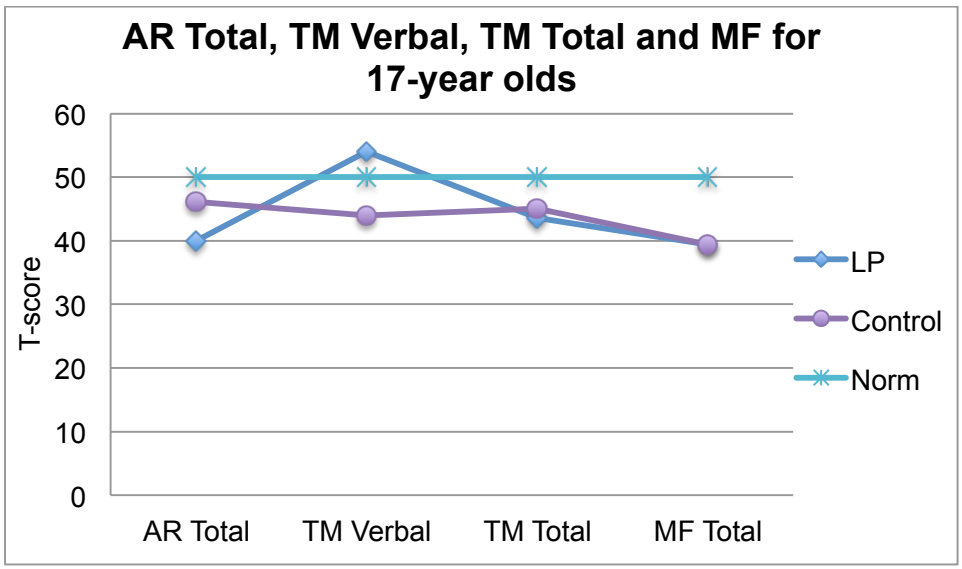

Figure 5.25. AR Total, TM Verbal, TM Total, and MF Total profiles of the 17-year-old participants.

In Figure 5.25, it is evident that the LiP participant's score is lower than the mean score of the matched controls and the ARN group on AR Total. However, the difference between the AR Total score of the LiP participant and the mean score of the controls is not significant. The LiP participant's score on TM Verbal is significantly higher than the mean score of the matched controls, but is not significantly different from the mean score of the ARN group. It is noticeable that the scores of the two controls are below the mean scores of the ARN group on all the social perception measures.

Summary of social perception profiles. Table 5.12 provides a summary of the effect sizes (d_1 and d_2) of every social perception construct of the 4-, 6-, 8-, 15- and 17-year-old participants to identify patterns in the findings. Effect sizes are marked with an asterisk

when both d_1 and $d_2 \geq 0.8$ (significant differences between the LiP participant's score and the mean scores of the control group and the ARN group on a particular measure). In some cases, the LiP participant performed better (fewer errors or higher scaled scores) than the controls and ARN groups did. Underlining effect sizes d_1 and/or d_2 in addition to marking the effect sizes with an asterisk will indicate these instances.

Table 5.12

Effect Sizes (d_1; d_2) of the 4-, 6-, 8-, 15- and 17-Year-Old LiP Participants on Measures of Social Perception

Social Perception Measures	**4-year-olds**		**6-year-olds**		**8-year-olds**		**15-year-olds**		**17-year-olds**	
	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**
Affect Recognition										
Happy Errors	0.9	0.1	0.0	0.6	1.3	0.5	0.0	0.0	0.0	0.0
Sad Errors	0.7	0.1	**1.0***	**1.2***	0.0	0.8	1.4	0.2	**5.5***	**3.8***
Neutral Errors	**1.7***	**1.2***	**3.3***	**2.2***	**3.3***	**3.8***	0.0	0.0	0.5	1.8
Fear Errors	**3.3***	**2.8***	1.7	0.5	0.0	0.1	1.7	0.5	**0.8***	**1.2***
Angry Errors	0.0	0.5	1.1	0.0	0.6	0.3	**1.7***	**1.8***	0.3	0.7
Disgust Errors	0.0	0.3	**1.3***	**0.9***	0.4	0.1	**0.8***	**1.1***	**0.8***	**1.1***
AR Total#	**1.6***	**0.9***	**1.6***	**1.5***	0.7	1.0	0.2	0.4	0.6	1.0
Theory of Mind										
TM Verbal	2.9	0.0	0.4	0.1	0.1	0.5	0.1	0.3	1.0	0.4
TM Total					0.1	0.3	0.1	0.3	0.1	0.6
Face Recognition										
MF Total			0.0	0.3	0.2	1.0	0.6	0.5	0.0	1.1

Note: * both d_1 and $d_2 \geq 0.8$; AR Total = Affect Recognition Total; TM Verbal = Theory of Mind Verbal; TM Total = Theory of Mind Total; MF Total = Memory for Faces Total.

In Table 5.12, it is evident that significant differences ($d \geq 0.8$) exist between LiP participants' scores and the mean scores of the matched controls (d_1), as well as between LiP participants' scores and the mean scores of the ARN group (d_2) on social perception measures, specifically recognition of facial emotion measures. Although a different profile

is evident for each LiP participant, it is noticeable that every LiP participant obtained scores that are significantly different from that of the control mean score (d_1) and norm group mean score (d_2) on one or more of the recognition of facial emotion measures. Each of the LiP participants performed significantly worse than their typically developing peers did on at least one of the error scales, indicating that each of the LiP participants found it more difficult than matched controls and the average individual in the ARN group did to recognise one or more facial expressions.

Compared to controls and the average individual in the ARN group, the 6- and 17-year-old LiP participants found it more difficult to recognise sad facial expressions, while the 4- and 8-year-olds found it more difficult to recognise neutral facial expressions. Both the 15- and 17-year-old LiP participants found it more difficult to recognise disgusted facial expressions, while the 15-year-old also found it difficult to recognise angry facial expressions compared to the controls and the ARN group. The only LiP participant who found it more difficult to recognise fearful facial expressions was the 4-year-old. Not one of the LiP participants made more errors than their typically developing peers did when required to recognise happy facial expressions.

It is evident that all the LiP participants made more errors compared to the matched controls and the average individual in the ARN group did on tasks requiring them to recognise negative facial expressions. However, no more errors were made than the matched controls and the average individual in the ARN group made when required to recognise a positive facial expression (happiness). Compared to their typically developing peers, the LiP participants did not find any specific negative facial expression more difficult to recognise.

It is interesting to note that the 6- and 17-year-old LiP participants performed significantly better compared to both the controls and the average individual in the ARN group on some measures of recognition of facial emotion. The 6-year-old LiP participant recognised neutral and disgusted facial expressions significantly better, while the 17-year-old LiP participant recognised fearful facial expressions significantly better than their typically developing peers did.

Finally, it is noticeable that there are no significant differences between any of the LiP participants' scores and the mean scores of the matched controls (d_1), as well as between

their scores and the mean scores of the ARN group (d_2) on measures of ToM (TM Verbal, TM Total) or face recognition (MF Total).

Social perception trajectories. One of the aims of the research was to explore developmental trends in the cognitive and psychosocial functioning of children and adolescents with LiP. To identify and describe developmental trends, graphs were plotted to represent the performance of the LiP participants on the social perception measures across the different age groups. No hypothesis is tested; therefore, this aspect of the research is purely explorative. Trajectories were plotted for every social perception construct. T-scores ($\overline{X} = 50$; $sd = 10$) were used to represent the performance and the mean scores of the LiP participants, the controls (Control) and the norm group (Norm).

Recognition of facial emotion (AR Error scales and AR Total). Figure 5.26 graphically compares the Happy Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.26.

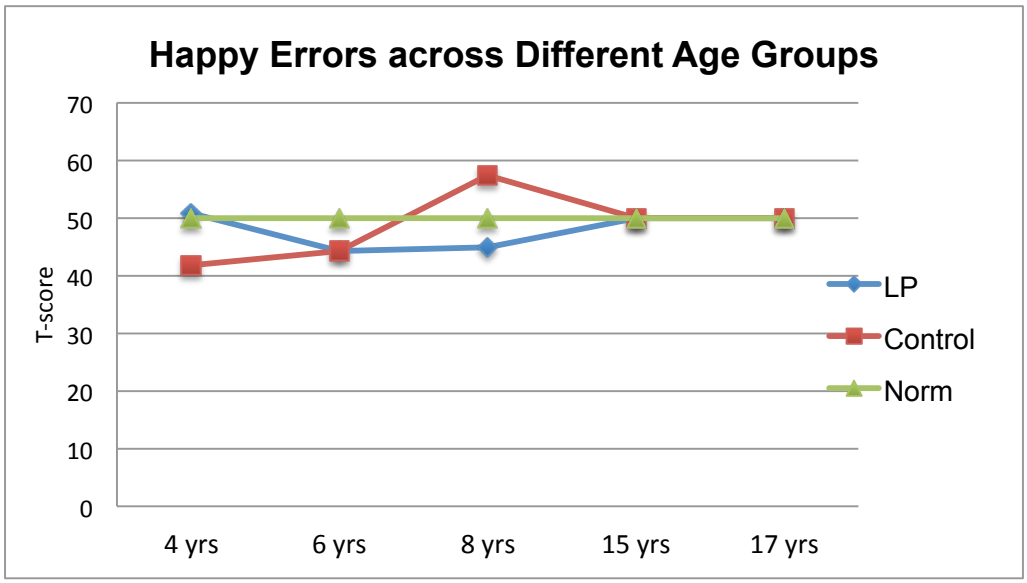

Figure 5.26. Happy Errors across the different age groups.

In Figure 5.26, it is evident that the 4-year-old ($d_1 = 0.9$) LiP participant made significantly more errors than the matched controls did when required to identify happy facial expressions, while the 8-year-old ($d_1 = 0.9$) LiP participant made significantly fewer

errors compared to the matched controls when required to identify happy facial expressions. Neither the 4-year-old ($d_2 = 0.1$) nor the 8-year-old ($d_2 = 0.5$) LiP participant obtained a score that is significantly higher (more errors) or lower (fewer errors) compared to the mean score of the ARN group. Therefore, not one of the LiP participants scored significantly below the mean score of the matched controls and the ARN group on Happy Errors.

The 4- and 6-year-old control participants scored below the mean score of the ARN group (fewer errors) on Happy Errors, while the 8-year-old controls scored above the mean score on this scale. No age-related trend is evident with regard to the recognition of happy facial expressions among the controls whose data are reflected in Figure 5.26.

Figure 5.27 graphically compares the Sad Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.27.

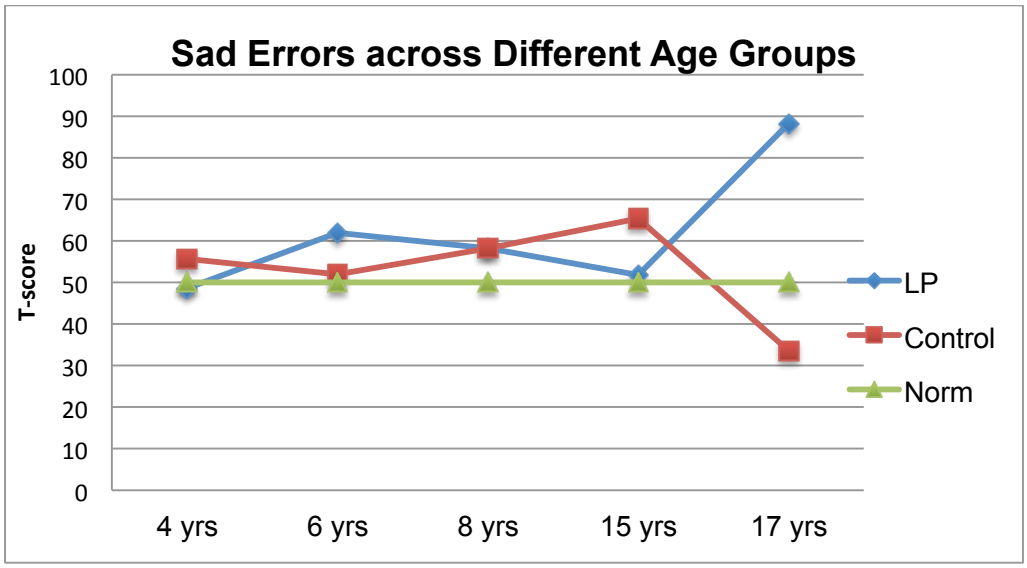

Figure 5.27. Sad Errors across the different age groups.

In Figure 5.27, it is evident that the scores of the 6-year-old ($d_1 = 1.0$) and 17-year-old ($d_1 = 5.5$) LiP participants on Sad Errors are significantly higher than the average score of the matched controls. The 15-year-old ($d_1 = 1.4$) LiP participant obtained a score that is significantly below (fewer errors) the average of the matched controls on Sad Errors. The 6-year-old ($d_1 = 1.2$) and 17-year-old ($d_1 = 3.8$) LiP participants also scored significantly

above (more errors) the mean score of the ARN groups on Sad Errors. The 8-year-old (d_2 = 0.8) LiP participant's score on Sad Errors is significantly above the mean score of the ARN group, but is the same as the mean score of the controls. Thus, no age-related trend is evident with regard to recognition of sad facial expressions among the LiP participants whose data are reflected in Figure 5.8.

The 8- and 15-year-old controls scored above the mean score of the ARN group on Sad Errors, while the 17-year-old LiP participant scored below the mean. No specific trend on the Sad Errors scale amongst the control participants is apparent.

Figure 5.28 graphically compares the Neutral Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.28.

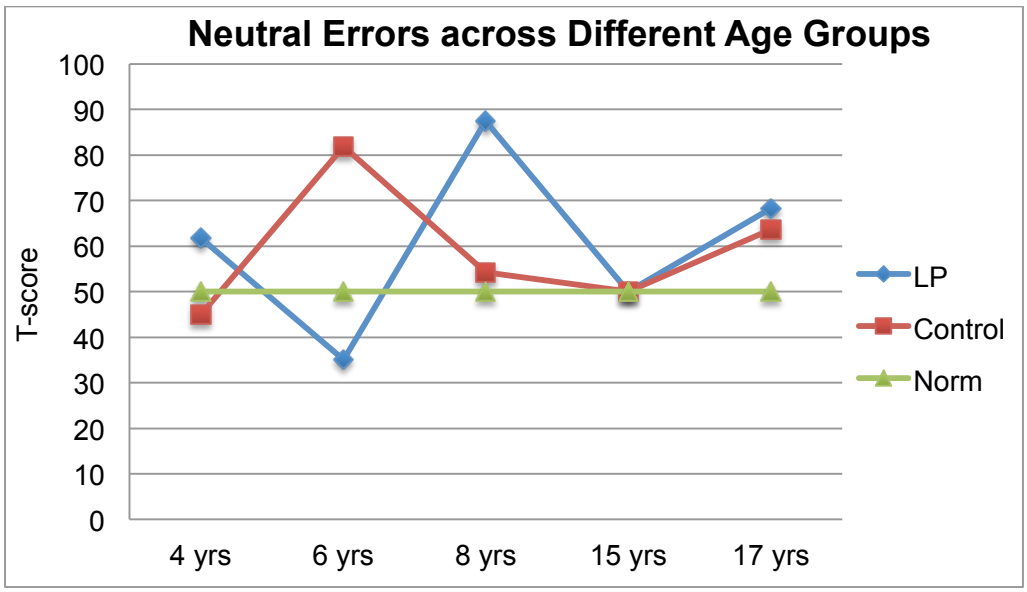

Figure 5.28. Neutral Errors across the different age groups.

In Figure 5.28, it is evident that the 6-year-old (d_1 = 3.3) LiP participant made significantly fewer errors on the Neutral Errors scale compared to the controls, while the 4-year-old (d_1 = 1.7) and 8-year-old (d_1 = 3.3) LiP participants made significantly more errors compared to the controls. The 4-year-old (d_2 = 1.2) and 8-year-old (d_2 = 3.8) LiP participants also scored above (more errors) the mean score of the ARN group on Neutral Errors, and the 6-year-old (d_2 = 2.2) LiP participant scored significantly below (fewer

errors) the mean score of the ARN group on this scale. Although the 17-year-old (d_1 = 0.5; d_2 = 1.8) LiP participant obtained a score that is significantly higher than the mean score of the ARN group on Neutral Errors, he performed similarly to the controls on this measure. Thus, no age-related trend is evident with regard to recognition of neutral facial expressions among the LiP participants whose data are reflected in Figure 5.28

It is further evident that the mean scores of the 6-, 8- and 17-year-old controls on the Neutral Errors scale are higher than the mean scores of the ARN group, while the 4-year-old control participant's score is lower than the mean score of the ARN group. Therefore, no age-related trend is evident with regard to recognition of neutral facial expressions by the control participants.

Figure 5.29 graphically compares the Fear Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.29.

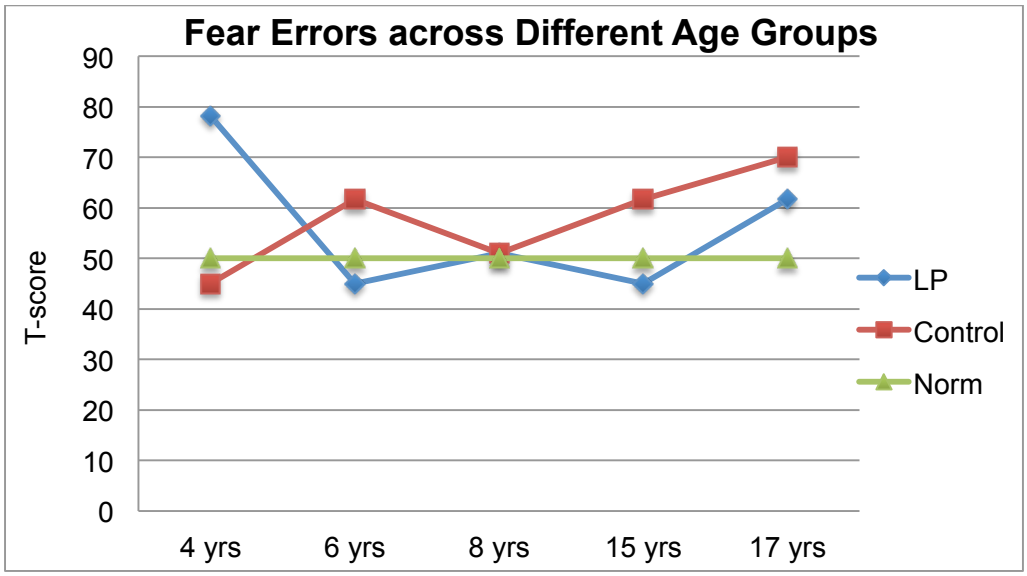

Figure 5.29. Fear Errors across the different age groups.

In Figure 5.29, it is evident that the 4-year-old (d_1 = 3.3) LiP participant's score on the Fear Errors scale is significantly above the mean score of the matched controls and the mean score of the ARN group. The 6-year-old (d_1 =1.7) and 15-year-old (d_1 = 1.7) LiP participants scored significantly below the mean scores of the matched controls, but their scores were not significantly below the mean score of the ARN group. Although the 17-

year-old LiP participant's score is significantly higher than the mean score of the ARN group (d_2 = 1.2), the score is also significantly lower than the mean score of the controls (d_1 = 0.8). Overall, only the youngest (4-year-old) LiP participant scored below both the mean score of the controls and the mean score of the ARN group.

The 6-, 15- and 17-year-old control mean scores are higher (more errors) than the mean scores of the ARN group, while the 4-year-old control mean score is lower (fewer errors) than the ARN mean score. No age-related trend among the control participants on Fear Errors is apparent.

Figure 5.30 graphically compares the Angry Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.30.

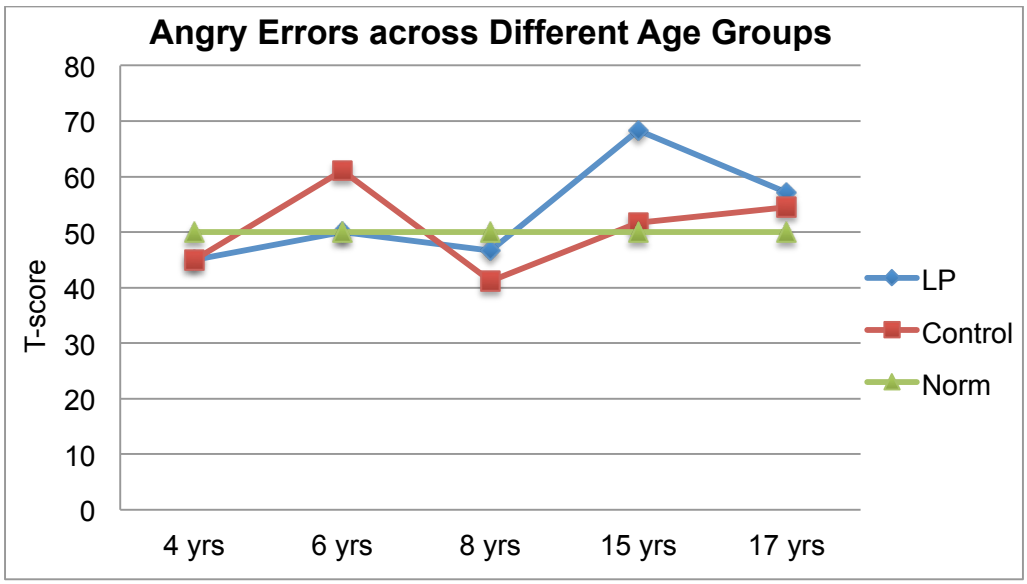

Figure 5.30. Angry Errors across the different age groups.

In Figure 5.30, it is evident that the 15-year-old (d_1 = 1.7) LiP participant's score on the Angry Errors scale is significantly higher, while the 6-year-old (d_1 = 1.1) LiP participant's score on this scale is significantly lower than the mean score of the matched controls. The 15-year-old (d_2 = 1.8) LiP participant's error score is also significantly higher compared to the mean score of the ARN group. Although the LiP participants' scores on the Angry Errors scale, relative to the mean scores of the ARN group, appear to

deteriorate (more errors) between the ages of 8 and 15 years, no age-related trend is evident if the scores are compared to the mean scores of the controls.

It is apparent that, compared to the mean scores of the ARN groups, the scores of the 6-, 15- and 17-year-old controls are higher. The 4- and 8-year-olds obtained scores lower than the ARN mean score. Thus, no age-related trend among the control participants with regard to recognition of angry facial expressions is evident.

Figure 5.31 graphically compares the Disgust Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.31.

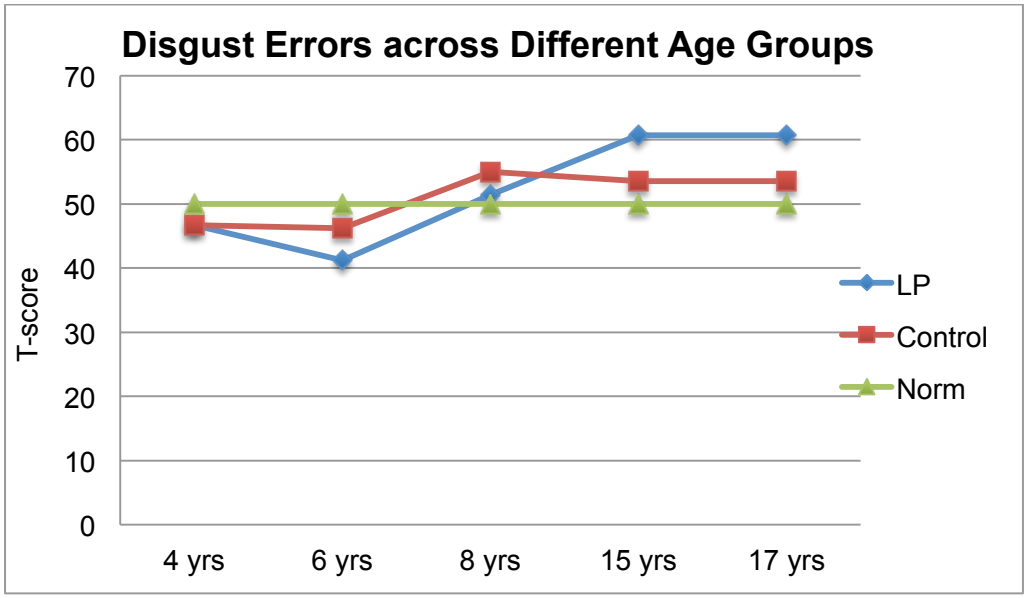

Figure 5.31. Disgust Errors across the different age groups.

In Figure 5.31, it is evident that the scores of the 15-year-old (d_1 = 0.8) and 17-year-old (d_1 = 0.8) LiP participants on Disgust Errors are significantly higher compared to the mean scores of matched controls, while the 6-year-old (d_1 = 1.3) LiP participant's score is significantly lower than the mean score of the controls. The scores of the 15-year-old (d_2 = 1.1) and 17-year-old (d_2 = 1.1) LiP participants on Disgust Errors are also significantly higher than the mean scores of the ARN group, while the 6-year-old (d_2 = 0.9) LiP participant's score on the same measure is also significantly below the mean score of the

ARN group. Thus, an increase in the error scores of the LiP participants between the ages of 6 and 15 years is evident.

An increase in the mean error scores of the control participants between the ages of 6 and 8 years is also evident on the Disgust Errors scale. The urban controls (4- and 6-year-olds) obtained scores on the Disgust Errors scale that are below the mean error scores of the ARN group. The 8-, 15- and 17-year-old rural controls obtained scores that are above the mean error scores of the ARN group. As there are differences between the urban and rural controls, these differences appear to explain the increase in mean error scores between the age of 6 and 8 years among the controls. However, these factors do not explain the increase in Disgust Errors scores between the ages of 6 and 15 years among the LiP participants, as the 8-year-old rural participant did not score significantly above either the mean score of the controls or the mean score of the ARN group.

Figure 5.32 graphically compares the AR Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) and the ARN group (Norm) across the different age groups.

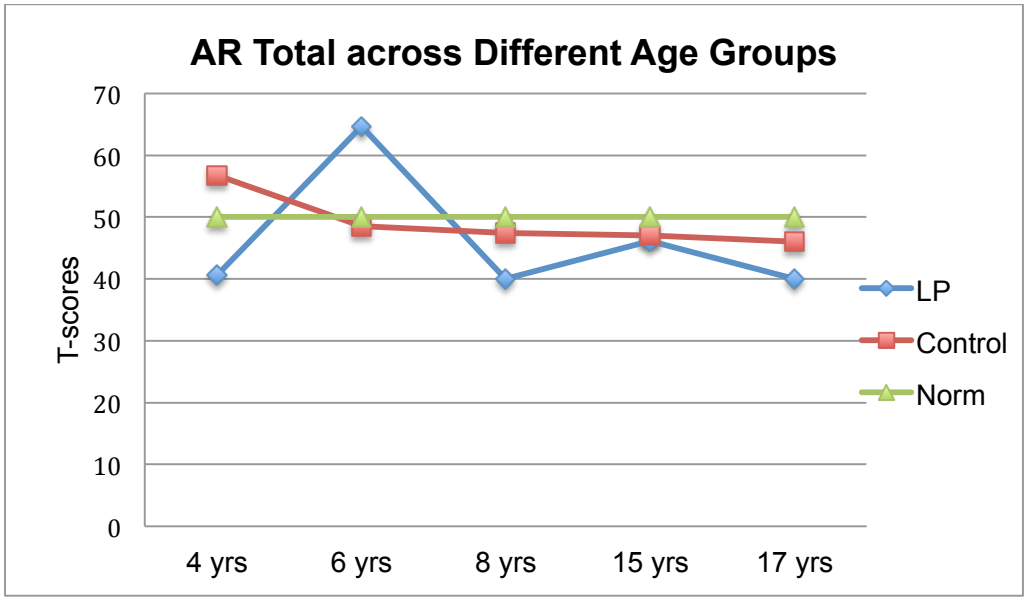

Figure 5.32. AR Total across the different age groups.

Figure 5.32 shows that the 4-year-old (d_1 = 1.6) LiP participant obtained a significantly lower score (indicating poorer recognition of facial emotion) on AR Total

compared to the mean score of the matched controls and the mean score of the ARN group. The 6-year-old (d_1 = 1.6) LiP participant obtained a significantly higher score than the mean score of the controls and a significantly higher score than the score of the ARN group on the same scale. The 8-year-old (d_2 = 0.9) and 17-year-old (d_2 = 1.0) LiP participants obtained scores that are significantly below the reported mean scores of the ARN group. However, their scores (8- year-old: d_1 = 0.7; 17-year-old: d_1 = 0.6) are not significantly below the mean scores of the controls. The 4-year-old participant is the only LiP participant that scored significantly below the mean scores of the controls and below the mean scores of the ARN group on AR Total. Thus, no-age-related trend is evident with regard to a general measure of recognition of facial emotion among the LiP participants whose data are reflected in Figure 5.32.

The mean scores of the controls on AR Total seem to deteriorate between the ages of 4 and 6 years, and then closely follow the trajectory of the reported mean scores of the ARN group. Therefore, the control participants generally performed somewhat similar to the average individual in the ARN group, except for the youngest control participants who performed better.

ToM (TM Verbal and TM Total). Figure 5.33 graphically compares the TM Verbal scores of the LiP participants (LP) to the mean scores of the matched controls (Control) and the ARN group across the different age groups.

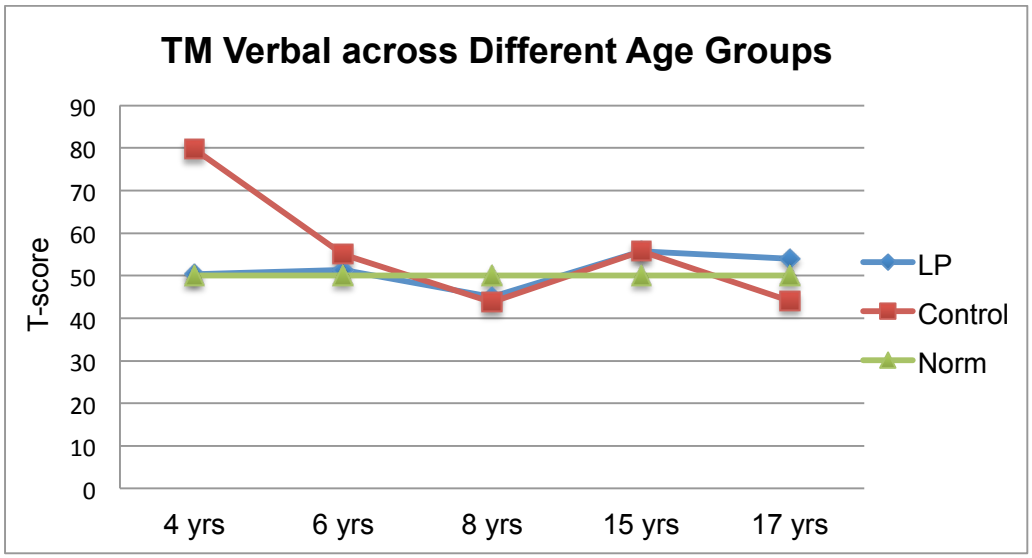

Figure 5.33. TM Verbal across the different age groups.

Figure 5.33 shows that the 4-year-old (d_1 = 2.9) LiP participant obtained a score that is significantly below the average of the matched controls, but this participant's (d_2 = 0.0) score is the same as the mean score of the ARN group. The 17-year-old (d_1 = 1.0) LiP participant obtained a score on TM Verbal that is significantly higher than the average of the controls, but this score is not significantly higher compared to the mean score of the ARN group. None of the other LiP participants (6-year-old: d_1 = 0.4; 8-year-old: d_1 = 0.1; 15-year-old: d_1 = 0.1) obtained scores that are significantly below or above the mean score of the matched controls. None of the LiP participants (4-year-old: d_2 = 0.0; 6-year-old: d_2 = 0.1; 8-year-old: d_2 = 0.1; 15-year-old: d_2 = 0.3; 17-year-old: 0.4) obtained scores on TM verbal that are significantly below or above the mean scores of the ARN group. None of the LiP participants' scores differs significantly from the mean scores of the controls and the mean scores of the ARN group.

The 4-year-old control participants scored above the mean score of the ARN group, while the 8-year-old and 17-year-old controls scored below the mean score of the ARN group. No specific trend among the controls with regard to TM Verbal could be identified.

Figure 5.34 graphically compares the TM Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.34. Norm group

mean scores for TM Total were not available for the younger age groups (4- and 6-year-olds); therefore, no data is represented for these two age groups.

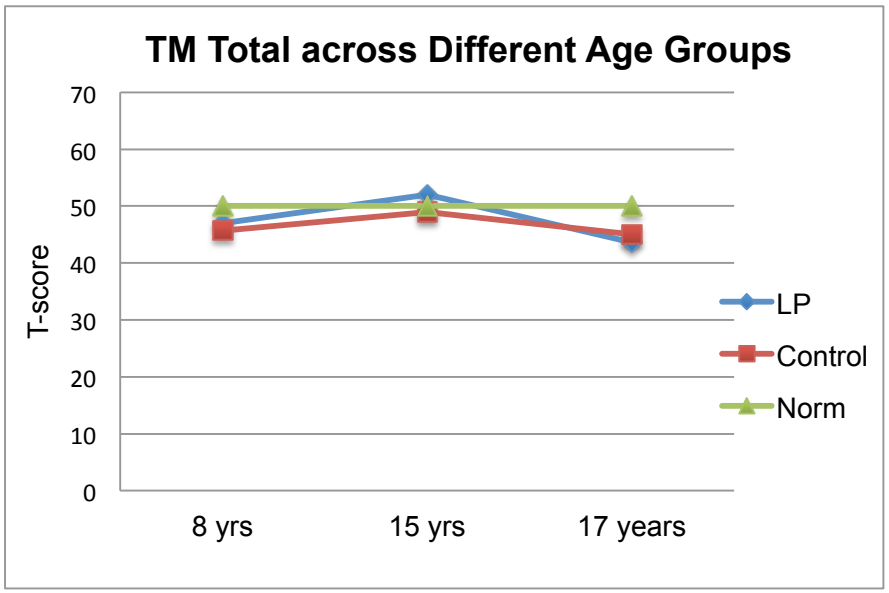

Figure 5.34. TM Total across the different age groups.

There are no significant differences between the LiP participants' and control participants' scores (8-year-old: $d_2 = 0.1$; 15-year-old: $d_2 = 0.1$; 17-year-old: $d_2 = 0.1$) on this measure. Furthermore, there are no significant differences between the LiP participants' scores (8-year-old: $d_2 = 0.3$; 15-year-old: $d_2 = 0.3$; 17-year-old: $d_2 = 0.6$) and the mean scores of the ARN group. Thus, none of the LiP participants scored significantly above or below the mean scores of the controls and the mean scores of the ARN group on a measure of ToM.

The 8- and 15-year-old controls scored below (but close to) the mean score of the ARN group, while the 17-year-old control scored below the mean score of the ARN group.

Face recognition (MF Total). Figure 5.35 graphically compares the MF Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.35. This measure was constructed and normed only for children who are 6 years and older; consequently, the test was not administered to the 4-year-old participants. Therefore, no data for the 4-year-old LiP participant are displayed.

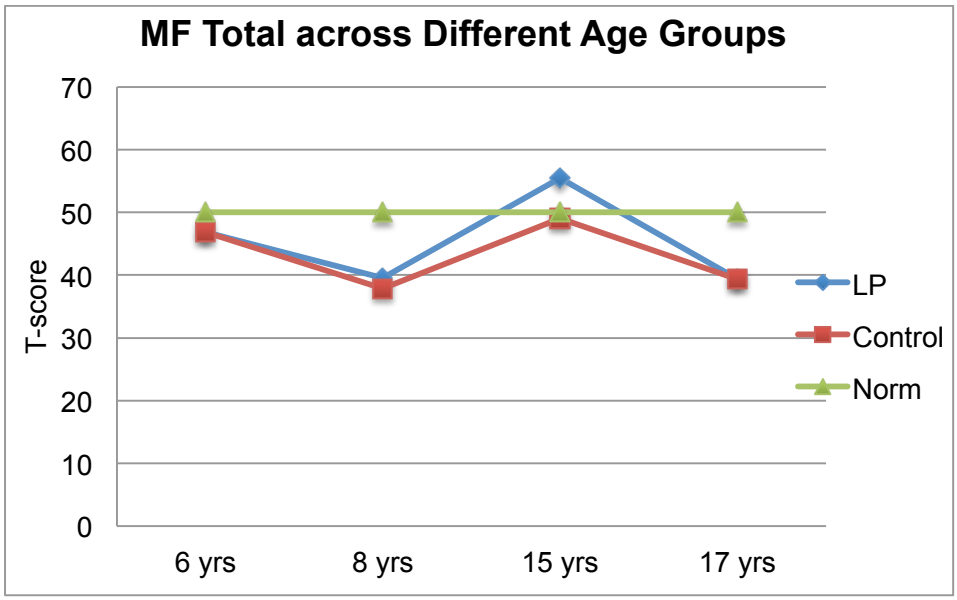

Figure 5.35. *MF Total across the different age groups.*

The 8-year-old (d_2 =1.0) and 17-year-old (d_2 =1.1) LiP participants obtained scores on MF Total that are significantly below the mean scores of the ARN group. However, it is evident in Figure 5.35 that none of the LiP participants (6-year-old: d_1 = 0.1; 8-year-old: d_1 = 0.2; 15-year-old: d_1 = 0.6; 17-year-old: d_1 = 0.0) obtained a score that is significantly below or above the mean scores of the controls on MF Total.

The 6-, 8- and 17-year-old control participants scored below the mean scores of the ARN group, but the mean score of the 15-year-olds is equivalent to the mean score of the ARN group. Therefore, all the LiP participants performed similarly to the matched controls in a task that requires recognition of and memory for faces. No age-related trend is evident with regard to the recognition of faces among the LiP or control participants whose data are reflected in Figure 5.8.

Summary of social perception trajectories.

Recognition of facial emotion. Compared to the mean scores of the controls and the age-appropriate norm group, only the 4-year-old LiP participant performed significantly worse, and the 6-year-old performed significantly better, on a measure of general recognition of facial emotion. Therefore, no age-related trend is evident with regard to general recognition of facial emotion among the LiP participants. The control participants generally performed equivalent to the average individual in the ARN group, except for the

youngest control participants who performed better. Therefore, the control participants have not been disadvantaged in this measure.

Recognition of happiness. No significant differences are evident between the LiP participants' scores and the mean scores of the matched controls and between the LiP participants' scores and the ARN group with regard to recognising happy facial expressions. The general tendency of the control participants was to score below (good performance) or equivalent to the mean scores of the ARN group on a task requiring them to recognise happy facial expressions, except for the 8-year-old control participants who made more errors in this task compared to the average number of errors reported for the ARN group.

Recognition of sadness. The 6- and 17-year-old LiP participants performed significantly worse (more errors) than the controls and the average person in the ARN group did when required to recognise sad facial expressions. Therefore, no age-related trend among the LiP participants is evident with regard to recognition of sad facial expressions. The 17-year-old LiP and control participants obtained noticeably different scores on the Sad Errors scale (LiP participant: significantly higher; control participant: noticeably lower).

Recognition of neutrality. It is evident that two LiP participants (the 4- and 8-year-olds) performed significantly poorer than their matched controls and the average person in the ARN group did when required to recognise neutral facial expression. The 6-year-old scored significantly below (fewer errors) the mean score of the matched controls and the mean scores of the ARN group. Thus, it is evident that there is no age-related trend among the LiP participants with regard to recognising neutral facial expressions.

In comparison to the mean scores of the ARN group, the scores of the 6- and 17-year-old control participants are higher (more errors), and no specific trend is evident in the performance of the control participants.

Recognition of fear. The youngest LiP participant (4-year-old) is the only LiP participant who performed poorer than both the controls and the average individual in the ARN group did on a scale measuring accurate recognition of fearful facial expressions.

Controls generally obtained scores that are above (6-, 15-year- and 17-year-olds) or equivalent (8-year-olds) to the mean score of the ARN group on Fear Errors, except for the 4-year-old controls who scored below (fewer errors) and the 8-year-old who performed similar to the mean score of the ARN group. No specific trend among the control participants with regard to fear recognition is evident.

Recognition of anger. The 15-year-old LiP participant was the only one who scored significantly above (more errors) both the mean score of controls and the mean scores of the ARN group. Therefore, no age-related trend among the LiP participants with regard to recognition of angry facial expressions is evident.

The 6-, 15- and 17-year-old controls obtained higher mean error scores than the average individual in the ARN group did, while the 4- and 8-year-olds obtained lower mean scores compared to the ARN group. No age-related trend among the controls in the recognition of anger was evident.

Recognition of disgust. Relative to the mean scores of the ARN group, an increase in errors on the Disgust Errors scale between the ages of 6 and 15 years is evident among the LiP participants. An increase in errors among the control participants between the ages of 6 and 8 years is also evident on the Disgust Errors scale. The 4- and 6-year-old controls obtained mean scores that are below (fewer errors) the mean score of the ARN group on the Disgust Errors scale, while the 8-, 15- and 17-year-old controls obtained scores that are higher (more errors). There are differences between the urban 4- and 6-year-old participants and the 8-, 15- and 17-year-old rural participants. It is likely that the evident increase in control mean scores between the ages of 6 and 8 years might be explained by these differences. Different from the control group, the 8-year-old rural LiP participant did not obtain a significantly higher error score than the ARN group did on the Disgust Errors scale. Therefore, the differences between the rural and urban LiP participants cannot explain the increase in errors among the LiP participants between the ages of 6 and 15 years.

ToM. None of TM Verbal and TM Total scores of the LiP participants was significantly above or below the mean scores of the controls and the mean scores of the ARN group. Therefore, the LiP participants' performance on two measures of ToM does

not differ significantly from the performance of the matched controls or the average individuals in the ARN group.

The 8- and 17-year-old controls scored below (fewer errors), and the 4-, 6- and 15-year-old controls scored above (more errors), the mean score of the ARN group on TM Verbal. Therefore, no age-related trend among the control participants with regard to TM Verbal is evident. The mean scores of the 8-, 15- and 17-year-old controls on TM Total closely follow the trajectory of the mean scores of the ARN group, indicating that these rural participants have not been disadvantaged in this measure.

Face recognition. Although the 8- and 17-year-old LiP participants obtained scores on a face recognition measure that are significantly below the mean scores of the ARN groups, the 8- and 17-year-old controls also scored below the mean scores of these groups. None of the LiP participants' scores on Face Recognition was significantly different from the mean scores of the controls and the reported mean scores of the ARN group. No age-related trend among the control participants with regard to the recognition and recall of faces is evident.

Conclusion: Social perception.

Significant differences. There are significant differences between the LiP participants' scores and the mean scores of the matched controls and between the LiP participants' scores and the mean scores of the ARN groups on measures of recognition of facial emotion, but no significant differences on measures of face recognition and ToM are evident.

The results on a general measure of recognition of facial emotion indicate that only the 4-year-old LiP participant's score is significantly lower than the mean scores of the controls and the ARN group. The results on the error scales of the recognition of facial emotion measure indicate that none of the LiP participants had difficulty in recognising happy (positive) facial expressions. However, all the LiP participants performed significantly worse than controls and the similarly-aged average person in the ARN group did in recognising at least one negative (sadness, anger, fear, disgust) and/or a neutral facial expression of emotion. However, there is no specific facial expression that all the LiP participants found difficult to recognise.

Two of the LiP participants performed better than the controls and the similarly aged average individual in the ARN group did when required to recognise certain facial expressions. The 6-year-old LiP participant performed better (fewer errors) when required to recognise neutral and disgusted facial expressions, while the 17-year-old LiP participant performed better when required to recognise fear.

Trends. There was a trend among the LiP participants not to perform significantly worse than their matched controls and the relevant norm groups did on measures of ToM and face recognition. No age-related trend among the LiP participants with regard to general recognition of facial emotion is evident.

No significant differences between the LiP participants' scores and the mean scores of both the matched controls and ARN groups across the different age groups on Happy Errors are evident. No age-related trends among the LiP participants with regard to recognition of sad, neutral, and angry facial expressions are evident. The youngest LiP participant (4-year-old) was the only LiP participant who performed worse than the typically developing children did when required to recognise fearful facial expressions.

Relative to the mean scores of the ARN group, an increase in errors on the Disgust Errors scale between the ages of 6 and 15 years is evident among the LiP participants. An increase in errors between the ages of 6 and 8 years is also evident among the control participants. Apparently, the evident increase in control scores between the ages of 6 and 8 years on Disgust Errors could be explained by differences between the urban and rural participants. However, the 8-year-old rural LiP participant did not obtain a significantly higher score than that of the ARN group on the Disgust Errors scale; therefore, these differences do not seem to explain the increase in errors among the LiP participants on the Disgust Errors scale.

Certain trends were observed with regard to the controls. Similar to the LiP participants, the controls also made more or fewer errors compared to the average individual in the ARN group when required to recognise different facial expressions. Not all of them made errors in recognising any specific facial emotion expression. No age-related trends among the controls other than on the Disgust Errors scale are evident. The trend of the control participants' performance on the AR Total and TM Total scales indicates that they were not disadvantaged on these measures.

Attention and Executive Function

The performance of the LiP children and adolescents on attention and executive function measures was compared to that of the matched controls and a norm group (the ARN group). The various aspects of attention and executive function measured include attention, processing speed, inhibition, switching, cognitive flexibility, and abstract thinking. The C-TRF, CBCL/1.5-5, TRF, and CBCL/6-18 were used to measure attention. NEPSY-II subtests (ST Total, ST Body Movement, ST Eye Opening, ST Vocalisation, IN Naming Errors, and IN Inhibition Errors) were used to measure inhibition. Cognitive flexibility and abstract thinking were measured by means of the IN Switching Errors and Animal Sorting Errors subtests of the NEPSY-II. Raw scores and scaled scores ($\overline{X}$ = 10; *sd* = 3) were used to compare the groups. Scores on all the tests were converted into McCall T-scores ($\overline{X}$ = 50; *sd* = 10) to compare the data in graphs.

Next, the differences in the mean scores of the 4-year-old LiP participant (compared to control and ARN group) on the attention and executive function measures/subtests will be reported and displayed graphically.

Four-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 4-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of memory and learning are reported in Table 5.13.

Table 5.13

Scores, Mean Scores, Standard Deviations, and Effect Sizes of the 4-Year-Old LiP Participant, Matched Controls, and Norm Group on Measures of Attention and Executive Function

Attention and Executive Function Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**		d_1	d_2
			$\overline{X}$	*sd*		
Attention						
Attention C-TRF	7.0	0.0	2.6	3.4	**2.1***	**1.3***
Attention CBCL	3.0	2.0	2.5	1.9	0.5	0.3
Executive function						
ST Total#	6.0	9.5	9.4	2.9	**1.2***	**1.2***
ST Body Movements	7.0	4.0	5.7	3.6	0.8	0.4
ST Eye Opening	11.0	1.5	4.5	3.8	**2.5***	**1.7***
ST Vocalisation	0.0	3.0	2.7	3.5	0.9	0.7

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; Attention C-TRF = Attention Problems C-TRF; Attention CBCL = Attention Problems CBCL; ST Total = Statue Total; ST Body Movements = Statue Body Movements; ST Eye Opening = Statue Eye Opening; ST Vocalisation = Statue Vocalisation.

In Table 5.13, it is apparent that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to the ST Total score ($d_1 = 1.2$; $d_2 = 1.2$), ST Eye Opening ($d_1 = 2.5$; $d_2 = 1.7$) and Attention C-TRF ($d_1 = 2.1$; $d_2 = 1.3$). Thus, the 4-year-old LiP participant scored significantly below the mean scores of the matched controls and the mean scores of the ARN group on tasks that tap the ability to inhibit motor responses to distractions. The LiP participant found it specifically difficult to inhibit the impulse to open her eyes in response to sounds. The responses of the LiP participant's teacher on the C-TRF indicate that the 4-year-old presented with more inattentive, hyperactive, and impulsive behaviour compared to matched controls and the average individual in the ARN group. However, parents did not rate the behaviour of the 4-year-old as problematic on the equivalent scale of the

CBCL/1.5-5 (Attention Problems). The 4-year-old LiP child's inattentive, impulsive, and hyperactive behaviour was more noticeable at school. Consequently, the H_0 hypothesis with regard to C-TRF Attention Problems, ST Total, and ST Eye Opening can be rejected.

Obtained differences on the Attention C-TRF, Attention CBCL and ST Error scales are visually represented in Figure 5.35. The score on ST Total (measuring the same construct as the ST Error scales) is interpreted differently from the other scores; therefore, the ST Total score is not represented in Figure 5.35. Data of the LiP child (LP), the ARN group (Norm) and the mean score of the controls (Control) are shown in Figure 5.35.

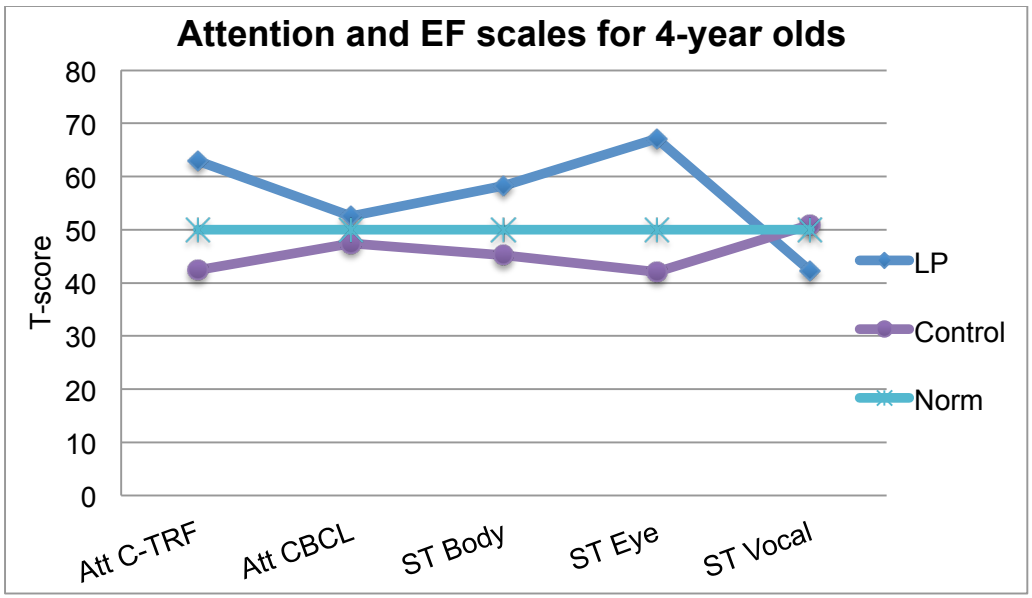

Figure 5.36. Attention and executive function profiles of the 4-year-old participants.

In Figure 5.36, it is evident that the LiP individual obtained higher scores and ratings (more errors, more problems) than matched controls did on all the executive function measures, except for ST Vocal and Attention CBCL. However, only scores on Attention C-TRF, ST Body Movement, and ST Eye Opening are significantly above the mean scores of the controls. It is noticeable that the scores of the two controls are below the mean score of the ARN group on Attention C-TRF, ST Body Movement, and ST Eye Opening.

Next, the differences in the scores of the 6-year-old LiP participant and the mean scores of the controls and the ARN group on the attention and executive function measures/subtests will be reported and displayed graphically.

Six-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 6-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of executive function are reported in Table 5.14.

Table 5.14

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 6-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Attention and Executive Function

Attention and Executive Function Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	d_1	d_2
Attention						
Attention C-TRF	3.0	0.0	2.6	3.4	0.9	0.1
Attention CBCL	5.0	0.0	2.5	1.9	**2.6***	**1.3***
Executive function						
ST Total#	11.0	9.5	10.8	2.3	0.7	0.1
ST Body Movements	4.0	3.5	2.7	2.6	0.2	0.5
ST Eye Opening	1.0	2.0	1.2	1.4	0.7	0.1
ST Vocalisation	1.0	1.5	1.6	2.5	0.2	0.2
INN Total Errors	3.0	3.0	4.9	3.4	0.0	0.6
INI Total Errors	11.0	11.0	10.4	7.6	0.0	0.1

Note: Data are presented as raw scores (different ranges) or scaled scores# (range 0-20, $\overline{X}$ = 10, *sd* = 3); * both d_1 and $d_2 \geq 0.8$; Attention C-TRF = Attention Problems C-TRF; Attention CBCL = Attention Problems CBCL; ST Total = Statue Total; ST Body Movements = Statue Body Movements; ST Eye Opening = Statue Eye Opening; ST Vocalisation = Statue Vocalisation; INN = Naming Total Errors; INI Total Errors = Inhibition Total Errors.

In Table 5.14, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2) with regard to the Attention Problems CBCL score ($d_1 = 2.6$; $d_2 = 1.3$). In comparison to her typically developing peers, the 6-year-old LiP participant received a significantly higher rating (significant higher μ) on the Attention Problems scale of the CBCL. This indicates that the LiP

participant's parents observed significantly more impulsive, hyperactive and inattentive behaviour at home compared to the parents of matched controls and the average parent in the ARN group. Consequently, the H_0 hypothesis with regard to CBCL Attention Problems can be rejected.

Obtained differences on the Attention C-TRF, Attention CBCL and ST Error scales are represented visually in Figure 5.37. The ST Total scaled score is interpreted differently from the raw error scores; therefore, the ST Total score will not be represented. Data for the LiP child (LP), the ARN group and the controls (Control), are shown in Figure 5.37.

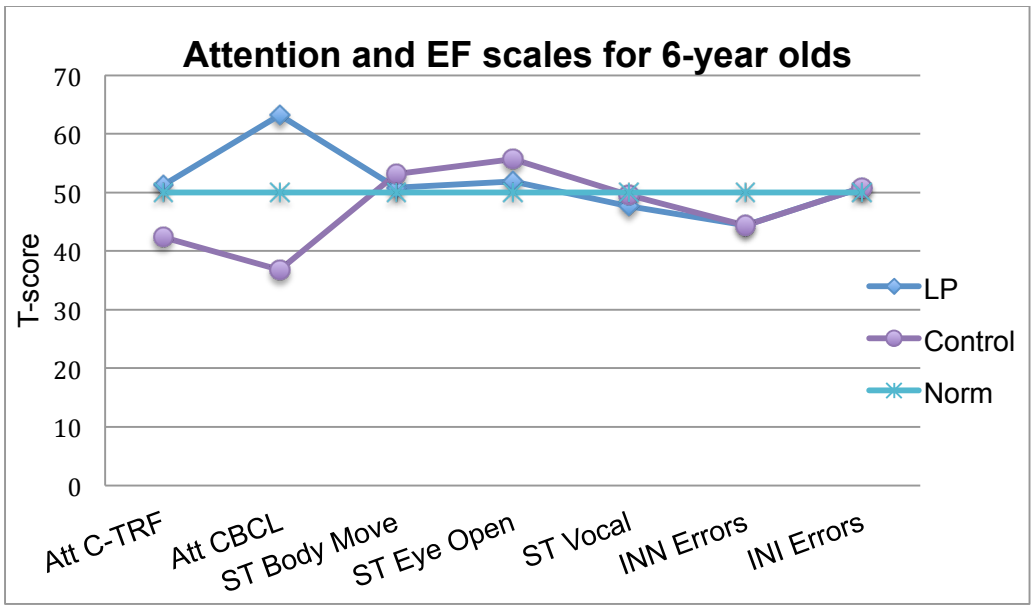

Figure 5.37. Attention and executive function profiles of the 6-year-old participants.

In Figure 5.37, it is evident that the LiP individual obtained a higher score than the mean score of the matched controls on Attention Problems C-TRF and Attention Problems CBCL. The LiP participant's teacher indicated that this participant presented with significantly more inattentive, hyperactive and impulsive behaviour at school compared to the matched controls. However, the LiP participant's score on this scale is not significantly higher than the mean score of the average individual in the ARN group. It is noticeable that the mean scores of the controls on Attention C-TRF and Attention CBCL are lower compared to the mean score of the ARN group (less impulsive, hyperactive, and impulsive behaviour was observed at school and at home).

Next, the differences in the mean scores of the 8-year-old LiP participant (compared to those of the control and ARN groups) on the attention and executive function measures/subtests will be reported and displayed graphically.

Eight-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 8-year-old LiP participant, the matched controls and the ARN group (Norm Group) on the measures of attention and executive function are reported in Table 5.15.

Table 5.15

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 8-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Attention and Executive Function

Attention and executive Function measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	***d_1***	***d_2***
Attention						
Attention TRF	18.0	10.5	11.3	11.0	0.7	0.6
Attention CBCL	4.0	2.5	4.1	3.2	0.5	0.0
Executive Function						
INN Total Errors	3.0	4.0	3.0	2.3	0.4	0.0
INI Total Errors	6.0	6.0	7.4	6.8	0.0	0.2
INS Total Errors	27.0	22.0	14.7	8.4	0.6	1.5
AS Total Errors	5.0	0.0	1.4	1.8	**2.8***	**2.0***

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Attention TRF = Attention Problems TRF; Attention CBCL = Attention Problems CBCL; INN = Naming Total Errors; INI Total Errors = Inhibition Total Errors; INS Total Errors = Switching Total Errors; AS Total Errors = Animal Sorting Total Errors.

In Table 5.15, it is evident that significant differences ($d \geq 0.8$) exist between the 8-year-old LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2) with regard to the AS Total Error score ($d_1 = 2.8$; $d_2 = 2.0$). The LiP participant made significantly more errors (significant higher μ) than the matched controls and the average person in the ARN

group did on the Animal Sorting task of the NEPSY-II. Therefore, the 8-year-old LiP participant's error score is significantly higher than the mean score of the controls and the mean score of the ARN group on a task that taps cognitive flexibility, self-monitoring, initiation, and abstract reasoning. Consequently, the H_0 hypothesis with regard to AS Total Errors can be rejected.

Figure 5.38 graphically compares the scores of the LiP participant (LP) to the mean scores of the matched controls (Control) across the measures of social perception that were administered. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.38.

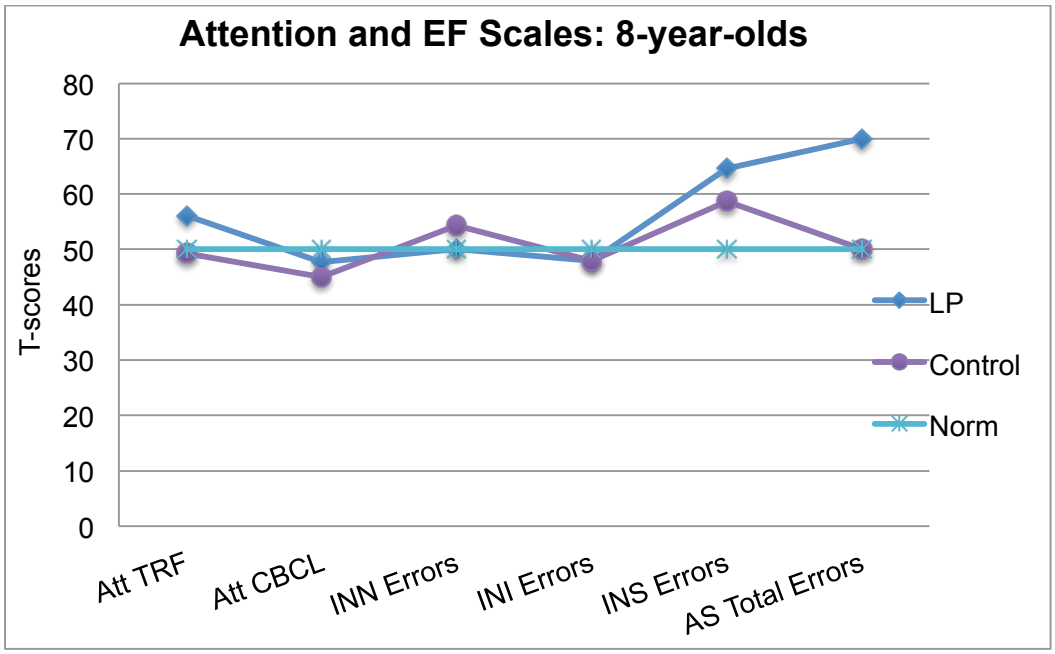

Figure 5.38. Attention and executive function profiles of the 8-year-old participants.

In Figure 5.38, it is evident that the LiP individual obtained higher T-scores on Attention Problems TRF (which is not significant), INS Errors (which is not significant) and AS Total (which is significant) compared to the matched controls. The LiP individual also obtained significantly higher T-scores than the ARN group did on the AS Total scale. It is noticeable in Figure 5.38 that the mean score of the two controls on INN and INS Errors is higher (worse performance) than the mean score of the ARN group. These are measures of processing speed and switching.

Next, the differences in the scores of the 15-year-old LiP participant compared to control and ARN group mean scores on the attention, and executive function measures/subtests will be reported and displayed graphically.

Fifteen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 15-year-old LiP participant, the two matched controls and the ARN group on the measures of attention and executive function are reported in Table 5.16.

Table 5.16

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 15-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Attention and Executive Function

Attention and executive Function measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	d_1	d_2
Attention						
Attention TRF	3.0	7.5	11.1	11.4	0.4	0.7
Attention CBCL	4.0	2.0	4.5	3.4	0.6	0.1
Executive Function						
INN Total Errors	2.0	5.5	0.5	1.0	**3.5***	**1.5***
INI Total Errors	6.0	9.0	1.9	2.2	**1.4***	**1.9***
INS Total Errors	9.0	22.0	6.0	5.7	2.3	0.5
AS Total Errors	6.0	2.5	1.4	1.6	**2.2***	**2.9***

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Attention TRF = Attention Problems TRF; Attention CBCL = Attention Problems CBCL; INN = Naming Total Errors; INI Total Errors = Inhibition Total Errors; INS Total Errors = Switching Total Errors; AS Total Errors = Animal Sorting Total Errors.

In Table 5.16, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the mean scores of the ARN group (d_2) with regard to the INN Total Errors score ($d_1 = 3.5$; d_2=1.5), the INI Total Errors score ($d_1 = 1.4$; $d_2 = 1.9$) and the AS Total Errors score ($d_1 = 2.2$; $d_2 = 2.9$). The LiP participant scored significantly below (fewer errors) the mean score of the matched controls on INN Total Errors, but

obtained a significantly higher score (more errors) than the mean score of the ARN group on the same measure. Similarly, the LiP participant obtained a score that is significantly below (fewer errors) the mean score of the matched controls on INS Total Errors, but obtained a score that is significantly higher than the mean score of the ARN group on the same measure. This indicates that the LiP participant performed significantly worse than the average person in the ARN group did on tasks that tap processing speed, inhibition and switching. However, the control participants performed worse than the LiP participant did on these measures of executive function. Therefore, the poor performance of the LiP participant is likely not due to the effect of LiP, but to factors that also affect the control participants. Both the LiP participant and the controls performed above (poorer performance) the mean score of the ARN group on a measure of processing speed (INN Total Errors). Therefore, a slow response speed may have affected the LiP and control participants' performance on the inhibition and switching measures negatively. The 15-year-old LiP participant obtained a score that is significantly higher (performed worse) than the mean scores of the matched controls and the ARN group on AS Total Errors, a task that taps self-monitoring, initiation, abstract reasoning, and cognitive flexibility. Consequently, the H_0 hypothesis with regard to INN Total Errors, INI Total Errors, and AS Total Errors can be rejected.

Figure 5.39 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) on measures of attention and executive function. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.39. A higher score represents a poorer performance or increased attention and executive function problems.

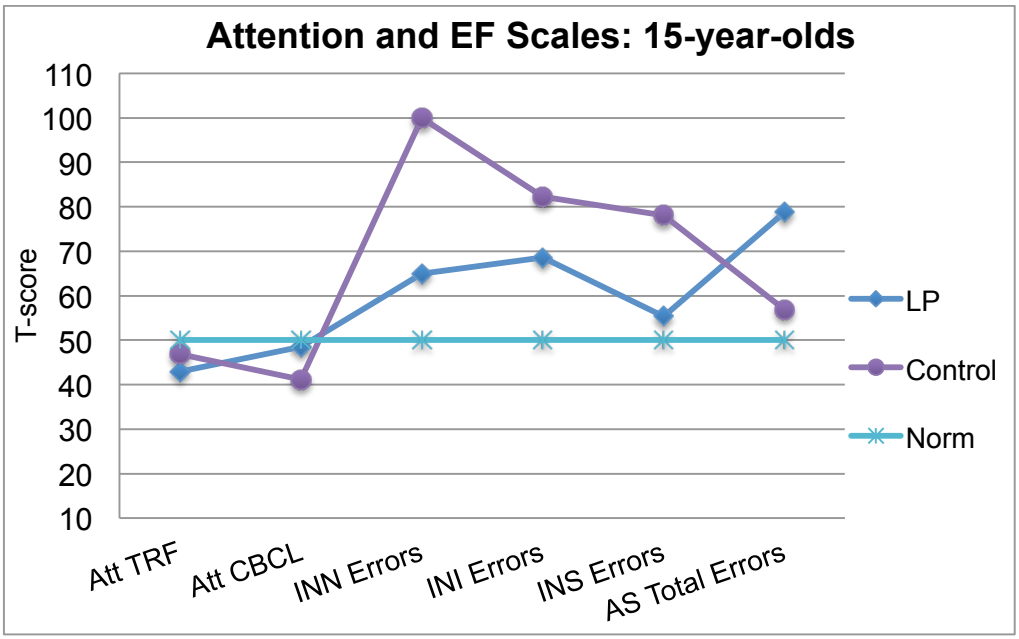

Figure 5.39. Attention and executive function profiles of the 15-year-old participants.

In Figure 5.39, it is evident that the LiP participant obtained higher scores than the matched controls did on Attention CBCL (which is not significant) and AS Total Errors (which is significant). The LiP participant made fewer errors (better performance) than the matched controls did on INN Errors (which is significant), INI Errors (significant) and INS Errors (significant), but made more errors on these scales than the average individual in ARN group did. It is noticeable that the scores of the two controls are above (worse performance) the mean score of the ARN group on INN Errors, INI Errors, INS Errors and AS Total Errors, tasks measuring executive function (processing speed, inhibition, switching and abstract thinking).

Next, the differences in the scores of the 17-year-old LiP participant compared to the mean scores of controls and the ARN group on the attention and executive function measures/subtests will be reported and displayed graphically.

Seventeen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 17-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of attention and executive function are reported in Table 5.17.

Table 5.17

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 17-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Attention and Executive Function

Attention and executive Function Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**		d_1	d_2
			$\overline{X}$	*sd*		
Attention						
Attention CBCL	12.0	2.0	4.5	3.4	**2.9***	**2.2***
Executive Function						
INN Total Errors	2.0	1.5	0.5	1.0	0.5	1.5
INI Total Errors	13.0	5.0	1.9	2.2	**3.6***	**5.0***
INS Total Errors	11.0	10.5	6.0	5.7	0.1	0.9
AS Total Errors	1.0	3.5	1.4	1.6	1.6	0.3

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Attention CBCL = Attention Problems CBCL; INN = Naming Total Errors; INI Total Errors = Inhibition Total Errors; INS Total Errors = Switching Total Errors; AS Total Errors = Animal Sorting Total Errors.

In Table 5.17, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to the Attention Problems CBCL scale ($d_1 = 2.9$; $d_2 = 2.2$) and the INI Total Errors scale ($d_1 = 3.6$; $d_2 = 5.0$). Therefore, the 17-year-old LiP participant obtained an error score that is significantly above (worse performance – significant higher μ) the mean score of the matched controls and the mean score of the ARN group in a task that taps the ability to inhibit responses (INI Errors). Parent ratings on the Attention Problems scale of the CBCL indicate that the 17-year-old LiP participant also exhibited more impulsive, hyperactive, and inattentive behaviour at home compared to the matched controls and the average individual in the ARN group. Consequently, the H_0 hypothesis with regard to Attention Problems CBCL and INI Total Errors can be rejected.

The obtained differences on the Inhibition Error scales and the Attention CBCL scales are represented visually in Figure 5.40 below. A higher score indicates worse performance

(INN Errors, INI Errors, INS Errors, and AS Errors) and problematic behaviour (inattentive, hyperactive, and impulsive behaviour). Figure 5.40 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) on measures of attention and executive function. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.40.

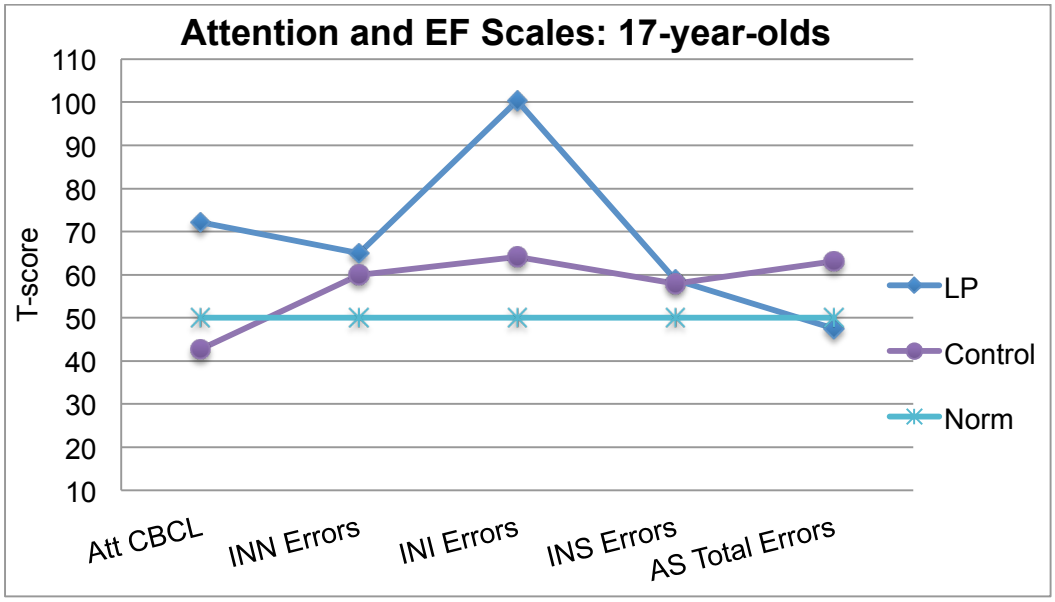

Figure 5.40. Attention and executive function profiles of the 17-year-old participants.

In Figure 5.40, it is evident that the LiP individual obtained a higher score than the matched controls did on the Attention Problems scale of the CBCL and the INI Errors scale. The LiP participant's score is also significantly higher than the mean score of the ARN group on these scales. The LiP participant obtained a lower score than the matched controls did on a task measuring cognitive flexibility (AS Total), but this score is not lower than the mean score of the ARN group. It is noticeable that the scores of the two controls are above (worse performance) the mean score of the ARN group on INN Errors, INI Errors, INS Errors, and AS Total Errors. These scales measure executive functions (processing speed, inhibition, switching).

Summary of attention and executive function profiles. Table 5.18 provides a summary of the effect sizes (d_1 and d_2) of every executive function construct in the various age groups to identify patterns in the performance of the different LiP participants. Effect sizes are marked with an asterisk when both d_1 and $d_2 \geq 0.8$. In addition to marking both

scores with an asterisk, the relevant effect sizes (d_1 and/or d_2) will be underlined when the LiP participant performed significantly better than the controls and the average individual in the ARN group did.

Table 5.18

Effect Sizes (d_1; d_2) of the 4-, 6-, 8-, 15- and 17-year-olds on Measures of Attention and Executive Function

Attention and Executive Function Measures	**4-year-olds**		**6-year-olds**		**8-year-olds**		**15-year-olds**		**17-year-olds**	
	***d*$_1$**	***d*$_2$**	***d*$_1$**	***d*$_2$**	***d*$_1$**	***d*$_2$**	***d*$_1$**	***d*$_2$**	***d*$_1$**	***d*$_2$**
Attention										
Attention CBCL	0.5	0.3	**2.6***	**1.3***	0.5	0.0	0.6	0.1	**2.9***	**2.2***
Attention C-TRF	**2.1***	**1.3***	0.9	0.1	0.7	0.6	0.4	0.7		
Executive Function										
ST Total#	**1.2***	**1.2***	0.7	0.1						
ST Body Movements	0.8	0.4	0.2	0.5						
ST Eye Opening	**2.5***	**1.7***	0.7	0.1						
ST Vocalisation	0.9	0.7	0.2	0.2						
INN Total Errors			0.0	0.6	0.4	0.0	**3.5***	**1.5***	0.5	1.5
INI Total Errors			0.0	0.1	0.0	0.2	**1.4***	**1.9***	**3.6***	**5.0***
INS Total Errors					0.6	1.5	2.3	0.5	0.1	0.9
AS Total Errors					**2.8***	**2.0***	**2.2***	**2.9***	1.6	0.3

Note: * Both d_1 and $d_2 \geq 0.8$; ST Total = Statue Total; ST Body Movements = Statue Body Movements; ST Eye Opening = Statue Eye Opening; ST Vocalisation = Statue Vocalisation; INN = Naming Total Errors; INI Total Errors = Inhibition Total Errors; INS Total Errors = Switching Total Errors; AS Total Errors = Animal Sorting Total Errors.

In Table 5.18, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participants' scores and the mean scores of the matched controls (d_1), as well as between the LiP participants' scores and the ARN group's mean scores (d_2) on the executive function measures. Although differences are evident for each LiP participant, no uniform profile of performance on the attention and executive function measures for all the participants is evident.

It is interesting to note that three of the LiP participants (4-, 6- and 17-year-olds) presented with significantly high ratings on a parent-rated measure of attention problems. The 4-year-old and 17-year-old LiP participants who obtained higher scores compared to the mean score of the controls and that of the ARN group on the Attention Problems syndrome scale also obtained scores that are above (worse performance) the mean error scores of these individuals on other measures of inhibition. The 4-year-old obtained an error score that is significantly above (worse performance) the mean score of the controls and that of the ARN group when she was required to inhibit responses to distractions on the Statue subtest. The 17-year-old participant obtained a significantly higher score than the controls and the average individual in the ARN group on a measure of inhibition of automatic responses.

As some executive functions develop fully only in older age groups, measures of switching response set are not readily available for younger children, and such a measure is also not included in the NEPSY-II. Therefore, the NEPSY-II AS subtest was constructed for children above the age of 6 years. Two of the three LiP participants (8- and 15-year-olds) to whom this subtest was administered scored above (more errors) the mean scores of the controls and the ARN group on this measure. Therefore, the 8- and 15-year-old participants performed worse than the controls and the similarly aged average individual in the ARN group did on a measure of cognitive flexibility, initiation of responses and conceptual reasoning. It is noticeable that there are no differences between the scores of any of the LiP participants and the mean scores of the matched controls (d_1) and between the score of the LiP participants and the mean score of the ARN group (d_2) on INS Total Errors (a measure of cognitive flexibility).

Finally, it is noticeable that the 15-year-old LiP participant was the only participant who obtained scores that are significantly below the mean score (better performance) of the matched controls on two measures of executive function (INN Errors and INI Errors). However, scores on these measures were not significantly below the mean scores of the ARN group.

Trajectories of attention and executive function. To identify developmental trends, graphs representing the performance of the LiP participants across the age groups on the different executive function measures were drawn. No hypothesis was tested; therefore,

this aspect of the research was purely explorative. Trajectories for every executive function construct were outlined. T-scores ($\overline{X}$ = 50; *sd* = 10) were used to represent the scores of the LiP participants, the mean scores of the controls (Control) and the mean scores of the ARN groups (Norm).

Attention (CBCL/1.5-5 and CBCL/6-18; C-TRF and TRF). Figure 5.41 graphically compares the Attention Problems CBCL/1.5-5 and CBCL/6-18 scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.41.

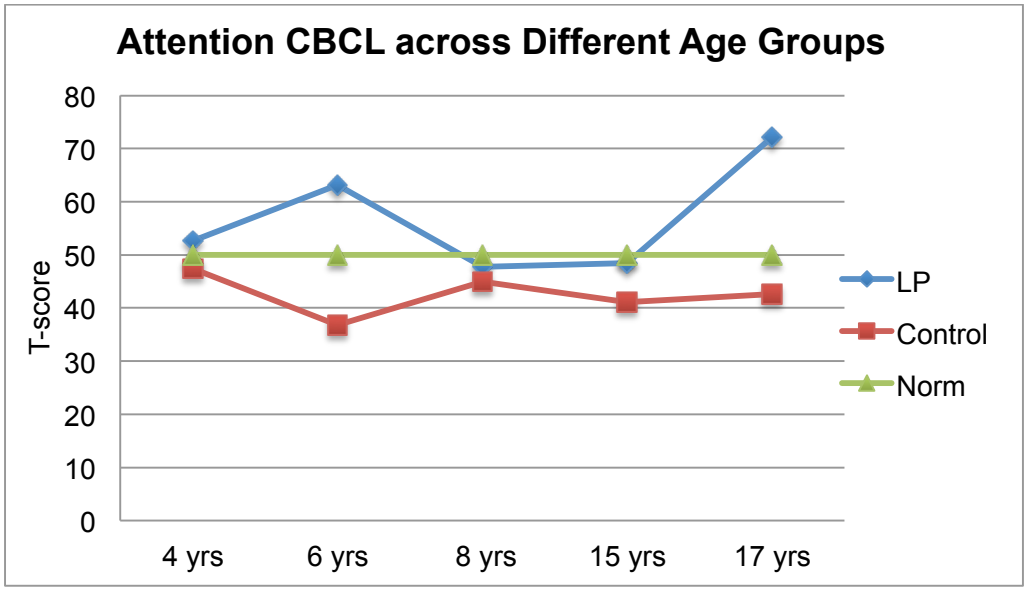

Figure 5.41. Attention CBCL across the different age groups.

In Figure 5.41, it is evident that the 6-year-old (d_1 = 2.6) and 17-year-old (d_1 = 2.9) LiP participants obtained significantly higher scores than the matched controls did on the CBCL scales. Furthermore, the scores of the 6-year-old (d_2 = 1.3) and 17-year-old (d_2 = 2.2) LiP participants on the Attention CBCL scale are also significantly above the mean score of the ARN group. Thus, no age-related trend is evident with regard to attention problems (CBCL) among the LiP participants.

In comparison to the reported mean scores of the ARN groups, none of the controls presented with higher scores on the CBCL Attention Problems scale. This was expected,

as potential controls were excluded from the study if they presented with any neuropsychiatric disorder (such as Attention Deficit Hyperactivity Disorder). These results indicate that the noted attention problems are likely associated with LiP rather than with another variable.

Figure 5.42 graphically compares the Attention Problems C-TRF or TRF scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.42. The 17-year-old LiP participant did not attend school; therefore, information on this participant's school functioning does not apply. Therefore, data for the 17-year-olds are not represented in Figure 5.42.

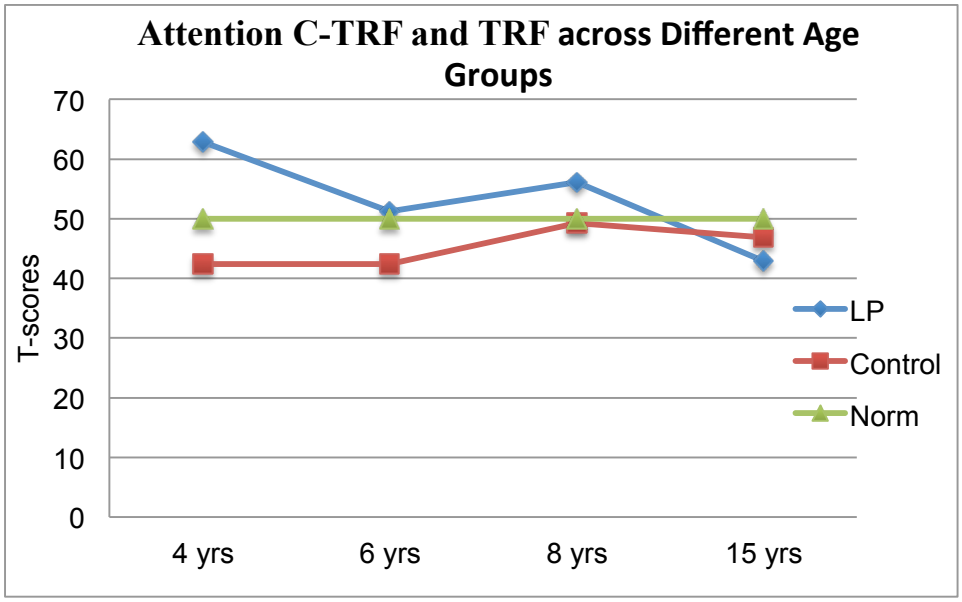

Figure 5.42. Attention C-TRF and TRF across the different age groups.

In Figure 5.42, it is evident that the 4-year-old (d_1 = 2.1) and 6-year-old (d_1 = 0.9) LiP participants obtained significantly higher ratings on the Attention Problems C-TRF compared to the matched controls. The score of the 4-year-old on the Attention Problems C-TRF scale (d_2 = 1.3) is also significantly above the mean score of the ARN group. The 6-, 8- and 15-year-old LiP participants did not present with significantly more attention problems compared to the average person in the ARN group. Thus, no age-related trend is evident with regard to attention problems (C-TRF) among the LiP participants whose data are reflected in Figure 5.42.

The controls obtained scores that are equivalent to (8-year-old or below (4-, 6- and 15-year-olds) the mean score of the ARN group on the Attention Problems C-TRF and TRF scales. Therefore, the screening method that was employed in this study was successful, as the aim was to exclude potential controls with neuropsychiatric disorders, such as ADHD, from the study.

Inhibition (ST Total scores). Figure 5.43 graphically compares the ST Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.43.

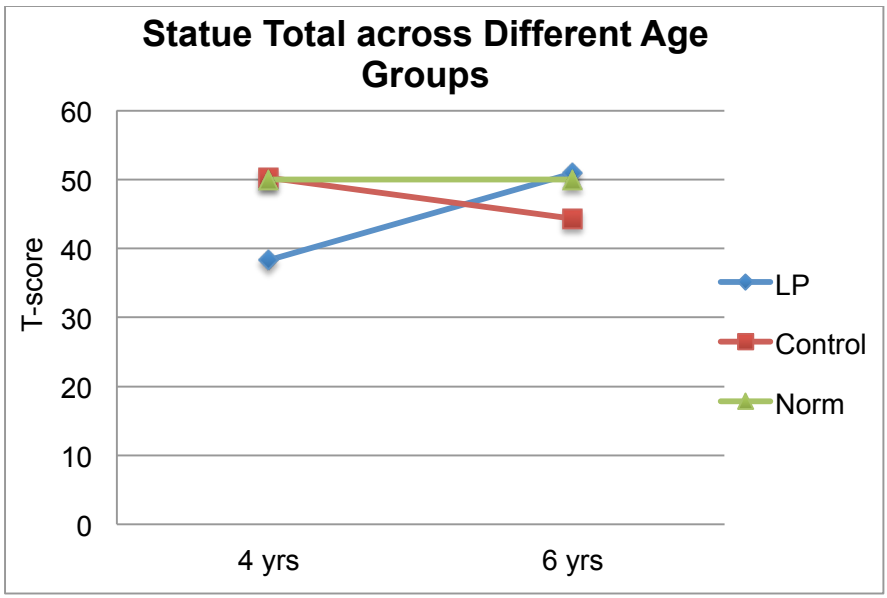

Figure 5.43. ST Total across the different age groups.

In Figure 5.43, it is evident that the 4-year-old (d_1 = 1.2; d_2 = 1.2) LiP participant obtained a significantly lower score in comparison to the mean score of the controls and the mean score of the ARN group on ST Total. Therefore, the younger urban female participant (4-year-old) performed worse than the matched controls and the average person in the ARN group did on a measure of behavioural inhibition. The older (6-year-old) urban female LiP participant's performance did not differ significantly from that of the typically developing children. No conclusions can be drawn with regard to possible age-related trends, as the graph depicts the performance of only two LiP participants.

The mean score of the 4-year-old controls is equivalent to the mean score of the ARN group, while the mean score of the 6-year-old controls is below the mean score of the ARN group. No conclusions can be drawn with regard to possible age-related trends.

Processing speed and inhibition (INN and INI Total Errors). Figure 5.44 graphically compares the INN Total scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.44. The Inhibition subtest of the NEPSY-II has not been constructed and normed for children younger than six years; therefore, the subtest was not administered to the 4-year-old participants.

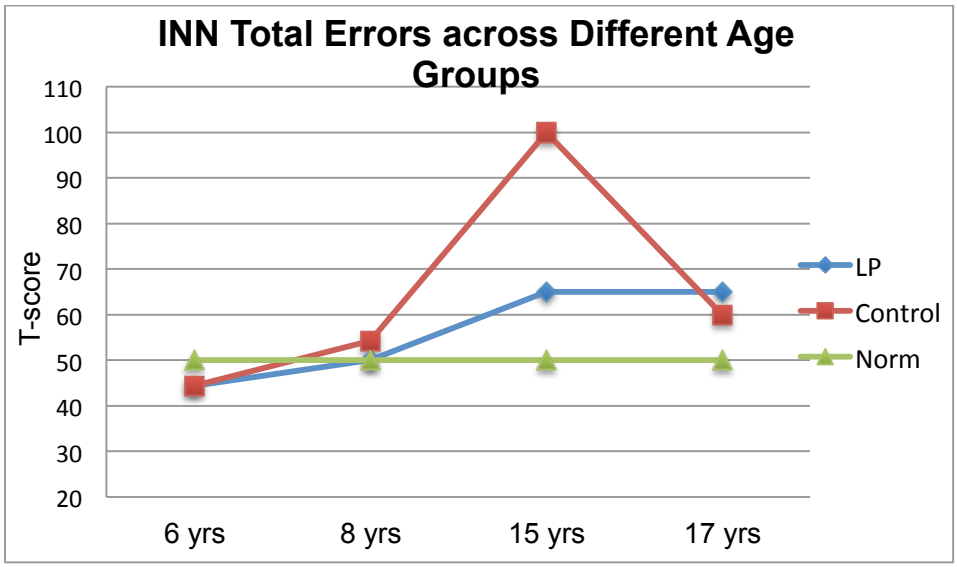

Figure 5.44. INN Total Errors across the different age groups.

In Figure 5.44, it is evident that the 15-year-old (d_2 = 1.5) and 17-year-old (d_1 = 1.5) LiP participants obtained significantly higher scores (worse performance) than the mean score of the ARN group on the INN Total Errors scale. However, the 15-year-old LiP participant's score (d_1 = 3.5) on this measure is significantly below the mean score of the matched controls (better performance). Therefore, although the 15-year-old LiP participant performed worse than the average individual in the ARN group did, the LiP participant performed significantly better than the controls did on this measure of processing speed. The 17-year-old LiP participant's score on INN Total Errors was not significantly different from the mean score of the controls. Thus, when the LiP

participants' scores are compared to the mean scores of the controls, no apparent age-related trend among the LiP participants with regard to processing speed (INN Total) is evident. However, when the LiP participants' scores are compared to the mean score of the ARN group, deterioration in scores between the ages of 8 and 15 years is apparent.

Figure 5.44 indicates that the scores of the 6- and 8-year-old LiP participants did not differ significantly from the mean score of the ARN group, while the 15- and 17-year-old LiP participants scored significantly above (more errors) the mean score of the ARN group. Therefore, deterioration in scores is evident between 8 and 15 years of age. However, a similar trend is apparent among the controls. The 15- and 17-year-old controls also scored above the ARN group mean (more errors) on INN Total Errors, while the scores of the 6- and 8-year-old controls are very similar to the mean scores of the ARN group. Therefore, the apparent increase (deteriorating performance) in the LiP participants' scores between the ages of 8 and 15 years on this scale does not seem to be related solely to the effect of LiP.

Figure 5.45 graphically compares the INI Total Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.45. The subtest INI Total Errors is not administered to children younger than six years; therefore, no data for the 4-year-old participants are presented.

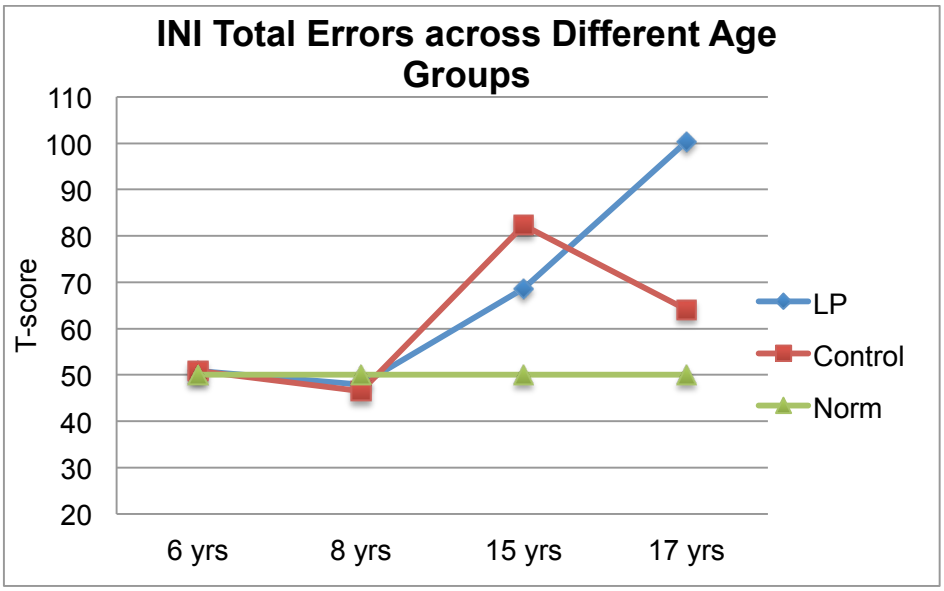

Figure 5.45. INI Total Errors across the different age groups.

The 15-year-old (d_1 = 1.4; d_2 = 1.9) LiP participant's score on INI Total Errors is significantly higher (worse performance) than the mean score of the ARN group. However, the 15-year-old LiP participant's score on this scale is significantly below the mean score of the matched controls (indicating better performance). In Figure 5.45, it is apparent that the score of the 17-year-old (d_2 = 5.0) LiP participant on INI Total Errors is significantly above the mean score of the ARN group (indicating poorer performance). The 17-year-old (d_1 = 3.6) LiP participant also obtained a significantly higher score than the mean score of the matched controls on INI Total Errors (indicating poorer performance). Therefore, the 17-year-old LiP participant, who was the oldest participant, was the only LiP participant who made more errors compared to matched controls and the average individual in the ARN group on a measure of inhibition.

A similar trend to what was identified on the INN Total Errors scale (Figure 5.44) is apparent on this scale. The scores of the 6- and 8-year-old LiP participants did not differ significantly from the mean scores of the ARN group. However, the scores of the 15- and 17-year-old LiP participants, similar to their performance on INN Total Errors, obtained error scores that are above the mean scores of the ARN group on INI Total Errors.

The increase in scores evident among the LiP participants between the ages of 8 and 15 years, relevant to the mean score of the ARN group, is also evident among the controls.

The 6-year-old and 8-year-old controls obtained scores that are equivalent to the mean scores of the ARN group, while the 15- and 17-year-old controls scored above the ARN group mean on this measure of inhibition (INI Total Errors). However, the increase in scores between the ages of 15 and 17 years among the LiP participants is not evident among the controls. The conclusion is that the apparent increase in the scores of LiP participants between the ages of eight and 15 years on this scale (indicating deteriorating performance) does not seem to be related solely to the effect of LiP.

Cognitive flexibility (INS Total Errors and AS Total). Figure 5.46 graphically compares the INS Total Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.46. This scale is not administered to children younger than seven years; therefore for the 4- and 6-year-olds are presented.

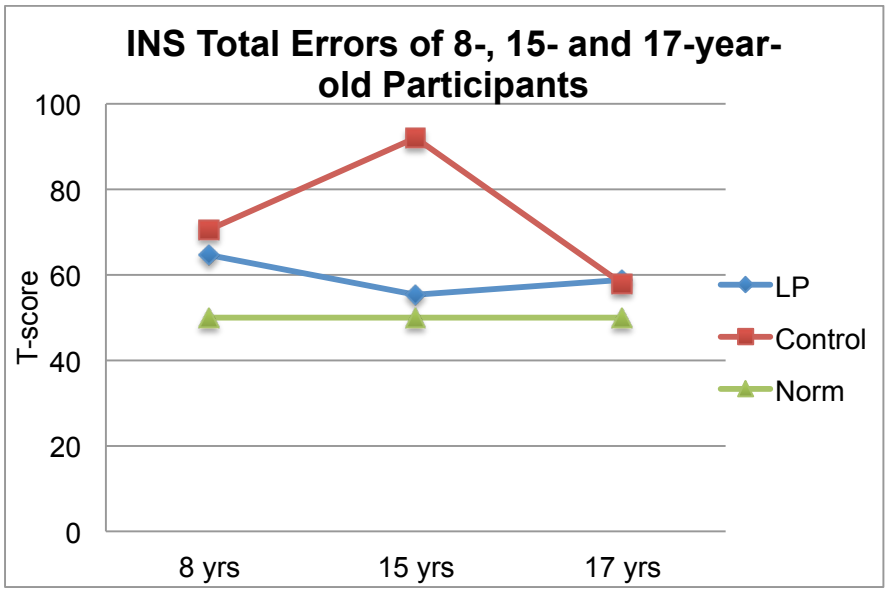

Figure 5.46. INS Total Errors across the different age groups.

In comparison to the reported mean scores of the ARN group, the scores of the 8-year-old (d_2 = 1.5) and 17-year-old (d_2 = 0.9) LiP participants are significantly higher (more errors). However, it is evident that none of the LiP participants has obtained a score on INS Errors that is significantly above the mean score of the matched controls (Figure 5.46). The 15-year-old (d_1 = 2.3) LiP participant's score on INS Total Errors is significantly below the mean score of the matched controls (indicating better

performance). All the controls also scored above (more errors) the mean scores of the ARN group on this measure of cognitive flexibility. In this instance, the matching of controls appears to have been essential, as it placed the LiP participants' performance in the context of the performance of individuals from a similar background.

Figure 5.47 graphically compares the AS Total Errors scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.47. This scale is not administered to children younger than seven years; therefore, no data for the 4- and 6-year-olds are presented.

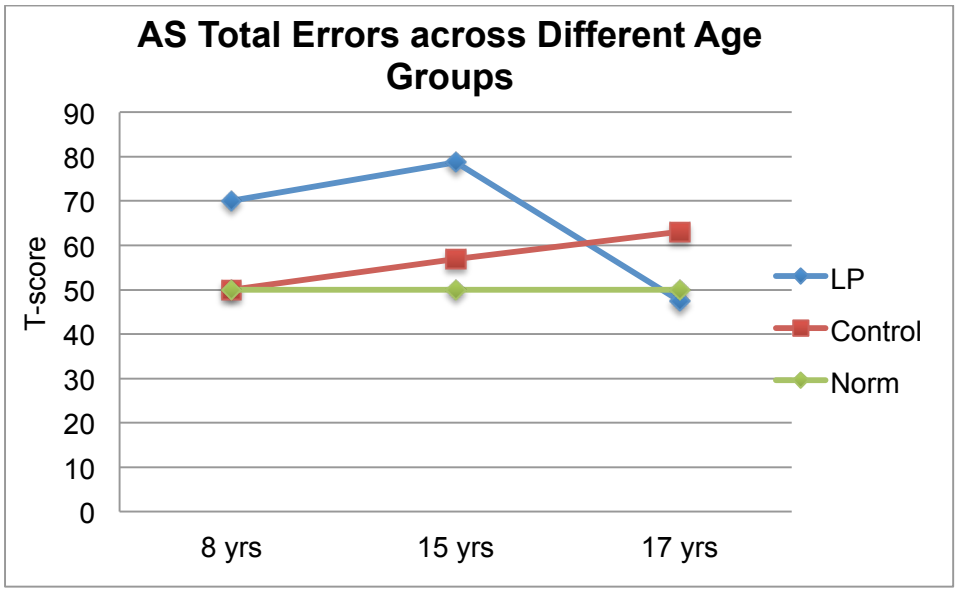

Figure 5.47. AS Total Errors across the different age groups.

In Figure 5.47, it is evident that the 8-year-old (d_1 = 2.8; d_2 = 2.0) and 15-year-old (d_1 = 2.2 d_2 = 2.9) LiP participants obtained higher error scores than the mean scores of the controls and the mean scores of the ARN group on AS Total Errors. Thus, there seems to be no specific age-related trend with regard to cognitive flexibility and abstract thinking among the LiP participants.

The 8-year-old control participants' score is equivalent to the ARN group mean, while the 15- and 17-year-old controls obtained higher scores than the average individual in the

ARN group did on AS Total. A similar tendency among the controls is evident on measures of processing speed (INN) and inhibition (INI) [Figure 5.44 and Figure 5.45].

Summary of attention and executive function trajectories.

Attention. Although the 4-year-old (at school) and the 6- and 17-year-old (at home) LiP participants presented with significantly more attention problems compared to their healthy peers, no age-related trends among the LiP participants with regard to attention problems are evident.

All the control participants obtained scores that are lower than or equal to the mean scores of the ARN groups on the ASEBA (CBCL/1.5, CBCL/6-18, C-TRF, TRF) Attention Problems scales. The controls were screened, and one of the criteria for exclusion was a neuropsychiatric disorder such as ADHD. The results of the control participants on the CBCL Attention Problems scale suggest that the screening method that was employed was successful.

Processing speed. The 6- and 8-year-old LiP participants obtained scores that are lower than (6-year-old) or equivalent to (8-year-old) the mean scores of the ARN group, while the 15- and 17-year-old LiP participants obtained higher error scores (indicating poorer performance) compared to the mean error scores of the ARN group. A similar trend is noted among the control participants, and none of the LiP participant's scores is significantly below the mean scores of the controls. Therefore, the apparent increase in LiP participants' scores between the ages of 8 and 15 years on a measure of processing speed does not seem to be related solely to LiP.

Inhibition. The 4-year-old LiP participant performed worse than the matched controls and the average individual in the ARN group in a task requiring behavioural inhibition (ST Total). In comparison to these typically developing peers, the 6-year-old did not perform worse on this measure.

In comparison to the ARN group mean on a specific measure of inhibition (INI), the 6- and 8-year-old LiP participants obtained equivalent scores, while the 15- and 17-year-old LiP participants obtained scores that are significantly higher. This trend is also evident among the control participants. However, the 17-year-old LiP participant's scores are significantly above the mean scores of the controls on this measure of inhibition (INI).

Therefore, the apparent increase in the scores of LiP participants between the ages of 8 and 15 years on a measure of inhibition does not seem to be related solely to LiP. However, an increase in scores between the ages of 15 and 17 years is evident among the LiP participants, but not among the control participants, on this measure.

Cognitive flexibility. None of the LiP participants scored above the mean score of the controls on the measure of cognitive flexibility (INS Total Errors), while the 8- and 17-year-old LiP participants scored significantly above the mean scores of the ARN group on INS Total Errors. This indicates that no particular trend on this measure of cognitive flexibility is evident.

The 8-, 15- and 17-year-old control participants all scored above the mean scores of the ARN group (indicating more errors) on the INS Total Errors scale. This indicates that it was pertinent to match LiP participants with controls in order to compare their performance on this scale with the performance of individuals from the same background.

The 8- and 15-year-old LiP participants obtained significantly higher error scores than the controls and the average individual in the ARN group did on another measure of cognitive flexibility (AS Total Errors). However, the 17-year-old LiP participant's score on this measure of abstract thinking and cognitive flexibility was significantly below the mean score of the matched controls (indicating better performance) and did not differ significantly from the mean score of the ARN group. Therefore, no particular age-related trend on this measure of cognitive flexibility and abstract thinking (AS Total Errors) was noted.

The LiP participants performed differently on the INS Total Errors and AS Total Errors scales. Therefore, the performance of the LiP participants on measures of cognitive flexibility depended on which particular instrument (INS Total versus AS Total) was used. An explanation may be that these two scales do not measure the same construct precisely.

In comparison to the mean scores reported for the ARN group on the AS Total scale, the 8-year-old controls obtained an equal score, while the 15- and 17-year-old controls obtained higher scores (more errors). This trend among the controls is also observed on all the other measures of executive function (INN Total, INI Total, and AS Total), except for the NEPSY-II INS Total subscale (cognitive flexibility and abstract thinking).

Conclusion: Attention and executive function.

Significant difference. Significant differences between the LiP participants and the matched controls and between the LiP participants and the ARN groups are apparent on the attention, processing speed, inhibition, and cognitive flexibility scales. No individual LiP child had difficulties that are apparent on all scales. Every LiP participant had a different executive function profile. The parents and teachers of three of the LiP participants (4-, 6- and 17-year-olds) indicated that they presented with significantly more attention problems than their peers did. Attention problems either at home (6- and 17-year-olds) or in school (4-year-old) were noted. The 4- and 17-year-old LiP participants, who received significantly higher scores on Attention Problems scales, also performed significantly worse than controls and the average individual in the ARN group did on measures of inhibition (Statue Total and INI Errors Total). None of the LiP participants performed worse than their typically developing peers did on a measure of processing speed. Two LiP participants (8- and 15-year-olds) performed significantly worse than controls and the average individual in the ARN group did on one measure of cognitive flexibility (AS Total). However, these LiP participants did not perform significantly worse than controls and the average person in ARN groups did on another measure of cognitive flexibility (INS Total Errors scale).

Trends. No age-related trends with regard to measures of attention among the LiP participants are evident. Factors that were unique to every LiP participant determined the extent of their attention problems, as observed by their parents and teachers. None of the controls scored below the mean score of the ARN group on measures of attention (CBCL; C-TRF).

In the graphs depicting the scores of the LiP and control participants on measures of processing speed and inhibition, it is apparent that the 6- and 8-year-old LiP participants obtained scores that are equal to or below the scores of the ARN groups (indicating better performance). The 15- and 17-year-old LiP participants obtained scores that are significantly above (more errors) the mean scores of the ARN groups on these measures. Therefore, an increase in scores between the ages of 8 and 15 years among the LiP participants on all measures of processing speed an inhibition is evident. Such an increase in scores between the ages of 8 and 15 years is also evident among the controls on these

measures. Therefore, the apparent increase in scores between 8 and 15 years does not seem to be the consequence of LiP-related factors alone.

The LiP participants (8-, 15- and 17-year-olds) scored above the mean score of the ARN group on a measure of cognitive flexibility (INS Total). However, the 8-, 15- and 17-year-old control participants also scored above the mean score of the ARN group on this measure (indicating more errors). It is also evident that none of the LiP participants did worse than his or her matched controls and the ARN group did on a measure of cognitive flexibility (INS Total Errors). Therefore, the apparent elevated scores of the 8-, 15- and 17-year-old LiP participants do not seem to be the consequence of LiP-related factors alone.

Although two LiP participants (the 8- and 15-year-olds) scored above the mean score of the matched controls and the mean score of the ARN group on a different measure of cognitive flexibility and abstract thinking (AS Total), the 17-year-old LiP participant did not score significantly above the mean score of these groups. Therefore, no age-related trend among the LiP participants on AS Total (cognitive flexibility and abstract thinking) is observed.

Psychosocial Functioning

Adaptive Behaviour

The performance of the LiP participants on measures of social adaptation was compared to that of the controls and a norm group (the ARN group). Scales of the Vineland-II were used to measure social adaptation. The Interpersonal Relationship scale measured social skills, the Play and Leisure Time scale measured play and leisure skills, and emotional control and coping skills were measured by means of the Coping Skills scale. School adjustment was measured by means of the TRF Adaptive Functioning scale. Raw scores were used to compare the performance of the LiP child with that of the controls and the ARN group. Scores on all the scales were transformed into T-scores ($\overline{X}$ = 50; *sd* = 10) and are displayed in the graphs.

Next, the differences in the mean scores of the 4-year-old LiP participant (compared to the control and ARN groups) on the adaptive behaviour measures/scales will be reported and displayed graphically.

Four-year-old LiP participant. The score, mean scores, standard deviations and effect sizes of the 4-year-old LiP participant, the two matched controls and the ARN group (obtained on the measures of adaptive behaviour) are reported in Table 5.19.

Table 5.19

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 4-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Adaptive Behaviour

Adaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**			
			$\overline{X}$	***sd***	***d*$_1$**	***d*$_2$**
Vineland-II Adaptive Behaviour Scales						
Interpersonal Rel	50.0	62.5	50.7	9.6	1.3	0.1
Play and Leisure	32.0	41.0	37.2	8.5	1.1	0.6
Coping Skills	41.0	34.5	25.5	10.0	0.7	1.6

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Play and Leisure Play and Leisure Time.

In Table 5.19, it is evident that no significant differences ($d \geq 0.8$) exist between the 4-year-old LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2). Consequently, the H_0 hypothesis is retained for all the adaptive behaviour scales.

Figure 5.48 graphically compares the scores of the LiP participant (LP) to the mean scores of the matched controls (Control) for the measures of adaptive behaviour that were administered. The mean scores of the ARN group (Norm) are also depicted in Figure 5.48.

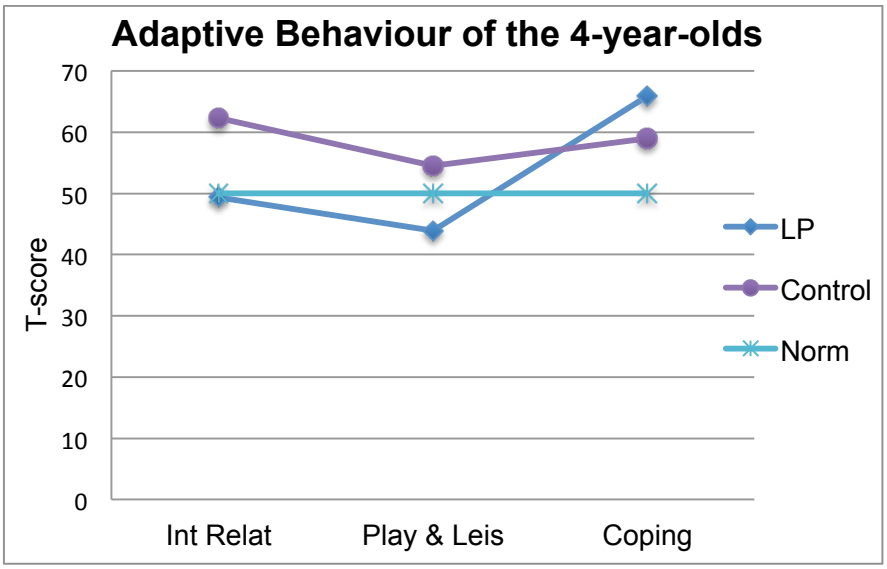

Figure 5.48. Adaptive behaviour profiles of the 4-year-olds.

In Figure 5.48, it is evident that the LiP participant obtained significantly lower scores than the matched controls on the Interpersonal Relationships and Play and Leisure Time subscales. However, these scores are not significantly below the ARN group mean on these measures. The 4-year-old LiP participant's score on a scale measuring coping skills (independent behaviour, emotional control and contextually appropriate behaviour) is above the mean score of the matched controls (which is not significant) and the mean score of the ARN group (which is significant). It is noticeable that the scores of the two controls on all the adaptive behaviour scales are higher than the mean scores of the ARN group.

Next, the differences in the mean scores of the 6-year-old LiP participant (compared to the control and ARN groups) on the adaptive behaviour measures/scales will be reported and displayed graphically.

Six-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 6-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of adaptive behaviour are reported in Table 5.20.

Table 5.20

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 6-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Adaptive Behaviour

Adaptive behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	d_1	d_2
Vineland-II Adaptive Behaviour Scales						
Interpersonal Rel	58.0	63.5	59.1	9.7	0.6	0.1
Play and Leisure	40.0	50.0	46.4	0.3	**1.3***	**0.8***
Coping Skills	38.0	39.5	36.2	11.8	0.1	0.2

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Interpersonal Rel = Interpersonal Relationships; Play and Leisure = Play and Leisure Time.

In Table 5.20, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2) with regard to the Play and Leisure Time scale ($d_1 = 1.3$; $d_2 = 0.8$). The 6-year-old LiP participant's parent's ratings of her adaptive behaviour on this scale is significantly worse (significant lower μ) than the mean ratings of the matched controls and mean ratings reported for the ARN group. According to the parent's rating, the LiP participant had fewer developed play skills (such as sharing toys) and fewer skills in playing games with others (such as following rules in games). Consequently, the H_0 hypothesis with regard to Play and Leisure Time can be rejected.

Figure 5.49 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) on the measures of adaptive behaviour that were administered. The mean scores of the ARN group (Norm) are also depicted in Figure 5.49.

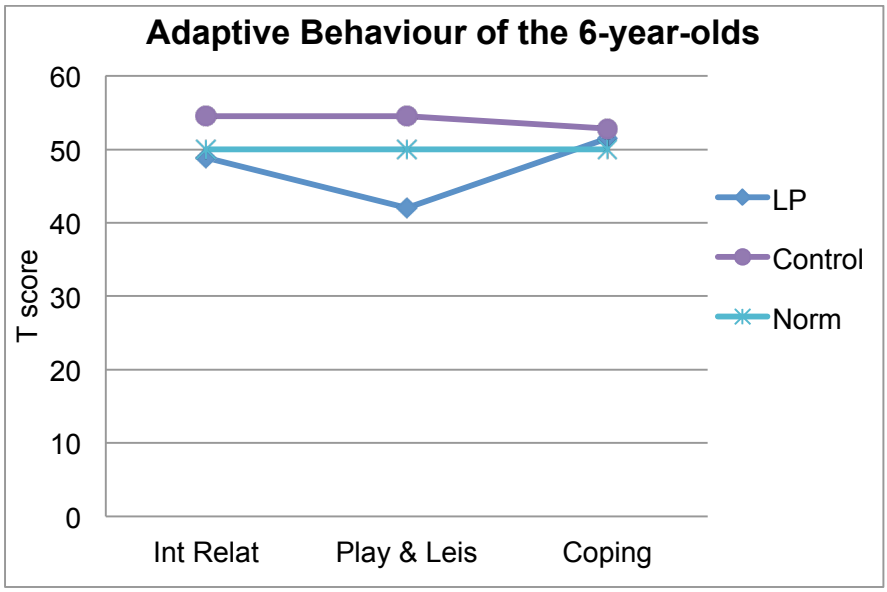

Figure 5.49. Adaptive behaviour profiles of the 6-year-olds.

It is evident in Figure 5.49 that the LiP participant obtained lower scores than the matched controls on the Interpersonal Relationships (which is not significant) and the Play and Leisure Time (which is significant) subdomain of the Vineland-II. It is noticeable that the mean scores of the controls on the three adaptive behaviour scales are all above the mean score of the ARN group.

Next, the differences in the mean scores of the 8-year-old LiP participant (compared to those of the control and norm groups) on the adaptive behaviour measures/subtests will be reported and displayed graphically.

Eight-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 8-year-old LiP participant, the two matched controls and the ARN group on the measures of adaptive behaviour are reported in Table 5.21.

Table 5.21

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 8-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Adaptive Behaviour

Adaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**		d_1	d_2
			$\overline{X}$	*sd*		
Vineland-II Adaptive Behaviour Scales						
Interpersonal Rel	69.0	66.0	63.0	8.7	0.3	0.7
Play and Leisure	50.0	48.5	50.2	7.0	0.2	0.0
Coping Skills	34.0	45.0	40.0	12.4	0.9	0.5
Teacher Report Form						
Adaptive Functioning TRF	16.0	16.0	17.5	5.2	0.0	0.3

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Interpersonal Rel = Interpersonal Relationships; Play and Leisure = Play and Leisure Time; Adaptive Functioning TRF = Adaptive Functioning Teacher Report Form.

In Table 5.21, it is evident that no significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1) and between the LiP participant's scores and the ARN group (d_2) on the adaptive behaviour scales. The results suggest that the LiP participant's adaptive behaviour was as good as that of his typically developing peers. Consequently, the H_0 hypothesis is retained.

Figure 5.50 graphically compares the performance of the LiP participant (LP) to the mean score of the matched controls (Control) on the measures of adaptive behaviour that were administered. The mean scores of the ARN group (Norm) are also depicted in Figure 5.50.

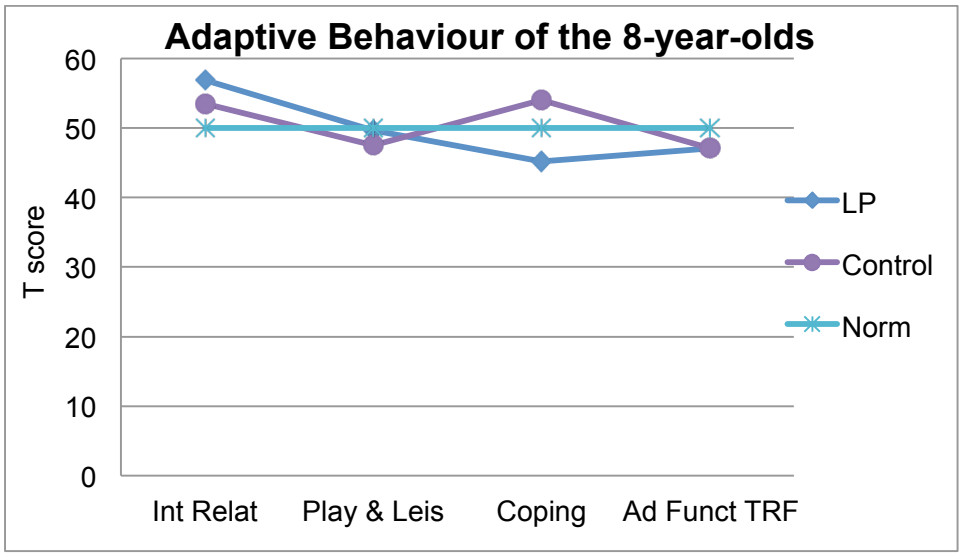

Figure 5.50. Adaptive behaviour profiles of the 8-year-olds.

In Figure 5.50, it is evident that, compared to matched controls, the LiP individual obtained a lower score on the Coping Skills scale. However, the score on the mentioned measure is not significantly below the mean score of the ARN group. The mean scores of the controls are close to the mean scores of the ARN group on the adaptive behaviour scale.

Next, the differences in the mean scores of the 15-year-old LiP participant (compared to those of the control and ARN groups) on the adaptive behaviour measures/subtests will be reported and displayed graphically.

Fifteen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 15-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of adaptive behaviour are reported in Table 5.22.

Table 5.22

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 15-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Adaptive Behaviour

Adaptive behaviour measures	**LP score (μ) (n = 1)**	**Control mean ($\overline{X}$) (n = 2)**	**Norm group** $\overline{X}$	***sd***	d_1	d_2
Vineland-II Adaptive Behaviour Scales						
Interpersonal Rel	65.0	73.0	70.7	5.1	**1.6***	**1.1***
Play and Leisure	58.0	56.5	58.7	3.9	0.4	0.2
Coping Skills	47.0	58.0	52.3	8.7	1.3	0.6
Teacher Report Form						
Adaptive Functioning TRF	17.5	16.5	17.8	5.9	0.2	0.1

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Interpersonal Rel = Interpersonal Relationships; Play and Leisure = Play and Leisure Time; Adaptive Functioning TRF = Adaptive Functioning Teacher Report Form.

In Table 5.22, it is evident that significant differences ($d \geq 0.8$) exist between the 15-year-old LiP participant's score and the mean score of the matched controls (d_1), as well as between the LiP participant's score and the ARN group's mean score (d_2) with regard to Interpersonal Relationships ($d_1 = 1.6$; $d_2 = 1.1$). The 15-year-old LiP participant obtained a significantly lower score than the mean score of the matched controls and the mean score of the ARN group on a measure of interpersonal skills. Consequently, the H_0 hypothesis with regard to Interpersonal Relationships can be rejected.

The obtained scores of the LiP participant (LP), mean scores of the ARN group (Norm) and averages of the controls (Control), are shown in Figure 5.51 below.

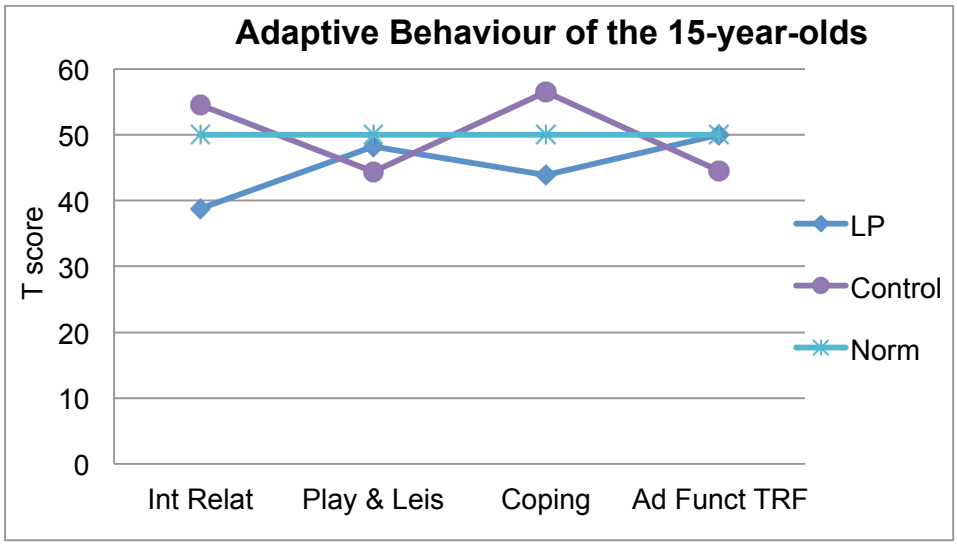

Figure 5.51. Adaptive behaviour profiles of the 15-year-olds.

In Figure 5.51, it is evident that the LiP individual obtained lower scores than the mean score of the controls on Interpersonal Relationships and Coping Skills. However, the score on the Coping Skills subdomain is not significantly lower than the mean score of the ARN group.

Mean scores of the controls are above the mean score of the ARN group on the Interpersonal Relationships and Coping Skills scales, but below the mean score of the ARN group on Play and Leisure Skills and Adaptive Functioning TRF (school adjustment).

Next, the differences in the mean scores of the 17-year-old LiP participant (compared to the scores of the control and ARN groups) on the adaptive behaviour measures/scales will now be reported and displayed graphically.

Seventeen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 17-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of adaptive behaviour are reported in Table 5.23. No data on the scholastic adjustment of the 17-year-olds was obtained, as the 17-year-old LiP participant did not attend school.

Table 5.23

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 17-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Adaptive Behaviour

Adaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**			
			$\overline{X}$	***sd***	***d*$_1$**	***d*$_2$**
Vineland-II Adaptive Behaviour Scales						
Interpersonal Rel	73.0	72.0	73.1	5.0	0.2	0.0
Play and Leisure	61.0	60.0	60.5	4.4	0.2	0.1
Coping Skills	42.0	52.0	55.5	6.5	**1.5***	**2.1***

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$; Interpersonal Rel = Interpersonal Relationships; Play and Leisure = Play and Leisure Time.

In Table 5.23, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's score and the mean score of the matched controls ($d_1 = 1.5$), as well as between the LiP participant's score and the ARN group's mean score ($d_2 = 2.1$) on the Coping Skills measure. The results indicate that the 17-year-old LiP participant found it more difficult (significant lower μ) to cope in social situations, regulate emotions, behave appropriately in different contexts and adapt to change. Consequently, the H_0 hypothesis with regard to Coping Skills can be rejected.

The obtained adaptive behaviour scores are also represented visually in Figure 5.52 below. Data for the LiP participant (LP) and the ARN group (Norm) and the average of the two controls (Control) are shown.

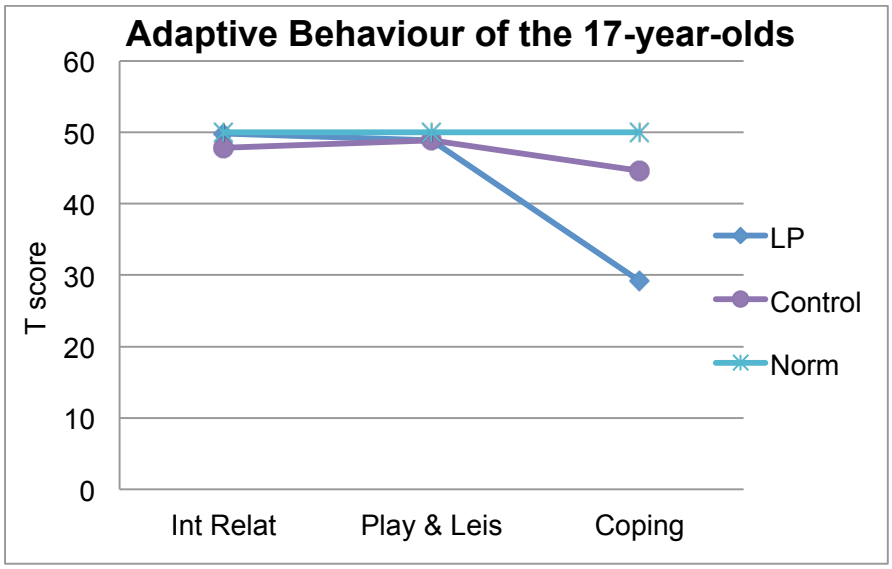

Figure 5.52. Adaptive behaviour profiles of the 17-year-olds.

In Figure 5.52, it is evident that the LiP individual scored below the mean scores of the matched controls and the ARN group on the Coping Skills subdomain. Therefore, the LiP participant performed worse than the matched controls did on a measure of coping skills (incorporating independence, adapting to change and being sensitive to others). It is noticeable that the mean score of the controls is similar to mean score of the ARN group on the Interpersonal Relationships and Play and Leisure Time scales, but below the mean score of the ARN group on the Coping Skills scale.

Summary of adaptive behaviour profiles. Table 5.24 provides a summary of the effect sizes (d_1 and d_2) of every adaptive behaviour construct in the different age groups to identify patterns of performance among the LiP participants. Effect sizes are marked with an asterisk when both d_1 and $d_2 \geq 0.8$.

Table 5.24

Effect Sizes (d_1; d_2) of the 4-, 6-, 8-, 15- and 17-year-olds on Measures of Adaptive Behaviour

Adaptive Behaviour Measures	4-year-olds		6-year-olds		8-year-olds		15-year-olds		17-year-olds	
	d_1	d_2	d_1	d_2	d_1	d_2	d_1	d_2	d_1	d_2
Vineland II-Adaptive Behaviour Scales										
Interpersonal Rel	1.3	0.1	0.6	0.1	0.3	0.7	**1.6***	**1.1***	0.2	0.0
Play and Leisure	1.1	0.6	**1.3***	**0.8***	0.2	0.0	0.4	0.2	0.2	0.1
Coping Skills	0.7	1.6	0.1	0.2	0.9	0.5	1.3	0.6	**1.3***	**2.3***
Teacher Report Form										
Adaptive Functioning TRF					0.0	0.3	0.2	0.1		

Note: * Both d_1 and $d_2 \geq 0.8$; Interpersonal Rel = Interpersonal Relationships; Play and Leisure = Play and Leisure Time; Adaptive Functioning TRF = Adaptive Functioning Teacher Report Form.

In Table 5.24, it is evident that significant differences (significantly lower scores) exist between the scores of all five the LiP participants on the adaptive behaviour measures and the mean scores of the matched controls (d_1). Significant differences between three of the LiP participants' scores and the ARN group's mean score (d_2) are also evident. However, each of the LiP participants has a different adaptive behaviour profile. The 17-year-old has significantly worse coping skills compared to the controls and the average person in the ARN group. The 6-year-old LiP participant presented with significantly less appropriate play behaviour and significantly less adequate leisure skills compared to controls and the average individual in the ARN group, while the 15-year-old LiP participant displayed significantly fewer efficient social skills compared to these individuals. It is noticeable that not one of the two LiP participants who attended school received lower scores on the Adaptive Functioning TRF scales than their typically developing peers did. This indicates that they adapted equally well to school as the matched controls and the average individual in the ARN group.

Adaptive behaviour trajectories. Graphs were drawn to represent the adaptive behaviour scores of the LiP and control participants across the different age groups,

thereby identifying developmental trends. No hypothesis is tested; therefore, this aspect of the research is purely explorative. Trajectories were plotted for every adaptive behaviour construct. T-scores ($\overline{X}$ = 50; *sd* = 10) were used to represent the performance of the LiP participants and the mean scores of the controls (Control) and the ARN group.

Interpersonal relationships. Figure 5.53 graphically compares the Interpersonal Relationships scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.53.

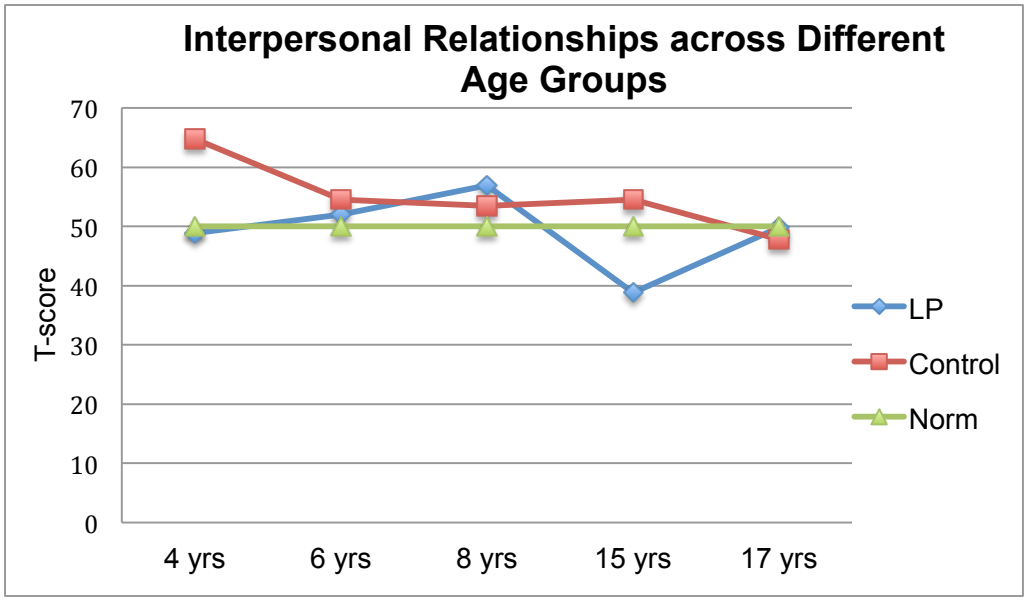

Figure 5.53. Interpersonal Relationships across the different age groups.

In Figure 5.53, it is evident that the 4-year-old (d_1 = 1.3) and 15-year-old (d_1 = 1.6) LiP participants obtained scores on the Interpersonal Skills subdomain that are below the mean scores of the matched controls. It is apparent that the 15-year-old LiP participant's score on Interpersonal Relationships (d_2 = 1.1) is also significantly below the mean score of the ARN group.

It is noticeable that the mean score of the 4-year-old control participants on Interpersonal Relationships is above the mean score of the ARN group, while the mean scores of the 6-, 8- and 15-year-old control participants are above but close to the mean scores of the ARN group. The 17-year-old control participant's mean score is below but

close to the reported mean score of the ARN group. Thus, no specific age-related trend is apparent with regard to social skills among the LiP or control participants whose data are represented in Figure 5.53.

Play and leisure time. Figure 5.54 graphically compares the Play and Leisure Time scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.54.

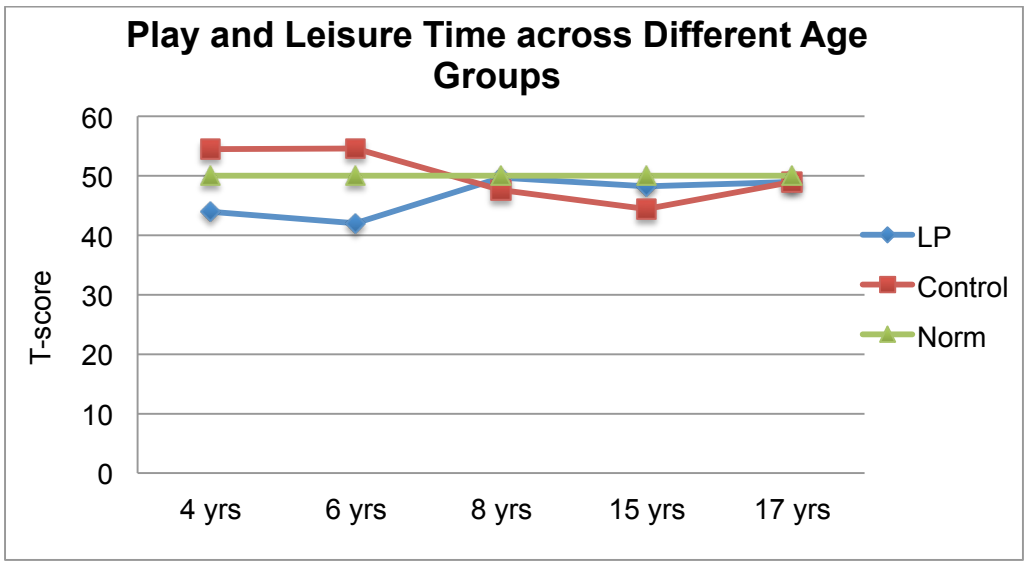

Figure 5.54. Play and Leisure Time across the different age groups.

In Figure 5.54, it is evident that the scores of the 4-year-old (d_1 = 1.1) and 6-year-old (d_1 = 0.8) LiP participants on the Play and Leisure Time subdomain are significantly below the mean scores of the matched controls. Therefore, the 4- and 6-year-old LiP participants have significantly lower scores compared to matched controls on a measure of appropriate play behaviour (such as symbolic play and taking turns) and leisure skills (such as knowing the rules of games). It is further evident that the 6-year-old (d_2 = 0.8) LiP participant's score on the Play and Leisure Time subdomain is below the mean score of the ARN group. The 4- and 6-year-old controls matched to LiP participants in these age groups obtained scores that are above the mean score of the ARN group on the Play and Leisure Time subdomain, whereas the scores of the 8-, 15- and 17-year-old control participants are close to this mean score. A significant difference in the play and leisure skills of the urban, female LiP children and those of the control participants is evident,

while such a significant difference is not evident between any of the rural LiP and control participants. As there are differences between the urban (4- and 6-year-old) and rural (8-, 15- and 17-year-old) LiP participants, this trend may indicate that LiP impact differently on the play and leisure skills of urban individuals than rural children and adolescents.

Coping skills. Figure 5.55 graphically compares the Coping Skills scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.55.

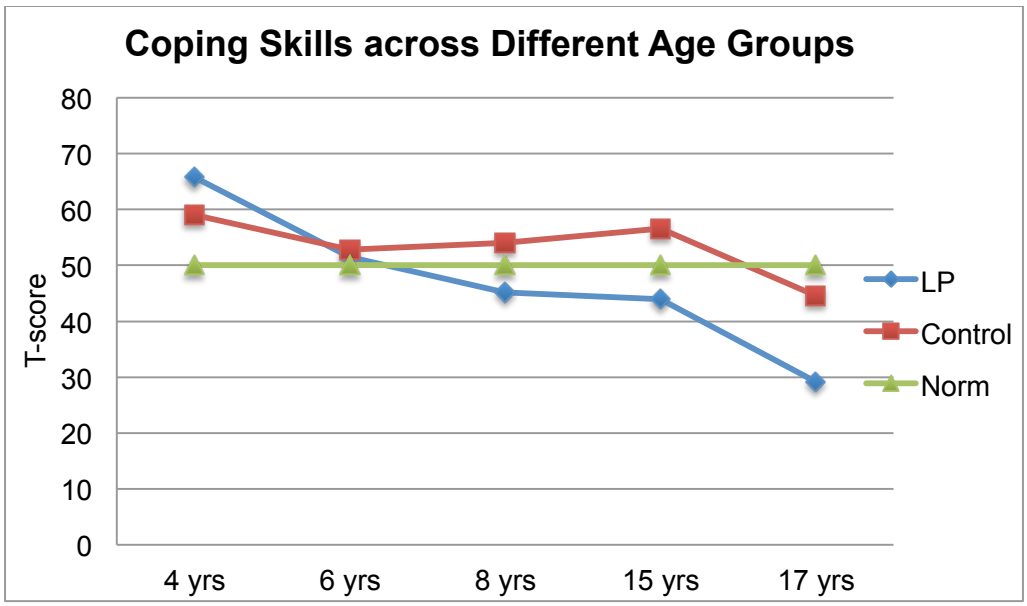

Figure 5.55. Coping Skills across the different age groups.

In Figure 5.55, it is evident that the 8-year-old ($d_1 = 0.9$), 15-year-old ($d_1 = 1.3$) and 17-year-old ($d_1 = 1.3$) LiP participants obtained significantly lower scores on the Coping Skills scale than the mean scores of the controls. Therefore, these LiP participants obtained significantly lower scores compared to matched controls on a measure of emotional regulation, contextually appropriate and flexible behaviour (adapting). The 4-year-old ($d_2 = 1.6$) LiP participant's score on Coping Skills is significantly above the mean score of the ARN group, while the 17-year-old ($d_2 = 2.3$) LiP participant's score on this subdomain is significantly below the mean score of the ARN group. Therefore, the 17-year-old LiP participant scored significantly below the mean score of the controls and the mean score of the ARN group on this measure of adaptive behaviour. The trajectory of the

LiP participants' scores on Coping Skills, in comparison to the mean scores of the ARN group, appears to follow a downward slope. The mean scores of the 4-, 6-, 8- and 15-year-old controls on Coping Skills are higher than the mean scores of the ARN group. However, the 17-year-old control participant scored below the mean score of the ARN group. Therefore, no specific trend among the control participants with regard to Coping Skills is evident.

Adaptive functioning TRF. Figure 5.56 graphically compares the Adaptive Functioning TRF scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.56. No data are displayed for the 4-, 6- and 17-year-olds that did not attend primary or high school; therefore, scholastic adjustment did not apply to them.

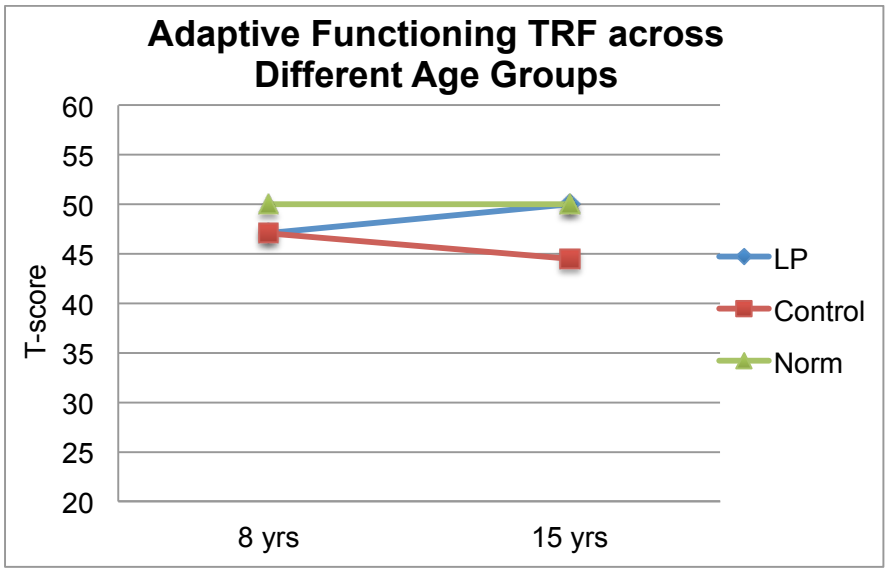

Figure 5.56. *Adaptive Functioning TRF across the Different Age Groups.*

In Figure 5.56, it is evident that the score of neither of the two LiP participants on Adaptive Functioning TRF is significantly below the mean score of their matched controls. Similarly, the score of neither of the LiP participants on Adaptive Functioning TRF is significantly below the mean score of the ARN group. The mean scores of the 8- and 15-year-old controls on the Adaptive Functioning TRF are below (but close to) the mean scores of the ARN group. Overall, the LiP participants appear to adjust equally well in school than their peers do.

Summary of adaptive behaviour trajectories.

Interpersonal skills. There is no specific age-related trend with regard to Interpersonal Skills among the LiP or control participants. The only LiP participant who scored significantly below the mean score of the ARN group and the mean score of the controls was the 15-year-old.

Playing and using leisure time. Significant differences between the play and leisure skills of the urban LiP and control participants are evident (the LiP participants obtained significantly lower scores), whereas no significant differences between the LiP and control participants are evident among the rural participants. The 4- and 6-year-old urban control participants scored above the mean score of the ARN group, while the 8-, 15- and 17-year-old control participants scored very similar to the means score of the ARN group. As there are differences between the urban (4- and 6-year-old) and rural (8-, 15- and 17-year-old) participants, this trend may be related to differences between the urban and rural participants.

Coping skills (adapting). The trajectory of the LiP participants' scores on Coping Skills, in comparison to the mean scores of the ARN group, follows a downward slope. The urban LiP participants (4- and 6-year-olds) scored above or similar to the ARN group mean, while the rural LiP participants scored below the mean score of the ARN group. This trend is not found among the control participants. Therefore, the decrease in the scores of the LiP participants may be associated with their having LiP.

School adjustment. Both LiP participants adjusted as well in school as their similarly aged peers (controls and ARN group). The controls in the 8- and 15-year-old age groups obtained lower mean scores than the average person in the ARN group did, but these scores are close to the mean score.

Conclusion: Adaptive behaviour.

Significant differences. Significant differences between the performance of the LiP participants and that of the matched controls and between the performance of the LiP participants and the average person in the ARN group are apparent on the adaptive behaviour scales. No individual LiP participant obtained low scores on all the adaptive behaviour scales. Compared to matched controls and the ARN groups, three of the LiP

participants (6-, 15- and 17-year-olds) obtained significantly lower scores, each on a different subdomain (6-year-old: Play and Leisure Time; 15-year-old: Interpersonal Relationships; 17-year-old: Coping Skills). The scores of the 4- and 8-year-old LiP participants do not differ significantly from the mean scores of the controls or the ARN group on any of the scales. There are no significant differences between the scores of the LiP participants who attended school and the mean scores of their matched controls or between the LiP participants' scores and the mean score of the ARN group on a measure of school adjustment.

Trends. Compared to the mean scores of the controls and the mean scores of the ARN group, different trends were noticed for each of the subdomains (Interpersonal Relationships, Play and Leisure Skills, and Coping Skills). No specific age-related trend among the LiP or control participants with regard to Interpersonal Relationships is evident. The scores of all the control and LiP participants, except for the 15-year-old LiP participant, are close to the mean score of the ARN group.

Significant differences (LiP participants' scores below the ARN group mean) between the scores of the urban LiP children and controls on a measure of play and leisure skills are evident, while there are no significant differences between the performance of the rural LiP participants and control participants on this subdomain. As there are differences in the background and characteristics between the urban (4- and 6-year-old) and rural (8-, 15- and 17-year-old) LiP participants, this trend may indicate that LiP impacts differently on the play and leisure skills of the urban participants compared to how it impacts on the rural LiP participants.

The trajectory of the LiP participants' scores on Coping Skills, in comparison to the mean scores of the ARN group, follows a downward slope. The trajectory of the averages of the controls' on Coping Skills does not follow this trend. Therefore, it is likely that the decrease in LiP Coping Skills scores may be attributed to the effect of the disorder on the LiP participants across the different age groups.

Maladaptive Behaviour

For each age group, separate comparisons were made between the performance of the LiP participants and that of the controls and the ARN group on measures of maladaptive

behaviour. The various maladaptive behaviour constructs were measured by means of the CBCL/1.5-5, CBCL/6-18, C-TRF, and TRF behaviour scales, depending on the age group of the participant. The ratings of parents and teachers on the Total Problems, Internalising Problems, Externalising Problems and Social Problems scales of the teacher (C-TRF or TRF) and parent (CBCL/1.5- or CBCL/6-18) checklists were employed to determine problem severity and the extent of internalising, externalising and social behaviour problems. Raw mean scores were used to compare the performance of the LiP participants with that of the controls and the ARN group. Raw scores on all the tests were transformed into T-scores ($\overline{X}$ = 50; *sd* = 10) to compare the scores graphically.

Next, the differences in the mean scores of the 4-year-old LiP participant (compared to the control and ARN group) on the maladaptive behaviour measures/subtests will be reported and displayed graphically.

Four-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 4-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of maladaptive behaviour are reported in Table 5.25.

Table 5.25

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 4-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm group**		d_1	d_2
			$\overline{X}$	*sd*		
CBCL/1.5-5 Syndrome Scales						
Total Problems	17.0	27.0	33.3	18.7	0.5	0.9
Internalising Problems	6.0	9.0	8.6	6.8	0.4	0.4
Externalising Problems	7.0	8.5	12.9	7.7	0.2	0.8
C-TRF Syndrome Scales						
Total Problems	55.0	9.0	19.6	20.9	**2.2***	**1.5***
Internalising Problems	13.0	6.0	6.4	6.9	**1.0***	**1.0***
Externalising Problems	12.0	0.0	8.0	10.1	1.2	0.4

Note: Data are presented as raw scores (different ranges); *both d_1 and $d_2 \geq 0.8$.

In Table 5.25, it is evident that significant differences ($d \geq 0.8$) exist between the 4-year-old LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) on the C-TRF Total Problems scale ($d_1 = 2.2$; $d_2 = 1.5$) and the C-TRF Internalising Problems scale ($d_1 = 1.0$; $d_2 = 1.0$). The 4-year-old LiP participant obtained a significantly higher score (significant higher μ) than the matched controls and similarly-aged average individual in the ARN group did on behaviour scales measuring total behaviour problems (severity of behaviour problems) and internalising behaviour problems (such as anxiety and depression) at school. Therefore, the LiP participant presented with more severe behaviour problems and more internalising behaviour problems compared to the matched controls and the average individual in the ARN group. Consequently, the H_0 hypothesis with regard to C-TRF Total Problems and C-TRF Internalising Problems can be rejected.

The scores obtained on the CBCL/1.5-5 scales are represented visually in Figure 5.57 below. Scores of the LiP child (LP), the ARN group (Norm) and the mean scores of the two controls (Control) are shown.

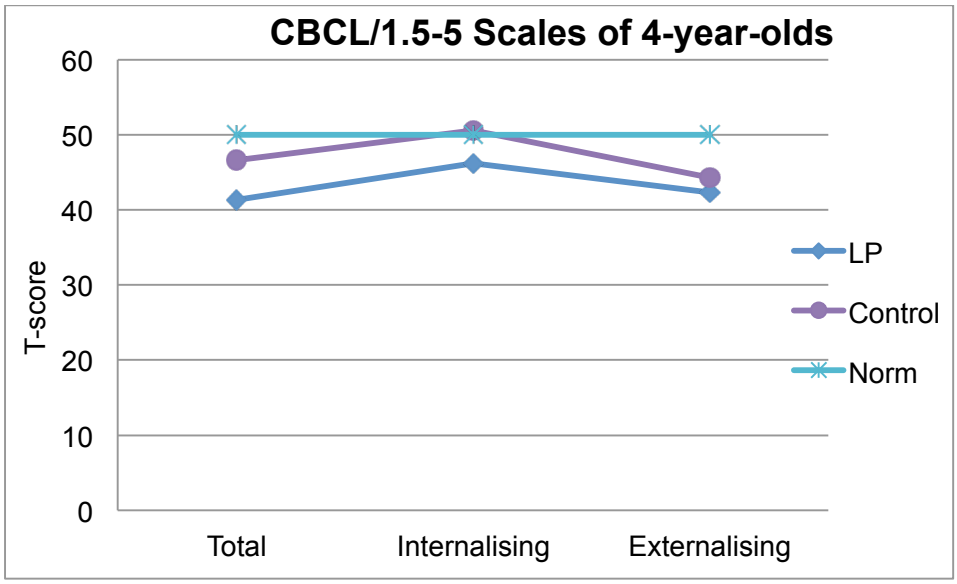

Figure 5.57. CBCL/1.5-5 scales of the 4-year-olds.

In Figure 5.57, it is evident that the 4-year-old LiP participant's scores on the CBCL/1.5-5 scales are below the mean scores of the matched controls (indicating less problem behaviour) on all three CBCL/1.5-5 problem scales (Total Problems, Internalising

Problems and Externalising Problems). However, the LiP participant's scores are not significantly below the mean scores of the ARN group on these scales. The mean scores of the two controls on the Total Problems and Internalising Problems scales are similar to the mean score of the ARN group and below the mean score of the ARN group on the Externalising Problems scale. This indicates that the controls did not present with problem behaviour at home.

The scores obtained on the C-TRF scales are represented visually in Figure 5.58 below. Scores of the LiP child (LP), mean scores of the ARN group (Norm) and mean scores of the two controls (Control) are shown.

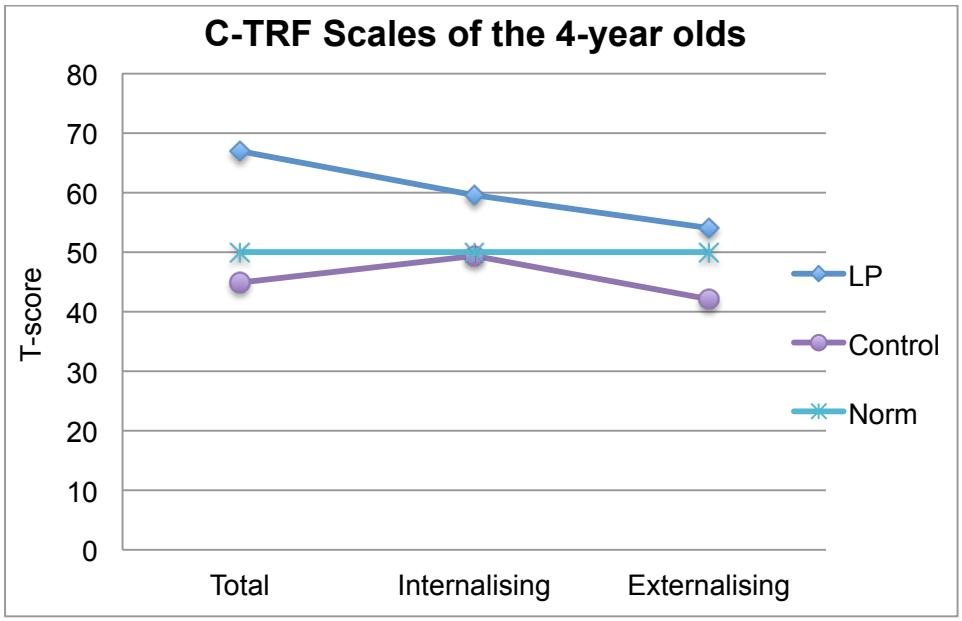

Figure 5.58. C-TRF scales of the 4-year-olds.

In Figure 5.58, it is evident that the LiP child obtained significantly higher scores than the matched controls did on all three the C-TRF behaviour problem scales (Total Problems, Internalising Problems and Externalising Problems). However, the score on the Externalising problems scale is not significantly above the mean score of the ARN group. It is noticeable that the mean scores of the two controls on the Total Problems, Internalising Problems and Externalising Behaviour Problems scales are similar to or below (less problem behaviour) the mean scores of the ARN group, indicating that they did not present with behaviour problems at school.

Next, the scores of the 6-year-old LiP participant (compared to the mean scores of the controls and the ARN group) on the maladaptive behaviour scales will be reported and displayed graphically.

Six-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 6-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of maladaptive behaviour are reported in Table 5.26.

Table 5.26

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 6-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group**			
			$\overline{X}$	***sd***	***d*$_1$**	***d*$_2$**
CBCL/1.5-5 Syndrome Scales						
Total Problems	26.0	3.0	33.3	18.7	1.2	0.4
Internalising Problems	4.0	1.0	8.6	6.8	0.4	0.7
Externalising Problems	11.0	0.5	12.9	7.7	1.4	0.2
C-TRF Syndrome Scales						
Total Problems	18.0	9.5	19.6	20.9	0.4	0.1
Internalising Problems	0.0	5.0	6.4	6.9	0.7	0.9
Externalising Problems	10.0	0.5	8.0	10.1	0.9	0.2

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$.

In Table 5.26, it is evident that no significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) on the CBCL/1.5-5 and C-TRF behaviour scales. Therefore, the 6-year-old LiP participant did not present with significantly more behaviour problems compared to the controls and the average individual in the ARN group. Consequently, the H_0 hypothesis is retained with regard to all the behaviour problem scales.

The scores and mean scores obtained on the CBCL/1.5-5 Syndrome scales are represented visually in Figure 5.59 below. Scores of the LiP child (LP), mean scores of the ARN group (Norm) and the mean scores of the two matched controls (Control) are shown.

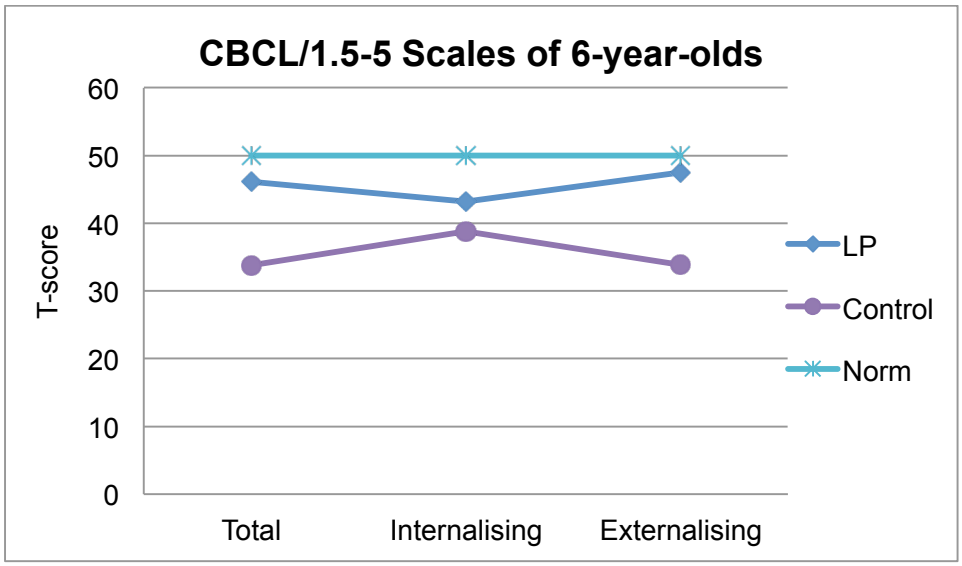

Figure 5.59. CBCL/1.5-5 scales of the 6-year-olds.

In Figure 5.59, it is evident that the 6-year-old LiP child obtained significantly higher scores than the mean scores of the matched controls on the CBCL/1.5-5 Syndrome scales (Total Problems and Externalising Problems). However, the LiP participant's scores on these scales are not higher than the mean scores of the ARN group. It is noticeable that the scores of the two controls are lower (indicating less behaviour problems) than the mean scores of the ARN group on all three CBCL/1.5-5 Syndrome scales.

Figure 5.60 graphically compares the performance of the LiP participant (LP) to the mean scores of the matched controls (Control) across the C-TRF behaviour problem scales. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.60.

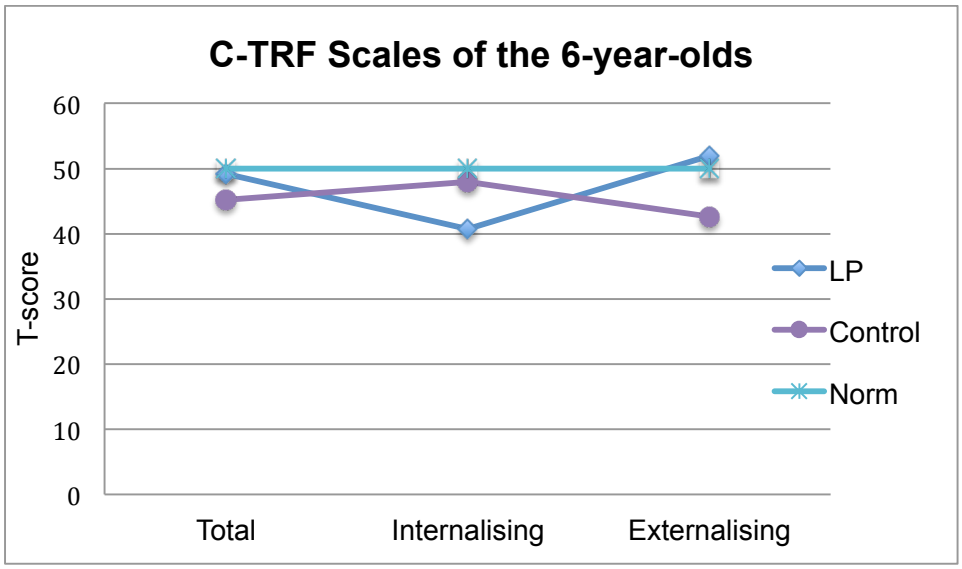

Figure 5.60. C-TRF scales of the 6-year-olds.

It is evident that the LiP individual obtained a higher score than the mean score of the matched controls on the Externalising Problems scale of the C-TRF. However, the LiP participant's score on this scale is not significantly higher than the mean score of the ARN group. The two controls scored below the mean score of the ARN group on the Externalising Problems scale, but similar to this group's mean score on the Total Problems and Internalising Problems scales.

Next, the differences in the mean scores of the 8-year-old LiP participant (compared to the mean scores of the control and norm groups) on the maladaptive behaviour measures/subtests will be reported and displayed graphically.

Eight-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 8-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of maladaptive behaviour are reported in Table 5.27.

Table 5.27

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 8-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	LP Score (μ) (n = 1)	Control Mean ($\overline{X}$) (n = 2)	Norm Group $\overline{X}$	Norm Group *sd*	d_1	d_2
CBCL/6-18 Syndrome Scales						
Total Problems	54.0	16.5	23.9	16.6	**2.3***	**1.8***
Internalising Problems	20.0	6.5	5.1	4.8	**2.8***	**3.1***
Externalising Problems	18.0	5.0	6.8	5.9	**2.2***	**1.9***
Social Problems	5.0	1.5	2.4	2.7	**1.3***	**1.0***
TRF Syndrome Scales						
Total Problems	57.0	20.5	24.1	23.0	**1.6***	**1.4***
Internalising Problems	18.0	8.5	4.6	5.4	**1.8***	**2.5***
Externalising Problems	20.0	6.5	5.5	7.4	**1.8***	**2.0***
Social Problems	4.0	1.0	1.4	2.3	**1.3***	**1.1***

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$.

In Table 5.27, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) on the following scales: CBCL Total Problems ($d_1 = 2.3$; $d_2 = 1.8$), CBCL Internalising Problems ($d_1 = 2.8$; $d_2 = 3.1$), CBCL Externalising Problems ($d_1 = 2.2$; $d_2 = 1.9$), CBCL Social Problems ($d_1 = 1.3$; $d_2 = 1.0$), TRF Total Problems ($d_1 = 1.6$; $d_2 = 1.4$), TRF Internalising Problems ($d_1 = 1.8$; $d_2 = 2.5$), TRF Externalising Problems ($d_1 = 1.8$; $d_2 = 2.0$) and TRF Social Problems ($d_1 = 1.3$; $d_2 = 1.1$). The 8-year-old LiP participant obtained significantly higher scores (significant higher μ) compared to the mean scores of similarly aged healthy controls on behaviour scales tapping severity of problem behaviour, externalising problems, internalising problems and social problems in the home and school settings. Consequently, the H_0 hypothesis with regard to all the CBCL and TRF syndrome scales (Total Problems CBCL, Internalising Problems CBCL, Externalising Problems CBCL, Social Problems CBCL,

Total Problems TRF, Internalising Problems TRF, Externalising Problems TRF and Social Problems TRF) can be rejected.

Figure 5.61 graphically compares the scores of the LiP participant (LP) on the CBCL behaviour problem scales to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.61.

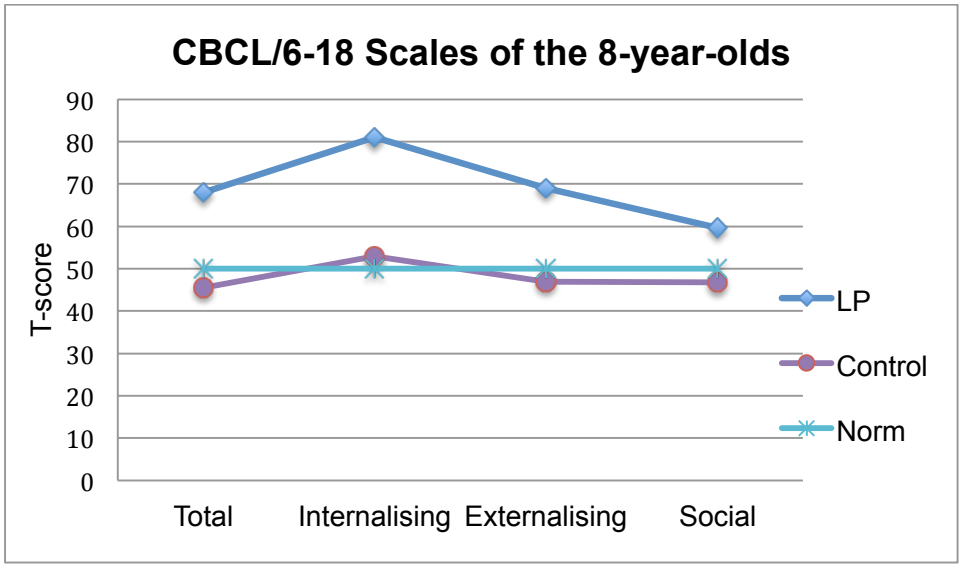

Figure 5.61. CBCL/6-18 scales of the 8-year-olds.

In Figure 5.61, it is evident that the LiP child obtained significantly higher scores than the matched controls and the ARN group did on all the CBCL/6-18 syndrome scales. The mean scores of the two controls are close to the mean scores of the ARN group on all the problem scales.

Figure 5.62 graphically compares the scores of the LiP participant (LP) on the TRF behaviour problem scales to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.62.

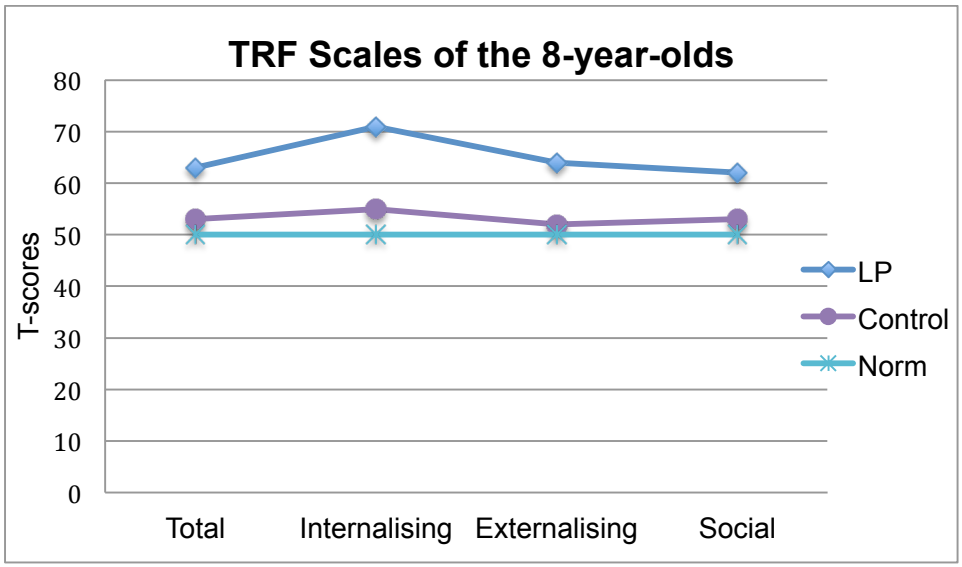

Figure 5.62. TRF scales of the 8-year-olds.

In Figure 5.62, it is evident that the LiP individual obtained significantly higher scores than the mean scores of the matched controls and the mean scores of the ARN group on all the TRF scales. This indicates that the LiP child had significantly more problems in general and presented with significantly more problems on each of the relevant scales (internalising problems, externalising problems and social problems) at school. It is noticeable that the mean scores of the two controls are somewhat above but close to the mean score of the ARN group on the TRF scales.

Next, the differences in the scores of the 15-year-old LiP participant, compared to the mean scores of the control and ARN group, on the maladaptive behaviour scales will be reported and displayed graphically.

Fifteen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 15-year-old LiP participant, the two matched controls and the ARN group on the measures of maladaptive behaviour are reported in Table 5.28.

Table 5.28

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 15-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	LP Score (μ) (n = 1)	Control Mean ($\overline{X}$) (n = 2)	Norm Group $\overline{X}$	Norm Group *sd*	d_1	d_2
CBCL/6-18 Syndrome Scales						
Total Problems	19.0	13.5	25.2	18.9	0.3	0.3
Internalising Problems	3.0	3.5	6.1	5.4	0.1	0.6
Externalising Problems	10.0	4.5	7.8	7.3	0.8	0.3
Social Problems	0.0	1.0	1.9	2.4	0.4	0.8
TRF Syndrome Scales						
Total Problems	21.0	20.0	23.8	25.8	0.1	0.1
Internalising Problems	8.0	8.5	4.4	5.8	0.1	0.6
Externalising Problems	6.0	3.0	5.3	8.1	0.4	0.1
Social Problems	3.0	1.0	1.3	2.5	0.8	0.7

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$.

In Table 5.28, no significant differences ($d \geq 0.8$) are evident between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) on any of the behaviour scales. Consequently, the H_0 hypothesis is retained with regard to all the CBCL/6-18 and TRF syndrome scales.

Figure 5.63 graphically compares the scores of the LiP participant (LP) on the CBCL/6-18 behaviour scales to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.63.

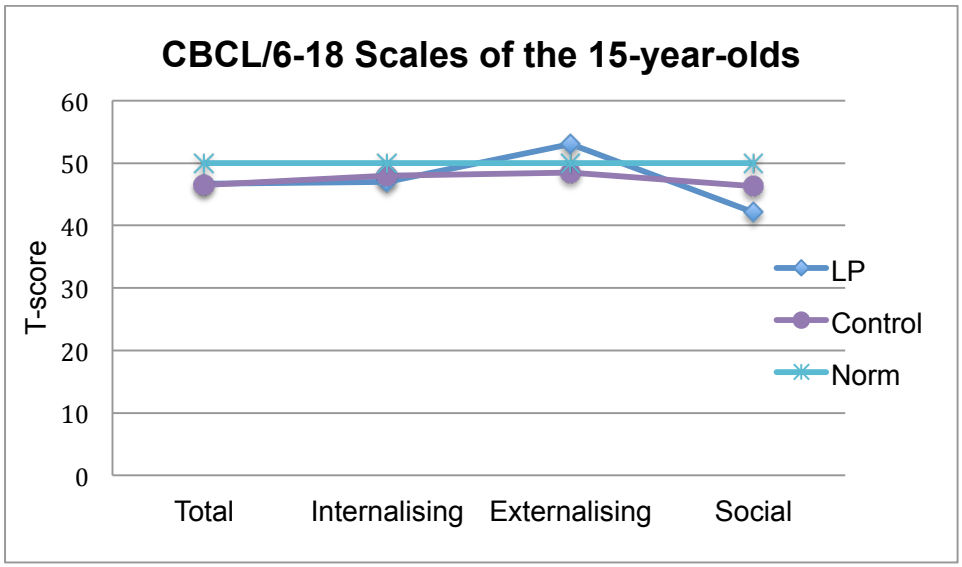

Figure 5.63. CBCL/6-18 scales of the 15-year-olds.

It is evident that the LiP participant obtained a higher score than the matched controls did on the CBCL Externalising Problems scale and a lower score than the matched controls did on the Social Problems scale. However, the LiP participant's scores on these scales are not significantly above or below the mean scores of the control or ARN group. The mean scores of the two controls are below, but close to, to the mean scores of the ARN group.

Figure 5.64 graphically compares the scores of the LiP participant (LP) on the C-TRF behaviour scales to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.64.

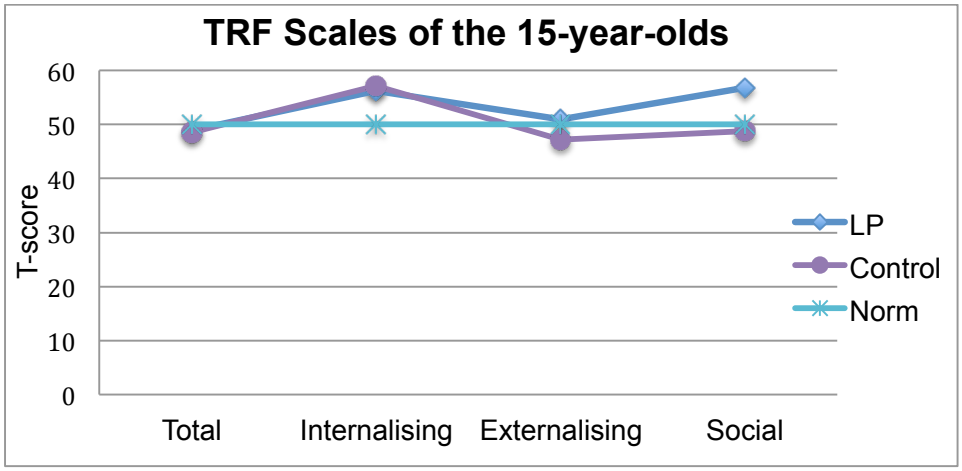

Figure 5.64. TRF scales of the 15-year-olds.

In Figure 5.64, it is evident that the LiP individual, compared to the matched controls, obtained a higher score (which is not significant) on the TRF Externalising Problems scale and a higher score (which is significant) on the TRF Social Problems scale. However, the LiP participant's scores are not significantly above the mean scores of the ARN group. It is noticeable that the mean score of the controls are above the mean score of the ARN group on the Internalising Problems scale, but none of the scores on the other scales are above the mean score of the ARN group.

Next, the differences in the scores of the 17-year-old LiP participant, compared to the mean scores of the control group and ARN group on the maladaptive behaviour scales, will be reported and displayed graphically.

Seventeen-year-old LiP participant. The scores, mean scores, standard deviations and effect sizes of the 17-year-old LiP participant, the two matched controls and the ARN group (Norm Group) on the measures of maladaptive behaviour are reported in Table 5.29.

Table 5.29

Scores, Mean Scores, Standard Deviations and Effect Sizes of the 17-Year-Old LiP Participant, Matched Controls and Norm Group on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	**LP Score (μ) (n = 1)**	**Control Mean ($\overline{X}$) (n = 2)**	**Norm Group** $\overline{X}$	***sd***	***d_1***	***d_2***
CBCL/6-18 Syndrome Scales						
Total Problems	81.0	26.0	25.2	18.9	**2.9***	**3.0***
Internalising Problems	20.0	11.0	6.1	5.4	**1.7***	**2.6***
Externalising Problems	28.0	10.5	7.8	7.3	**2.4***	**2.8***
Social Problems	9.0	1.0	1.9	2.4	**3.3***	**3.0***

Note: Data are presented as raw scores (different ranges); * both d_1 and $d_2 \geq 0.8$.

In Table 5.29, it is evident that significant differences ($d \geq 0.8$) exist between the LiP participant's scores and the mean scores of the matched controls (d_1), as well as between the LiP participant's scores and the ARN group's mean scores (d_2) with regard to Total

Problems (d_1 = 2.9; d_2 = 3.0), Internalising Problems (d_1 = 1.7; d_2 = 2.6), Externalising Problems (d_1 = 2.4; d_2 = 2.8) and Social Problems (d_1 = 3.3; d_2 = 3.0). Therefore, the 17-year-old LiP participant obtained higher scores (significant higher μ), compared to the mean scores of matched controls and the ARN group, on behaviour scales measuring problem severity, internalising behaviour problems, externalising behaviour problems and social problems. Consequently, the H_0 hypothesis with regard to CBCL Total Problems, CBCL Internalising Problems, CBCL Externalising Problems and CBCL Social Problems can be rejected.

Figure 5.65 graphically compares the scores of the LiP participant (LP) on the CBCL behaviour scales to the mean scores of the matched controls (Control). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.65.

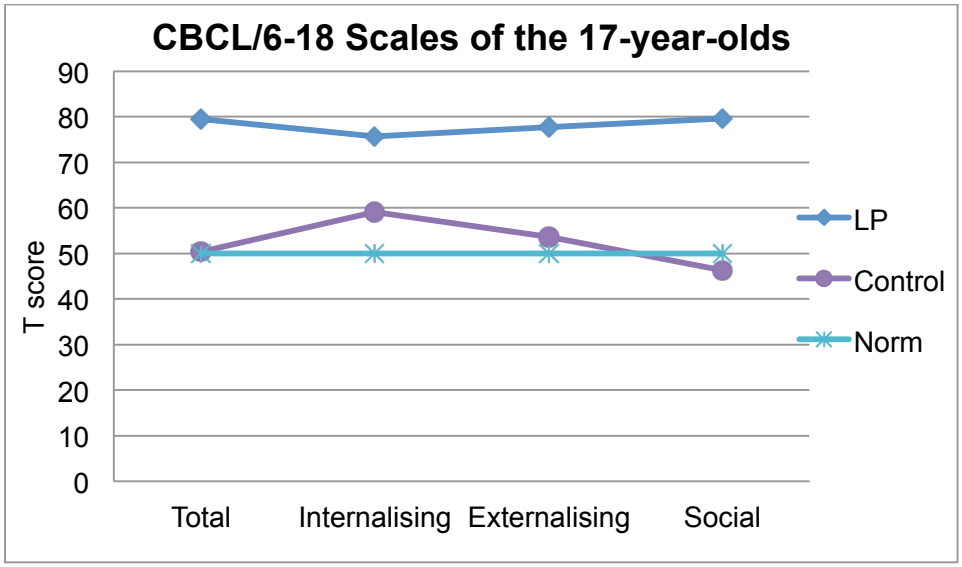

Figure 5.65. CBCL/6-18 scales of the 17-year-olds.

It is evident that the LiP individual's scores on all the CBCL/6-18 scales are significantly higher than the mean scores of the matched controls and the ARN group. It is noticeable that the mean score of the two controls on the Internalising Problems scale of the CBCL/6-18 is above the mean score of the ARN group.

Summary of maladaptive behaviour profiles. Table 5.30 provides a summary of the effect sizes (d_1 and d_2) for every maladaptive behaviour construct across the different

age groups to identify patterns among the performance of the different LiP participants. Effect sizes are marked with an asterisk when both d_1 and $d_2 \geq 0.8$.

Table 5.30

Effect Sizes (d_1; d_2) of the 4-, 6-, 8-, 15- and 17-Year-Olds on Measures of Maladaptive Behaviour

Maladaptive Behaviour Measures	**4-year-olds**		**6-year-olds**		**8-year-olds**		**15-year-olds**		**17-year-olds**	
	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**	***d*1**	***d*2**
CBCL Syndrome Scales										
Total Problems	0.5	0.9	1.2	0.4	**2.3***	**1.8***	0.3	0.3	**2.9***	**3.0***
Internalising	0.4	0.4	0.4	0.7	**2.8***	**3.1***	0.1	0.6	**1.7***	**2.6***
Externalising	0.2	0.8	1.4	0.2	**2.2***	**1.9***	0.8	0.3	**2.4***	**2.8***
Social Problems					**1.3***	**1.0***	0.4	0.8	**3.3***	**3.0***
C-TRF Syndrome Scales										
Total Problems	**2.2***	**1.5***	0.4	0.1	**1.6***	**1.4***	0.1	0.1		
Internalising	**1.0***	**1.0***	0.7	0.9	**1.8***	**2.5***	0.1	0.6		
Externalising	1.2	0.4	0.9	0.2	**1.8***	**2.0***	0.4	0.1		
Social Problems					**1.3***	**1.1***	0.8	0.7		

Note: * Both d_1 and $d_2 \geq 0.8$; Internalising = Internalising Problems; Externalising = Externalising Problems.

In Table 5.30, it is evident that significant differences ($d \geq 0.8$) exist between three of the LiP participants' scores on the maladaptive behaviour measures and the mean scores of the controls matched to them (d_1), as well as between the scores of the three LiP participants and the mean scores of the ARN group (d_2). The 8- and 17-year-old LiP participants obtained higher scores on all the problem scales of the CBCL/6-18 (Total Problems, Internalising Problems, Externalising Problems and Social problems), indicating a wide

range of behaviour problems at home. Compared to typically developing peers, the 4-year-old LiP participant presented with significantly more total and internalising behaviour problems at school, while the 8-year-old LiP participant obtained significantly higher scores on all the problem scales of the TRF (behaviour problems at school). However, parents rated the problem behaviour of the 4-year-old differently from the teachers. More problems than are typical for 4-year-old children were not noted at home.

Certain patterns in the performance of the 4-, 8- and 17-year-old LiP participants on the CBCL and C-TRF or TRF are noticeable. All three LiP participants who presented with significant behaviour problems on either or both of the CBCL and C-TRF behaviour checklists have high scores on the Total Problems scale. This indicates that they generally presented with behaviour problems that were more severe compared to typically developing peers. Two of the LiP participants (8- and 17-year-olds) also presented with pervasive behaviour problems (i.e. problems are evident on all the scales of the behaviour checklists).

Maladaptive behaviour trajectories. Graphs were drawn to represent the LiP and control participants' scores on maladaptive behaviour measures across the different age groups. This was done to identify developmental trends. No hypothesis is tested; therefore, this aspect of the research is purely explorative. Trajectories were plotted for each maladaptive behaviour construct. T-scores ($\overline{X} = 50$; $sd = 10$) were used to represent the scores of the LiP participants, the mean scores of the control participants (Control) and the norm group (Norm).

Total problems. Figure 5.66 graphically compares the CBCL/1.5-5 and CBCL/6-18 Total Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) and the ARN group (Norm Group) across the different age groups.

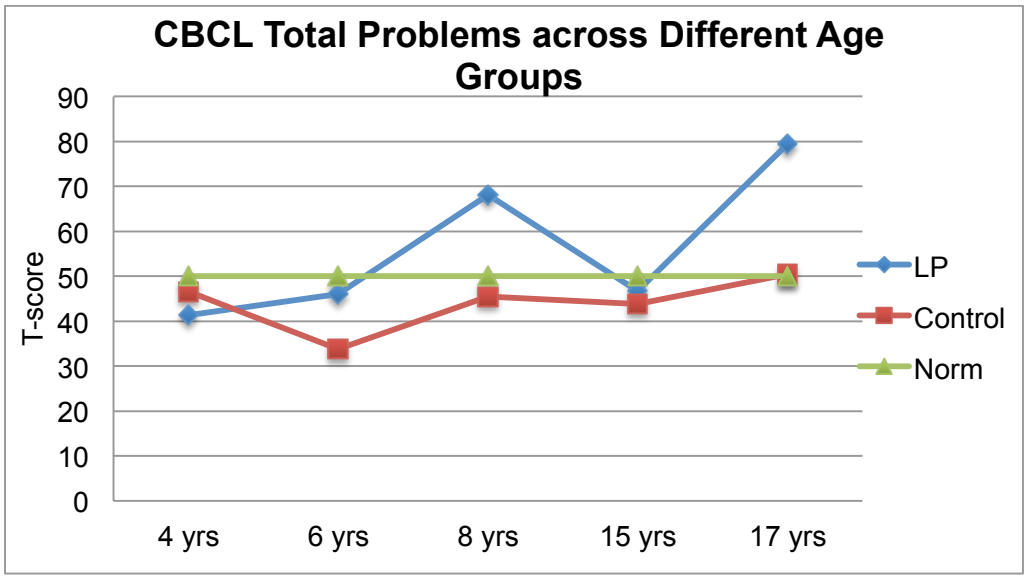

Figure 5.66. CBCL Total Problems across the different age groups.

It is evident in Figure 5.66 that the 6-, 8- and 17-year-old LiP participants have higher mean scores on the CBCL Total Problems scale than the controls have. The scores of the 8-year-old (d_2 = 1.8) and 17-year-old (d_2 = 3.0) LiP participants are also significantly above the mean scores of the ARN group. The controls matched to the LiP participants generally have scores that are lower or similar to the mean score of the norm group on the CBCL Total Problems scale. No specific age-related among the LiP participants trend with regard to total problems seems evident.

Figure 5.67 graphically compares the C-TRF and TRF Total Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.67. The 17-year-old LiP participant did not attend school; therefore, the TRF was not completed for the 17-year-old participants.

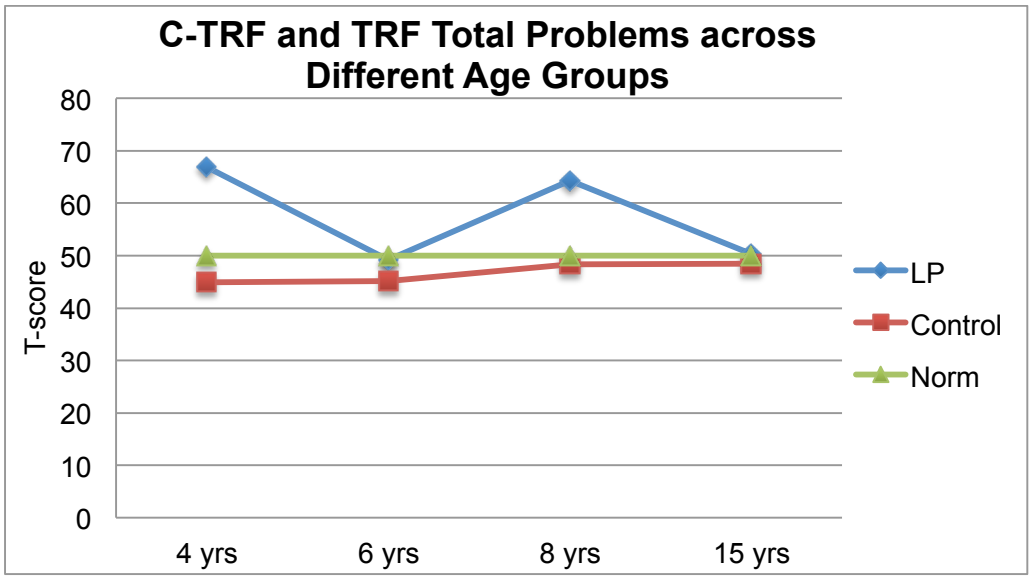

Figure 5.67. C-TRF and TRF Total Problems across the different age groups.

It is evident in Figure 5.67 that the scores of the 4-year-old (d_1 = 2.2) and 8-year-old (d_1 = 1.6) LiP participants on the C-TRF and TRF Total Problems scales are significantly higher compared to that of the controls. The scores of the 4-year-old (d_2 = 1.5) and 8-year-old (d_2 = 1.4) LiP participants on the Total Problems scales of the C-TRF and TRF are also above the mean score of the ARN group. Therefore, the 4- and 8-year-old LiP participants presented with significantly more behaviour problems at school than the matched controls and the average person in the ARN group did. Thus, it appears that no age-related trend is evident with regard to TRF problem severity among the LiP participants for whom data is reflected in Figure 5.67. The scores of the controls on C-TRF and TRF Total Problems closely follow the trajectory of the mean scores of the ARN group on this scale.

Internalising problems. Figure 5.68 graphically compares the CBCL/1.5-5 and CBCL/6-18 Internalising Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN (Norm) group are also depicted in Figure 5.68.

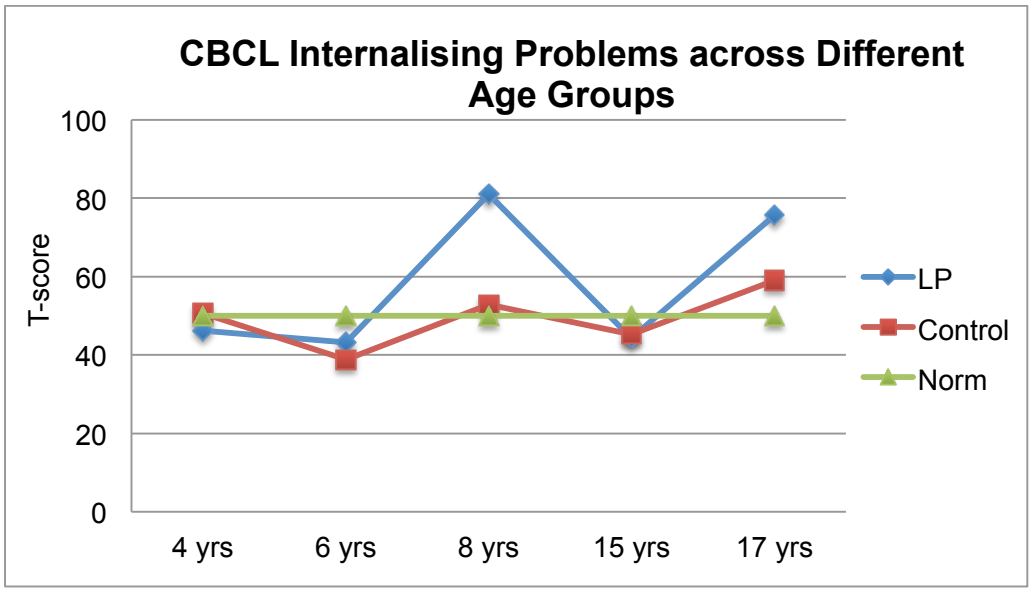

Figure 5.68. CBCL Internalising Problems across the different age groups.

In Figure 5.68, it is evident that that the scores of the 8-year-old (d_1 = 2.8) and 17-year-old (d_1 = 1.7) LiP participants on CBCL Internalising Problems are above the mean scores of the matched controls. The 8-year-old (d_2 = 3.1) and 17-year-old (d_2 = 2.6) LiP participants' scores on CBCL Internalising Problems are also significantly above the reported mean scores of the ARN group. Therefore, the 8- and 17-year-old LiP participants presented with significantly more internalising behaviour problems than typically developing peers did. Thus, it appears that no age-related trend among the LiP participants with regard to internalising problems is evident.

The mean score of the 17-year-old controls on the CBCL Internalising Problems scale is higher than the reported mean score of the ARN group. The other control participants all scored similarly to or below this mean score. No age-related trend with regard to internalising problems among the control participants is evident.

Figure 5.69 graphically compares the C-TRF and TRF Internalising Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups (excluding the 17-year-olds). In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.69.

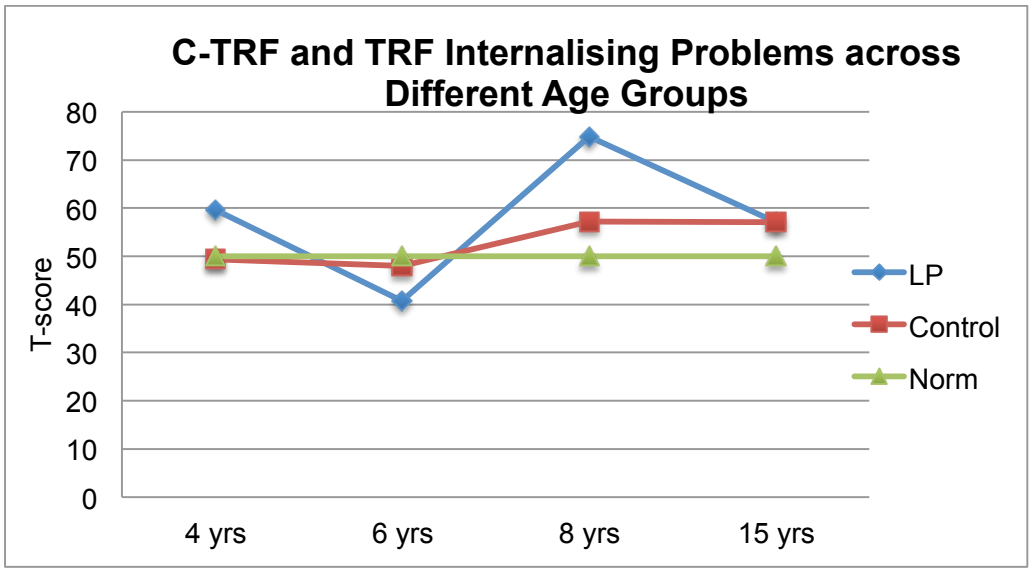

Figure 5.69. C-TRF and TRF Internalising Problems across the different age groups.

It is evident in Figure 5.69 that the 4-year-old (d_1 = 1.0) and 8-year-old (d_1 = 1.8) LiP participants have significantly higher scores compared to the matched controls on the C-TRF and TRF Internalising Problems scale. It is also apparent that the scores of the 4-year-old (d_2 = 1.0) and 8-year-old (d_2 = 2.5) LiP participants on C-TRF and TRF Internalising Problems are significantly above the mean score of the ARN group, while the score of the 6-year-old (d_2 = 0.9) LiP participant is significantly below this mean score. Thus, no age-related trend with regard to teacher-rated internalising problems among the LiP participants is evident.

The scores of the 4- and 6-year-old control participants on the C-TRF Internalising Problems scale are similar or close to the mean scores of the ARN group, while the 8- and 15-year-old matched controls' scores on this scale are above the mean score. As the urban 4- and 6-year-old control participants and the rural 8- and 15-year-old control participants differed with regard to certain characteristics, it is evident that these factors may explain the increase in scores on the Internalising Problems scale among the control participants between the ages of 6 and 8 years. However, these factors alone do not seem to explain the significantly higher Internalising Problems scores of the LiP participants (4- and 8-year-old), as there is no age-related trend with regard to the Internalising Problem scores of the LiP participants.

Externalising problems. Figure 5.70 graphically compares the CBCL/1.5-5 and CBCL/6-18 Externalising Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.70.

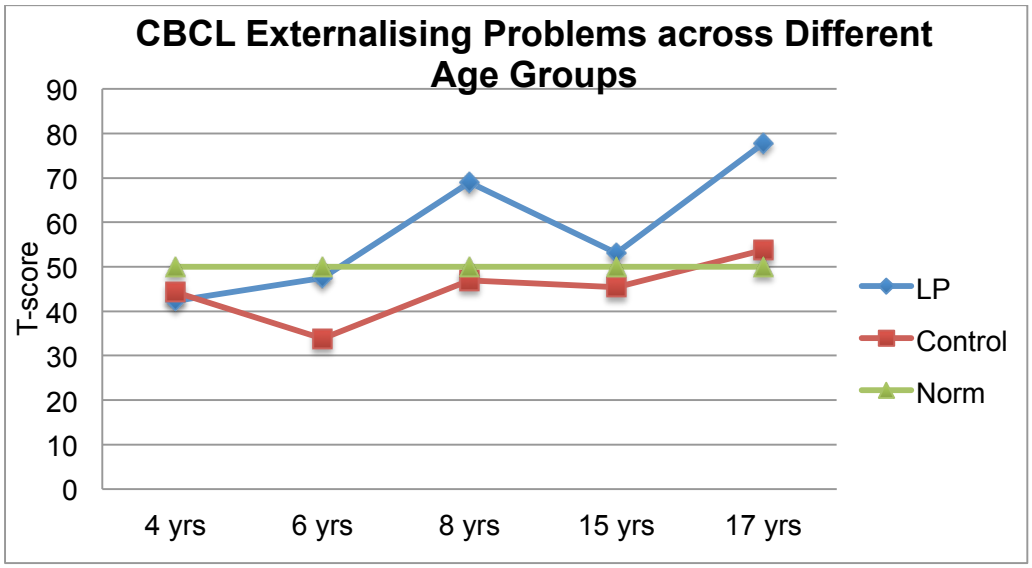

Figure 5.70. *CBCL Externalising Problems across the different age groups.*

In Figure 5.70, it is evident that the 6-year-old (d_1 = 1.4), 8-year-old (d_1 = 2.2), 15-year-old (d_1 = 0.8) and 17-year-old (d_1 = 2.4) LiP participants have significantly higher scores compared to the mean scores of the controls on the CBCL Externalising Problems scale. Further, it is apparent that the 8-year-old (d_2 = 1.9) and 17-year-old (d_2 = 2.8) LiP participants also have significantly higher scores compared to the mean score of the ARN group. Thus, it appears that no age-related trend with regard to CBCL Externalising Problems among the LiP participants is evident. The controls obtained lower or very similar scores on the CBCL Externalising Problems scale compared to the average person in the ARN group.

Figure 5.71 graphically compares the C-TRF and TRF Externalising Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.71.

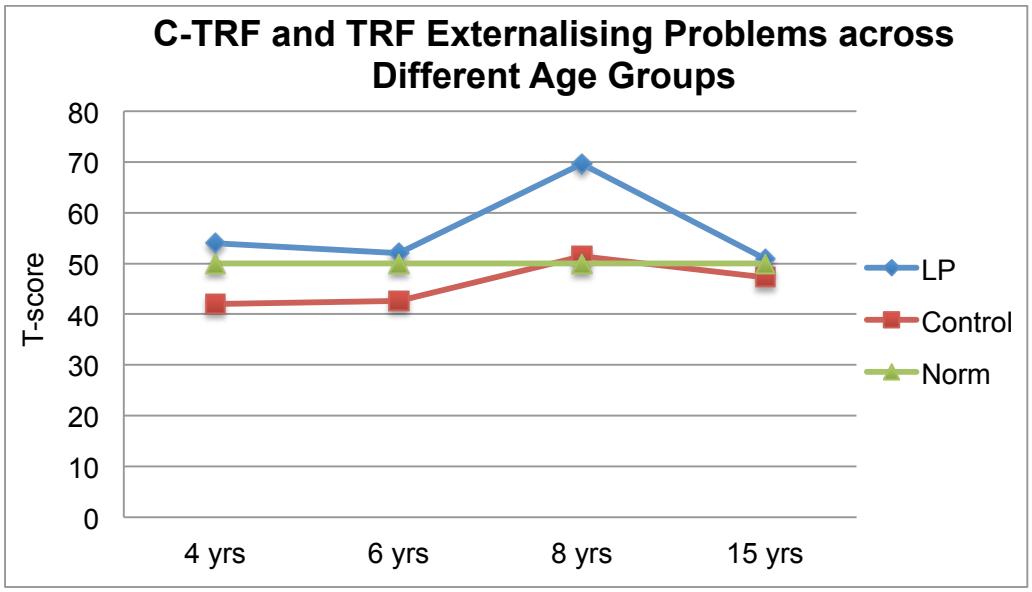

Figure 5.71. C-TRF Externalising Problems across the different age groups.

In Figure 5.71, it is evident that the scores of the 4-year-old (d_1 = 1.2), 6-year-old (d_1 = 0.9) and 8-year-old (d_1 = 1.8) LiP participants on the C-TRF and TRF Externalising Problems scale are significantly higher than the mean scores of the controls. Further, it is apparent that the score of the 8-year-old (d_2 = 2.0) LiP participant on the C-TRF and TRF Externalising Problems scale is significantly higher than the mean score of the ARN group. Thus, no age-related trend with regard to externalising problems among the LiP participants is evident.

The scores of the controls on the C-TRF and TRF Externalising Problems scale are below (4- and 6-year-olds) or very similar (8-year-old and 15-year-olds) to the mean score of the ARN group. This indicates that they did not have externalising behaviour problems.

Social problems. Figure 5.72 graphically compares the CBCL/6-18 Social Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.72. The CBCL/1.5 does not include a Social Problems scale; therefore, no data for the 4- and 6-year-old participants with regard to social problems. are available.

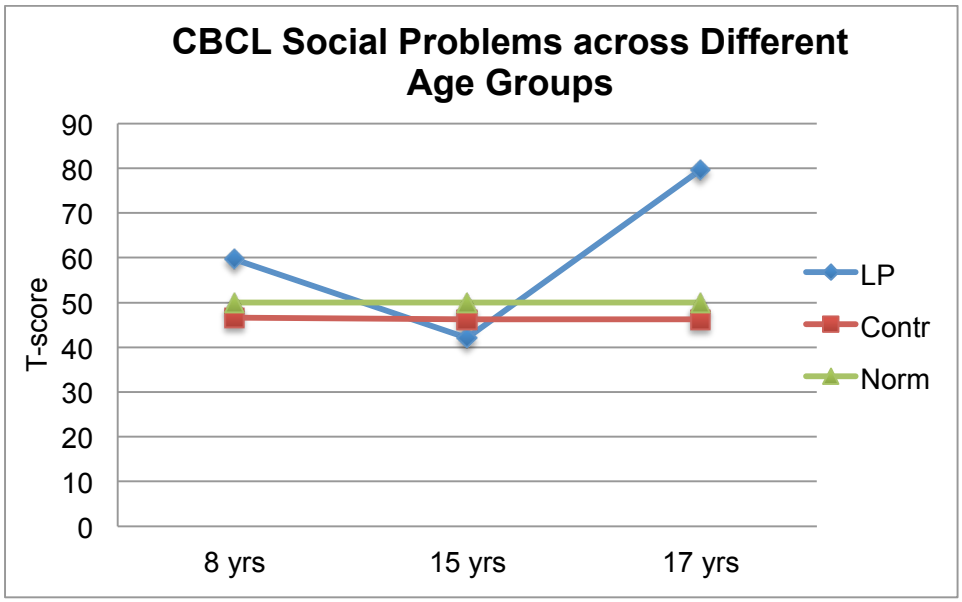

Figure 5.72. *CBCL Social Problems across the different age groups.*

In Figure 5.72, it is evident that the 8-year-old (d_1 = 1.3) and 17-year-old (d_1 = 3.3) LiP participants have significantly higher scores on the CBCL Social Problems scale compared to the mean scores of the matched controls. It is also apparent that the scores of the 8-year-old (d_2 = 1.0) and 17-year-old (d_2 = 3.0) LiP participants on the CBCL Social Problems scale are significantly above the mean score of the ARN group. Thus, it appears that no age-related trend with regard to social problems among the LiP participants is evident. The scores of the 8-, 15- and 17-year-old controls on CBCL Social are below (but close to) the ARN group mean scores.

Figure 5.73 graphically compares the TRF Social Problems scores of the LiP participants (LP) to the mean scores of the matched controls (Control) across the different age groups. In addition, the mean scores of the ARN group (Norm) are also depicted in Figure 5.73. The C-TRF checklist does not include a Social Problems scale; therefore, no data are available for the 4-year-old and 6-year-old participants. The 17-year-old LiP participant did not attend school; therefore, no data were gathered for the 17-year-old participants.

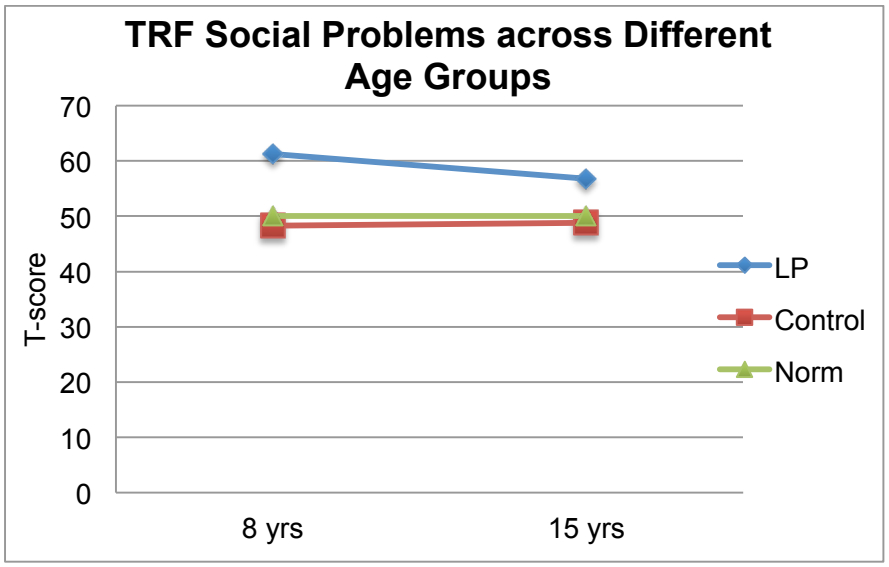

Figure 5.73. TRF Social Problems across the different age groups.

In Figure 5.73, it is evident that the scores of the 8-year-old (d_1 = 1.3) and 15-year-old (d_1 = 0.8) LiP participants are significantly higher than the mean scores of the matched controls on the TRF Social Problems scale. The score of the 8-year-old (d_1 = 1.1) LiP participant is also significantly above the mean score of the ARN group. As only two age groups are represented in the graph, it is difficult to ascertain a specific age-related trend. The controls matched to the 8-year-old and 15-year-old LiP participants obtained mean scores very similar to that of the mean score of the ARN group on the TRF Social Problems scale.

Summary of maladaptive behaviour trajectories. The graphs indicate that no age-related trends are evident on either the CBCL or TRF and C-TRF scales with regard to problem severity, internalising problems, externalising problems, or social problems among the LiP participants. The scores of the controls on the Total Problems, Externalising Problems and Social Problems scales of the CBCL and C-TRF closely follow or are below the trajectory of the mean scores of the ARN group, indicating that the controls did not present with externalising or social problems. The mean score of the 17-year-old control on the CBCL Internalising Problems scale is above the mean score of the ARN group, but the other control participants all scored similar to or below this mean score. Therefore, no age-related trend among the control participants with regard to internalising problems, as observed at home, is evident. However, an increase in scores on

the Internalising Problems C-TRF and TRF scales is evident among the controls between the ages of 6 and 8 years. The urban 4- and 6-year-old controls scored below or similar to the mean score of the ARN group on C-TRF Internalising Problems, but the 8- and 15-year-old controls scored above the mean score on the TRF scale. As the urban 4- and 6-year-old control participants and the rural 8- and 15-year-old control participants differed with regard to socioeconomic background and certain characteristics, it is evident that these factors may explain the increase in scores on Internalising Problems between the ages of 6 and 8 years among the controls. However, these factors do not seem to explain the significantly higher Internalising Problems scores of the LiP participants (4- and 8-year-olds) – there is no visible age-related trend with regard to internalising problems among the LiP participants.

Conclusions: Maladaptive behaviour.

Significant differences. Three of the LiP participants (4-, 8- and 17-year-olds) presented with significant behaviour problems in comparison to the matched controls and the average person in the ARN group. All three these participants have high scores (relative to the mean score of the ARN group) on the Total Problems scale and the Internalising Problems scale. The 8- and 17-year-old LiP participants have significantly higher scores compared to those of the matched controls and the similarly-aged norm groups on all the syndrome scales that were utilised in the study (Internalising Problems, Externalising Problems, Social Problems), indicating pervasive behaviour problems. The 17-year-old LiP participant did not attend school; therefore, his behaviour problems were only noted at home. The 8-year-old LiP participant presented with similar behaviour problems at home and at school (internalising problems, externalising problems and social problems), while the 4-year-old LiP participant's problem behaviour was noticeable only at school (total problems and internalising behaviour problems). The 6-year-old LiP participant does not have significantly higher scores than the mean score of the ARN group on the Total, Internalising and Externalising Problems scales of the CBCL/1.4 and C-TRF. However, she has significantly higher scores on the CBCL/1.5-5 Attention Problems scale compared to her typically developing peers. This means that the 15-year-old LiP participant was the only individual who did not present with significant behavioural difficulties when compared to the matched controls and the ARN group.

Trends. No age-related trends with regard to problem severity, externalising problems, and social problems among the LiP participants are noticeable. Generally, the controls obtained similar or lower scores compared to the mean scores of the ARN group. Low scores on the behaviour problems checklists among the controls were expected, as potential control candidates were excluded from the study when they presented with clinically significant scores on the CBCL DSM-orientated scales (corresponding to criteria for specific DSM disorders). No age-related trends with regard to problem severity, externalising problems, and social problems among the control participants are noticeable. However, an increase in scores on the Internalising Problems scale of the C-TRF and TRF is noticeable between the ages of 6 and 8 years among the controls. This trend appears to reflect a difference in the levels of internalising behaviour among the urban (4- and 6-year-old) versus the rural (8- and 15-year-old) control participants. As this trend is not observed on the C-TRF and TRF Internalising Problems scales among the LiP participants, it is evident that the high scores of the three LiP participants on the Internalising Problems scales cannot be explained purely by differences between the urban and rural participants. Overall, the high scores of the LiP participants (4-, 8- and 17-year-olds) on behaviour problem scales appear to be a consequence of LiP-related factors, and the varying results on these scales do not appear to be a consequence of gender, cultural or socioeconomic factors.

Summary of Results

Overall, significant differences between the scores of the LiP participants and those of their typically developing peers are evident on certain neuropsychological measures (verbal and visual memory, recognition of facial emotion, attention, inhibition, and cognitive flexibility) and behaviour-rating instruments (adaptive functioning and maladaptive behaviour). None of the LiP participants scored significantly below the mean scores of the matched controls and the similarly aged average person in the ARN group on measures of face recognition, visual-verbal paired associative learning, ToM, processing speed and school adjustment.

Age-related trends (urban participants: better performance compared to the mean score of the ARN group; rural participants: worse performance compared to the mean score of the ARN group) among the LIP participants with regard to verbal free recall, cognitive

flexibility and recognition of disgusted facial expressions were noted. These trends were also noted among the control participants. Differences (relative to the mean score of the ARN group) between the scores of urban and rural participants were also noted with regard to verbal recognition memory, verbal free and cued recall, visuospatial memory, and internalising problems (at school) among the control participants but not among the LiP participants. Therefore, rural participants appear to have been disadvantaged on several neuropsychological measures (verbal memory, cognitive flexibility, recognition of disgusted facial expressions) but not on others (AR Total and TM Total). Therefore, matching the LiP participants to controls proved to be important because it placed the LiP participants' performance on neuropsychological and psychosocial measures in their specific cultural and socioeconomic context.

Trends with regard to processing speed and inhibition (increase of errors between 8 and 15 years of age relative to the ARN group) and coping skills among the LiP participants do not appear to be related to differences between the urban and rural participants. Trends with regard to processing speed, inhibition, cognitive flexibility and abstract thinking (AS Total) and all visual memory measures (decrease in scores between the ages of 8 and 15 years) among the control participants also do not appear to be related to differences between urban and rural participants. The research results are summarised below. The summary will serve as a basis for the discussion of the results in the next chapter.

Neuropsychological Functioning

Memory and learning. Significant differences in the performance of the LiP participants and the performance of the typically developing children are evident on measures of verbal (free recall and recognition) and visual (short- and long-term memory) memory. This result indicates that, although different neural mechanisms are suggested to underlie the different types of memory (verbal versus visual, long-term versus short-term, visual-spatial versus visual content), various types of memory functions can be affected in children and adolescents with LiP. However, visual-verbally paired associative memory is not affected.

Age-related trends among the LiP participants differ on measures of verbal versus visual measures. Differences between the urban participants (4- and 6-year-olds) and the

rural participants (8-, 15- and 17-year-olds) appear to explain the decrease in the performance of the LiP and control participants on a measure of verbal free recall. Differences between the urban and rural participants do not appear to explain the performance of the control participants (a decrease in scores between the ages of 8 and 15 years) on measures of visual memory. However, certain differences in performance of the urban versus the rural LiP participants are evident on the visual memory measures. Compared to typically developing peers, the 4- and 6-year-old LiP participants performed significantly worse on measures of short-term (4- and 6-year-olds) and long-term (6-year-old) visual memory for content and position. However, compared to the mean scores of matched controls and the ARN group, the 8- and 17-year-old LiP participants performed significantly better on long-term visual memory measures. The 15-year-old LiP participant performed inconsistently: significantly worse on measures of short-term and long-term visual memory for content, but significantly better than typically developing peers did on a measure of short-term spatial memory. Opposite trends among the control participants versus the LiP participants with regard to short-term spatial memory were also especially noticeable, with urban controls performing above the mean score of the ARN group and the urban LiP participants scoring below this mean score. Therefore, the effect of LiP may be different among the urban participants than among the rural participants, especially with regard to spatial memory. Ultimately, LiP appears to have different effects on the verbal memory performance of the participants as opposed to their visual memory performance.

Social perception. Compared to the matched controls and the average individual in the ARN group, the LiP participants performed significantly different on a measure of recognition of facial emotion. However, results on the face recognition and ToM measures suggest that the LiP participants are generally as able as typically developing children to recognise faces and to attribute mental states to themselves and others and to understand that others have desires, intentions, and beliefs that are different from their own.

Results on the recognition of facial emotion measure indicate that, compared to the controls and the average individual in the ARN group, none of the LiP participants had difficulty in recognising happy (positive) facial expressions. However, they performed worse on tasks requiring them to recognise neutral and negative (sad, fearful, angry, and disgusted) facial expressions. Each of the LiP participants recognised at least one (neutral

or negative) facial expression significantly worse than the typically developing individuals (controls and ARN group) did. There is no specific facial expression that all the LiP participants recognised less well than typically developing peers did. Interestingly, given the hypothesised importance of the amygdala in recognising fearful facial expressions, only the 4-year-old LiP participant found it significantly more difficult to recognise fearful facial expressions.

In some instances, the LiP participants recognised fearful (17-year-old), neutral and disgusted facial expressions (6-year-old) significantly better than their matched controls and the average person in the ARN group did. Only the 4-year-old scored significantly below the mean scores of both the ARN group and the controls on a general measure of recognition of facial emotion.

Overall, no specific age-related performance trends on any of the recognition of facial emotion error scales were noticeable, except for Disgust Errors. An increase in scores on the Disgust Errors scale between the ages of 6 and 8 years, as well as between the ages of 8 and 15 years is evident among the LiP participants. A similar increase in errors on this scale between the ages of 6 and 8 years is evident among the control participants. As there are differences between the urban participants (4- and 6-year-olds) and the rural participants (8-, 15- and 17-year-olds), it is possible that these factors affected the participants' performance on the Disgust Errors scale.

The lack of significant differences between the results of the LiP participants and the control groups on a measure of face recognition indicates that evident challenges in recognition of facial emotion among the LiP participants cannot be explained by deficits in face recognition or visual-spatial processing.

Attention and executive function. Significant differences between the scores of the LiP participants and the mean scores of the matched controls and the LiP participants and between the mean scores of the ARN groups are apparent on the attention, inhibition, and cognitive flexibility measures. Results vary between individuals. Specific LiP individuals presented with significant hyperactive, impulsive, and inattentive behaviour at home (6- and 17-year-olds) and at school (4-year-old). The 4- and 17-year-old LiP participants who obtained significantly higher scores than their typically developing peers did on the Attention Problems behaviour scales also performed significantly worse on measures of

inhibition (Statue Total and INI Errors Total). All the control participants presented with less inattentive and impulsive behaviour than the average person in the ARN groups did. This was expected, as potential control participants were excluded from the study if they presented with Attention Deficit Hyperactive Disorder or any other neuropsychiatric disorder.

The two measures of cognitive flexibility that were used in the study are constructed and normed for children and adolescents older than 6 years. The LiP participants (8-, 15- and 17-year-olds) performed inconsistently on the two measures. Compared to matched controls and the average individual in the ARN groups, the 8- and 15-year-old LiP participants performed significantly worse on one measure of switching, initiation and abstract thinking (AS subscale of NEPSY-II). However, not one of the LiP participants older than 6 years performed worse than their similarly aged typically developing peers did on another measure of cognitive flexibility (INS Total Errors scale).

A particular trend in performance on most measures of executive function (INN, INI, and INS) among the LiP participants is evident. The 4-, 6- and 8-year-old LiP participants tended to obtain scores similar to the ARN groups on measures of inhibition and cognitive flexibility. However, the 15- and 17-year-old LiP participants obtained significantly higher scores (with more errors indicating worse performance) compared to the typically developing individuals on these measures. This general tendency is also evident among control participants on measures of processing speed, inhibition, and cognitive flexibility (INN, INI, AS Total) and therefore may not be an age-related phenomenon unique to LiP individuals. The higher error scores of the 15- and 17-year-old LiP and control participants (above the ARN group mean scores), compared to the lower error scores (below the ARN group mean scores) of the 4-, 6- and 8-year-old participants on most measures of executive function cannot be explained by differences between the urban and rural participants.

Psychosocial Functioning

Adaptive behaviour. Significant differences between the ratings on adaptive behaviour scales of three of the LiP participants (6-, 15- and 17-year-olds) and those of the matched controls and between the ratings of the LiP participants and those of the average individuals in the ARN groups are apparent. Each of these three LiP participants (6-, 15-

and 17-year-olds) presented with a significantly lower score on a different adaptive behaviour subdomain (6-year-old: play and leisure skills, 15- year-old: social skills and 17-year-old: coping skills). Results on the TRF adaptive scale suggest that all the school-attending LiP participants adjusted as well at school (academic achievement, appropriate behaviour, learning as hard as others, happiness) as the matched controls and the average individual in the ARN group.

While no noticeable trend with regard to social skills, play and leisure skills, or school adjustment among the LiP participants is apparent, the graph representing LiP Coping Skills scores indicates a downward slope. A similar trend with regard to coping skills is not noticeable among the control participants. Therefore, differences between the urban and rural participants do not appear to explain the LiP participants' decreasing scores on the Coping Skills subdomain of the Vineland-II. Therefore, age-related changes or a barrier in the development of coping skills (emotional regulation and flexible behaviour) may be present among the LiP participants.

Maladaptive behaviour. It is evident that certain LiP individuals (4-, 8- and 17-year-olds) presented with significantly more behaviour problems compared to matched controls and the average individual in the ARN group. Compared to these typically developing individuals, the three LiP participants (4-, 8- and 17-year-olds) presented with significantly more total and internalising problems. The 4-year-old LiP participant's total and internalising behaviour problems were apparent only at school and not at home. In addition to a high frequency of total and internalising problems, the 8-year-old LiP participant presented with externalising and social problems at school and at home, while the 17-year-old LiP participant presented with more externalising and social behaviour problems at home than his typically developing peers did.

No noticeable age-related trends are evident on the Total Problems, Externalising Problems, Internalising Problems and Social Problems syndrome scales among the LiP participants. Therefore LiP-related factors unique to each individual may underlie these behaviour problems.

Compared to the mean scores of the ARN group, the 8-year-old (at school and at home), 15-year-old (at school) and 17-year-old (at home) rural control participants presented with higher scores on the Internalising Behaviour Problems scale. However, the

4- and 6-year-old urban controls did not score above the mean score of the ARN group on the Internalising Behaviour Problems scale. Most likely, this trend among the control participants relates to the effect of environmental differences (rural versus urban). This trend is not evident among the LiP participants; therefore, it is unlikely that the internalising problems of the 4-, 8- and 17-year-old LiP participants can be explained by their rural or urban status respectively. Although the Internalising Problems scores of the rural control participants are higher than the mean score of the ARN group, a possible diagnosis of anxiety or mood disorders among the control participants is not apparent on the CBCL DSM scales.

Conclusion

The results of the study were reported in this chapter. The results obtained on the neuropsychological instruments and adaptive and maladaptive behaviour checklists were presented for each construct and each age group separately. The scores obtained on the neuropsychological measures and behaviour checklists were presented in tables and graphs. Significant differences between the scores of the LiP participants and the mean scores of matched controls and between the scores of the LiP participants and the mean scores of the ARN group are evident on measures of memory and learning, recognition of facial emotion, attention and executive function, adaptive behaviour and maladaptive behaviour.

For each construct, graphs were drawn to represent the performance of the LiP and control participants across the age groups to identify trends. Trends were noted on certain measures (verbal free recall and recognition of disgust) among the LiP and control participants, and these trends suggest differences between the performance of the urban and control participants. Trends across the age groups with regard to certain constructs (visual memory, coping skills, internalising problems) among the LiP and control participants show a more complex relationship with factors that distinguish the urban and rural participants. A summary of the significant results and trends was provided at the end of each section (each construct) and at the end of the chapter to form a basis for the discussion of the results. The research results presented in this chapter are discussed in the next chapter.

Chapter 6

Discussion of Results

The primary aim of the study was to determine whether children and adolescents with LiP have increased neuropsychological and psychosocial deficits compared to healthy controls. The secondary aim of the study was to compare the performance of the LiP and control participants across the different age groups in order to explore trends in their neuropsychological and psychosocial development. The children and adolescents with LiP were compared to match controls as well as to relevant norm groups (the samples on which the various instruments were normed) with regard to memory and learning, attention and executive function, social perception and psychosocial adjustment. The results of these analyses have been reported in Chapter 5. In this chapter, the main findings with respect to the neuropsychological functioning and psychosocial adjustment of the LiP participants will be highlighted and discussed.

Neuropsychological Functioning

The main findings with respect to memory and learning, social perception, attention and executive function will be discussed next.

Memory and Learning

Each of the LiP participants in the current study performed significantly worse than controls and the age-appropriate norm group did on at least one verbal or visual memory measure. Overall, variable levels of verbal and visual memory functioning among the children and adolescents with LiP were found, and this finding is in line with reports in the literature of variable visual and verbal memory functioning among adults and children with LiP (Brand et al., 2007; Emsley & Paster, 1985; Hurlemann et al., 2010; Hurlemann et al., 2007; Siebert et al., 2003; Strange, Hurlemann, & Dolan, 2003; Thornton et al., 2008; Tranel & Hyman, 1990).

Deficits in short-term memory of non-emotional verbal information were noted among three of the LiP participants (6-, 8- and 17-year-olds). Significant differences between the scores of the LiP participants and the mean scores of the typically developing children

(control and norm groups) are evident with regard to verbal recognition (6- and 8-year-olds) and free recall (17-year-old) measures. Although only two of the LiP participants in the current study performed worse than their typically developing peers did on a measure of verbal recognition, it has to be taken into account that the verbal recognition measure normally is administered only to 4- to 8-year-olds (Korkman et al., 2007a). Therefore, the LiP participants (15- and 17-year-olds) who were not evaluated by means of the verbal recognition measure might also have performed poorly compared to their typically developing peers.

Only the 17-year-old LiP participant performed worse than matched controls did on a measure of verbal free recall (story). Although this participant was matched to his controls with regard to intelligence, he had a lower level of education. The LiP participant left school in Grade 9 (therefore he completed only Grade 8), while the two controls matched to him were still in school (Grades 11 and 12 respectively). Some aspects of verbal memory ability have been associated with level of education, as a broader knowledge base (semantic memory) was suggested to contribute to better long-term memory functioning (Maril et al., 2010; Reis, Guerreiro, & Petersson, 2003). Therefore, a lower education level could explain why the 17-year-old LiP participant performed worse than his peers did on the verbal free recall measure. However, the MRI scan of the 17-year-old showed bilateral amygdala damage and this (or less visible brain damage) might provide another explanation for the 17-year-old LiP participant's poor performance on the verbal free recall measure. Adults with LiP, who were matched to controls with similar education level, have also been reported to perform poorly on measures of short-term verbal memory (Siebert et al., 2003; Thornton et al., 2008).

The literature suggests a strong connection between verbal and visual memory deficits and hippocampal damage in children (De Haan et al., 2006; Isaacs et al., 2003; Jambaqué et al., 2006). Therefore, visual and verbal memory deficits among the children and adolescents with LiP in the current study would suggest hippocampal involvement. In the current study, neuroimaging was done on four children with LiP, and two of them presented with bilateral amygdala lesions and no visible hippocampal lesions, and results for two of them were inconclusive. Reports could be found of other individuals with LiP who had memory problems and presented with amygdala but not hippocampal lesions (Emsley & Paster, 1985). It has been suggested that hippocampal damage that is not

visible on CT or MRI scans may explain memory problems among individuals with LiP and amygdala damage (Emsley & Paster, 1985; Newton et al., 1971). The amygdala and hippocampus are closely connected (Tohno et al., 2013), and it is also possible that not only the hippocampus but also the amygdala plays a role in verbal and visual memory of non-emotional material. Recently, Chau and Galvez (2012) concluded that the amygdala might play an important role in learning and remembering non-emotional material by prioritising and consolidating behaviourally relevant material. Even though one needs to be cautious with localising and interpreting function, there does seem to be some indication that memory functions (normally dependent on the hippocampus and/or the amygdala), were affected negatively in the children and adolescents with LiP in the current study.

The MRI scan of the 17-year-old showed bilateral amygdala damage that was more extensive compared to the amygdala damage (partial damage) of the younger (8-year-old) child. It is therefore possible that the 17-year-old LiP participant performed worse than the younger LiP individuals on a measure of short term verbal memory due to deterioration of this function. However, there was no obvious decrease or increase in scores on visual and verbal memory measures that could be explained by age. In the literature on LiP, reports of memory deterioration could not be found, except for a discussion of deteriorating autobiographical memory in an adult with LiP (Wiest et al., 2006). Autobiographical memory was hypothesised to be impaired in individuals with LiP due to amygdala damage (Markowitsch, 2008; Markowitsch & Staniloiu, 2011); therefore, progressive amygdala damage might explain the deteriorating autobiographical memory in this particular case.

Age-related performance trends among the LiP participants differed on measures of verbal versus visual memory. Differences in gender, culture, language and socioeconomic status between the urban female participants (4- and 6-year-olds) and the rural, male participants (8-, 15- and 17-year-olds) seem to explain the decline in the performance of the LiP and control participants on a measure of verbal free recall. However, differences between the urban and rural participants do not appear to explain the performance of the LiP and control participants (as compared to the average person in the norm group) on measures of visual memory in a similar manner. This may be because factors such as language and culture affect individuals' performance in verbal and non-verbal tests differently (Farah et al., 2006).

The age-related trend with regard to visual memory noticed among the control participants (decrease of scores between the ages of 8 and 15 years) differs from the trend among the LiP participants (improvement in scores between the ages of 6 and 8 years). The 4- and 6-year-old LiP participants performed significantly worse than typically developing peers did on measures of short-term (4- and 6-year-olds) and long-term (6-year-old) visual memory for content and position. However, the 8-, 15- and 17-year-old LiP participants performed significantly better than typically developing peers did on a measure of spatial memory. The results suggest that LiP might have affected the memory performance of the two female urban participants (worse performance) differently from the male rural participants (better performance), especially with regard to spatial memory. Gender differences (such as the involvement of the left hippocampal region in males, but not in females) in the neural substrate of spatial cognition are mentioned in the general literature on neuropsychology (Grön, Wunderlich, Spitzer, Tomczak, & Riepe, 2000; Newhouse, Newhouse, & Astur, 2007). Therefore, the better performance of male LiP participants (compared to controls and the norm group) and the poorer performance of female participants on measures of visual memory (especially spatial memory) may be explained by gender differences. Gender differences in the neuropsychological functioning of individuals with LiP have not been explored in other studies; therefore, the current results cannot be compared to previous research results. Conclusions with regard to differences in the performance of males and females and performance on verbal versus visual measures need to be viewed with caution, considering the small group of participants and the qualitative nature of evaluating the data.

The results on the visual memory measures further indicate that enhanced performance on memory measures may be evident in certain children and adolescents with LiP. This is in line with the suggestion that, in some instances, brain injury, or pathology can cause enhancement of certain cognitive functions. This may occur by means of different processes, such as functional brain reorganisation or paradoxical facilitation (Toomela et al., 1999). Morgan et al., (2012) describe paradoxical facilitation of working memory in individuals with LiP. The paradoxical functional facilitation of working memory in three adults with LiP was explained by an interactive, dynamic model of brain function (Raichle, 2010; Sporns, Chialvo, Kaiser, & Hilgetag, 2004; Stevens, 2009): Reduced interference of the involuntary attention system (vigilance) due to basolateral amygdala damage paradoxically facilitated better top-down attention control (Morgan et al., 2012). However,

the underlying brain mechanisms involved in short-term and long-term visual memory (declarative memory) are not the same as those involved in working memory. Therefore, the same explanation for facilitation of working memory in a group of individuals with LiP and basolateral amygdala damage would not apply to the current findings.

It is noticeable that the same LiP participants who performed significantly better than their peers did on a measure of visual-spatial memory (8-, 15- and 17-year-olds), did not obtain significantly higher scores on a measure of face memory (socially significant stimuli). Therefore the performance of the LiP participants on visual memory measures possibly depended on the type of visual stimuli that they had to remember. Adolphs, Tranel et al., (1999) found that two individuals with LiP and bilateral amygdala damage showed a preference for nonsense figures, patterns and landscapes that others normally do not prefer. Therefore, it is possible that individuals with LiP prefer different types of visual stimuli (such as more abstract, nonsense patterns and figures) compared to typically developing individuals, and they may remember these types of visual stimuli better than their peers may. However, this will not explain why the male LiP participants in this study performed better than their peers did on visual memory measures, while the female LiP participants performed significantly worse than their peers did when required to remember the same type of visual information.

No specific memory and learning profile (such as exclusively verbal or exclusively visual memory deficits) is evident for all the participants. However, all the LiP participants performed within the expected limits (their scores were not significantly different from the mean score of the controls and the relevant norm group) on a visual-verbal associative learning task. Unlike this result, difficulties with learning have been identified in a group of adults with LiP (Thornton et al., 2008). However, the learning task that was used in the study by Thornton et al. (2008) exclusively included verbal information and required learning of a list, whereas the learning task in the current study included visual material (pictures of neutral faces) and required associative learning. The specific visual-verbal associative memory task that was presented to the children and adolescents in the current study required them to associate drawings of neutral faces with names. Therefore, it is relevant to note that the LiP participants also presented with intact recognition of neutral faces (on the MF subtest of the NEPSY-II).

The recognition of facial emotion test that was administered to the participants in the current study includes a memory task. The children and adolescents with LiP performed significantly worse than typically developing peers did on error scales of the recognition of facial emotion task. The neutral nature of the photos and drawings used in the face recognition and verbal-visual associative learning task compared to the emotional nature of the photos used in the recognition of facial emotion measure may explain why the children and adolescents with LiP (often associated with amygdala damage) did not find it difficult to recognise neutral faces or associate names with neutral faces, but found it difficult to recognise facial expressions. It is important to note that the MF subtest of the NEPSY-II, used to measure memory for faces, was found to be less reliable in certain age groups (5 to 8 years and 11 to 12 years). However, literature supports the hypothesis that amygdala damage may underlie worse performance on tasks requiring learning of affective as opposed to neutral information (Boucsein, Weniger, Mursch, Steinhoff, and Irle, 2001). Boucsein et al. (2001) found a relationship between amygdala damage (often associated with LiP) and impairment in the associative learning of emotional faces as opposed to associative learning of neutral faces.

The findings of Boucsein et al. (2001) and others (Calder & Young, 2005; Kosaka et al., 2003; LaBar & Cabeza, 2006; Masaki et al., 2006) suggest that the underlying neural structure involved in remembering or recognising neutral faces compared to remembering or recognising emotional faces is different. Therefore, declarative memory for emotional material can be deficient while, in the same individual, episodic memory for non-emotional material is intact (LaBar & Cabeza, 2006; Masaki et al., 2006). Findings from studies on the neuropsychological functioning of adults with LiP support this hypothesis (Hurlemann et al., 2007; Thornton, 2006; Tranel & Hyman, 1990). Amygdala damage has been associated with LiP and was hypothesised to underlie difficulties among individuals with this disorder in recognising facial expressions and remembering emotionally significant material (Adolphs et al., 1997; Adolphs et al., 1999; Adolphs & Tranel, 2000; Siebert et al., 2003).

The conclusion is that the children and adolescents with LiP, similar to adults with the disorder, had variable levels of visual and verbal memory dysfunction. Age-related trends (decrease in scores on a measure of free recall) in performance on memory measures appear to be related not only to LiP, but also to cultural, language and socio-economic

differences between the rural and urban participants. Performance trends suggest that LiP possibly affects visual memory functioning differently from verbal memory functioning, with verbal memory performance being more susceptible to the additional influence of language, cultural and socio-economic factors on test performance. On the other hand, the effect of LiP on visual memory performance possibly depends on the gender of the person. It is hypothesised further that some of the LiP participants' memory for abstract visual material was better than the memory of their peers, while they performed equally well on a measure of memory for faces due to the difference in the type of visual information that needed to be remembered (socially significant versus abstract). Certain memory functions (visual-verbal associative learning and face memory) were found to be intact among all the participants. There appeared to be a pattern of intact face recognition and name-face associative learning, but significantly worse performance when required to identify facial expressions. It is hypothesised that the intensity of affective processing that is required determined the level of success on these measures, with intact performance on learning and memory tasks involving neutral faces.

These results extend knowledge of memory and learning in LiP to include an understanding of these functions among children and adolescents. It suggests that memory and learning deficits may occur even in preschool children with LiP. Therefore, the onset of memory and learning difficulties in LiP may be at a young age. Memory difficulties acquired at such a young age potentially can affect school learning and cognitive development of children negatively. A decrease of scores on memory and learning measures across the different age groups was not evident. This may suggest that memory difficulties are not exacerbated over time. However, in the absence of longitudinal follow-up studies of these children's memory functioning, this result is not conclusive.

Social Perception

Overall, results on the recognition of facial emotion measure in the current study vary. The youngest of the five LiP participants obtained a significantly lower total score on recognition of facial emotion compared to the scores of the control and the ARN groups. This indicates that she found it significantly more difficult than typically developing peers did to recognise facial emotional expressions in general. Based on their scores, it seems that the other four LiP participants did not find it significantly more

difficult than typically developing peers to recognise facial emotion expressions in general. Nevertheless, Brand et al. (2007) found that, similar to four of the LiP participants in the current study, a 17-year-old adolescent with LiP obtained an average total score ($p = 27$) on a general measure of recognition of facial emotion test. This suggests that she generally did not find it difficult to recognise facial emotion expressions. She also did not find it difficult to name different facial emotion expressions. The author (Brand et al., 2007) did not provide separate scores for recognition of each of the facial emotion expressions, which would have provided more information on which facial expressions had been identified correctly and which not.

In the current study, error scores for the different facial expressions were analysed separately and yielded results that provide further insight into recognition of facial emotion among the LiP participants. Data reported by Korkman et al. (2007a) suggest that the reliability of the AR Total score is somewhat questionable, especially in the 4- to –6-year-old age range. For this reason, it is probably more pertinent to trust the results on the error scales, which have been shown to be reliable indices of recognition of facial emotion deficits. Scores obtained on the different error scales indicate that none of the LiP children and adolescents found it more difficult than their typically developing peers did to recognise happiness, while each of the LiP participants had difficulty (performed significantly worse than their peers did) in recognising at least one of the negative or neutral facial expressions. These results are in line with the literature on typical development of children, suggesting that happiness is very seldom confused with negative emotions (Gao & Maurer, 2009; Golouboff et al., 2008; Herba et al., 2006; Montirosso, Peverelli, Frigerio, Crespi, & Borgatti, 2010). These findings are also in line with the results of most studies on recognition of facial emotion in individuals with LiP, which indicate that these individuals had intact recognition of positive emotions and deficits in recognising negative facial emotion expressions (Adolphs, Tranel et al., 1999; Siebert et al., 2003). However, Thornton (2006) found deficits in recognition of positive facial expressions (happiness) among a group of individuals with LiP. Happiness was intact in children and adolescents with LiP, but not in adults with the disorder. Therefore, Thornton (2006) concludes that the ability to recognise happiness may diminish with age in individuals with LiP, possibly due to progressive amygdala lesions. In the current study is no indication of regression in the ability to recognise happiness across the different age groups. However, regression of the ability to recognise happiness may occur at a much

older age (the age range of individuals with LiP in Thornton's study was from 10 to 65 years). Cornish et al. (2005) found a strong relationship between general regression in performance on emotion recognition tasks and age (age range 20 to 67 years) among a group of adults with fragile-X, who also had structural amygdala abnormalities. The regression was not obvious for any particular facial expression and rather appeared to be general (therefore, including both positive and negative facial expressions). In contrast, in normal aging, regression in the ability to recognise facial expressions is suggested to be specific to certain facial expressions, specifically fear and anger (Calder et al., 2003). The results of the current study, the research by Cornish et al. (2005) and Thornton (2006) and literature on the decline of facial expression recognition with age in typically developing individuals (Calder et al., 2003) evoke several questions with respect to recognition of facial emotion functioning across the lifespan in individuals with LiP. Understanding of the nature of the recognition of facial emotion ability of individuals with LiP across the lifespan may provide valuable information with respect to brain-cognition relationships in LiP.

It has been suggested that different neural systems are involved in recognising different facial expressions and also positive versus negative facial expressions (Calder et al., 2001; Gray et al., 1997; Phan et al., 2002; Phillips, Drevets, Rauch, & Lane, 2003b). This may explain why the children and adolescents in the current study found it difficult to recognise negative but not positive facial emotion expressions. Research on lesions and neuroimaging confirm that the amygdala is involved primarily in the perception and production of negative emotions, especially fear and anger (Costafreda, Brammer, David, & Fu, 2008; Fitzgerald et al., 2006; Schaefer et al., 2002). Therefore, Amygdala lesions should affect the recognition of negative (especially fearful and angry) facial emotion expressions rather than the recognition of positive expressions. In line with this hypothesis, it was found most often that adults with LiP and bilateral amygdala damage had deficits in recognising negative rather than positive facial emotion expressions (Blair et al., 1999; Calder et al., 2001; Sato & Murai, 2004; Wright, Martis, Shin, Fischer, & Rauch, 2002).

Several studies indicate that adults with LiP and amygdala damage found it specifically difficult to recognise fear in comparison to intact or less impaired recognition of other facial emotion expressions (Adolphs, 2004; Calder et al., 1996; Morris et al.,

1996; Phillips et al., 1998; Tranel & Hyman, 1990). This is postulated to be due to the critical role of the amygdala in processing fear and threat-related stimuli (Adolphs, 2004; Anderson & Phelps, 2001; Tranel & Hyman, 1990). However, only one LiP participant (4-year-old) in the current study found it specifically more difficult than controls and the similarly aged average person in the norm group did to recognise fearful facial expressions. Each of the other four LiP participants found it difficult to recognise a different negative facial expression. This finding seems to be in line with reports of variable ability to recognise fearful facial expression among adults with LiP and amygdala damage, ranging from severely impaired to essentially normal (Adolphs, Tranel et al., 1999; Hurlemann et al., 2007). Given the hypothesis that the amygdala to a great extent is involved in recognising fearful expressions (Calder et al., 1996; Tranel & Hyman, 1990), there is no clarity on why the recognition of fearful expressions is defective in some individuals with amygdala damage and not in others.

An explanation for the variability in the ability to recognise fearful facial expressions in individuals with LiP may involve brain plasticity. Research outcomes in studies of adults with LiP suggest that plasticity allows development of an alternative neural network for the recognition of fear or the development of cognitive strategies that compensate for their deficits (Becker et al., 2012; Hurlemann et al., 2007). However, there is no clarity with regard to the role of age of onset of amygdala damage, additional brain damage, or disconnection between brain structures in the development of these compensatory mechanisms in LiP. Better recovery or positive development of function after early onset of brain injury compared to later injury may occur due to greater brain plasticity during this developmental stage (Kolb & Gibb, 2007; Kolb et al., 2000; Reilly, Levine, Nass, & Stiles, 2008; Stiles et al., 2005). However, poor recovery or abnormal development following early injury has also been suggested due to the vulnerability of the brain at a younger age (Anderson, 2003; Anderson et al., 2010; Anderson et al., 2009; Kolb & Gibb, 2007; Kolb et al., 2000; Krägeloh-Mann et al., 1999; Max, Bruce, Keatley, & Delis, 2010; Reilly et al., 2008; Stiles et al., 2005). The relationship between age, vulnerability, and plasticity has been debated extensively in the general literature (Anderson et al., 2010; Kolb & Gibb, 2007; Stiles, 2000). The outcome of brain injury during childhood and adolescence is most likely not determined by one factor (such as age), but rather by a combination of factors. Understanding of plasticity and functional development in

individuals with LiP would be possible only with longitudinal research and a combination of imaging and cognitive measurement.

It has to be noted that surprise is not one of the emotions to be recognised on the affect recognition task of the NEPSY-II (AR subtest); therefore, results with regard to recognition of positive emotions are incomplete. Recognition of surprised expressions was found to be deficient in some individuals with LiP (Adolphs, Tranel et al., 1999; Thornton, 2006). Surprise is not always observed to be a positive facial expression. A particular surprise may be positive or negative; therefore, aspects of surprised and fearful facial expressions are very similar. Gao & Maurer (2009) suggest that children confuse surprised and fearful facial expressions. Therefore, adding surprised faces to a recognition of facial emotion task will provide additional information with regard to the processing of facial emotion expressions among children and adolescents with LiP.

Regression in performance (an increase in scores on the Disgust Errors scale between the ages of 6 and 8 years) among the LiP participants with regard to the recognition of disgusted facial expressions was noted. However, a similar increase in errors on this scale between the ages of 6 and 8 years is also evident among the control participants. As there are gender, cultural and socioeconomic differences between the urban female participants (4- and 6-year-olds) and the rural male participants (8-, 15- and 17-year-olds), it is possible that these factors had some effect on their performance on the Disgust Errors scale. Reports of recognition of facial emotion in individuals with LiP indicate that the recognition of disgust is often impaired (Adolphs, Tranel et al., 1999; Thornton, 2006), but not always (Siebert et al., 2003). However, no reference is made to the decrease of scores in LiP or control participants in these studies. Similarly, no mention is made in these studies with regard to the relationship between the recognition of disgust and factors such as intelligence, language, or culture. In the general literature, there is a debate about cultural differences in recognition of the different facial expressions, with some studies showing differences between cultures in the recognition of emotions (Jack, Blais, Scheepers, Schyns, & Caldara, 2009; Jack, Caldara, & Schyns, 2012) and others indicating that the basic facial expressions (happiness, anger, fear, sadness, disgust and surprise) are universal; therefore, culture does not affect the recognition of these expressions (Sauter, Eisner, Ekman, & Scott, 2010). A compromise between these viewpoints indicates that, whereas facial expressions of emotion embody universal signals, culture-specific learning

moderates the expression and interpretation of these emotions (Elfenbein & Ambady, 2003; Mandal & Ambady, 2004). Therefore, a variable such as culture could have influenced the performance of the LiP participants when required to recognise disgusted facial expressions. However, there is no specific research documenting the influence of culture on the interpretation and recognition of facial expressions in the South African context.

All the LiP participants in this study performed similarly to controls and a normative sample on the ToM subtest of the NEPSY-II. Similar to this result, a study on two adults with LiP and amygdala damage indicates that they did not present with ToM deficits (Paul et al., 2010). However, an adolescent with LiP performed below expectation on a test of ToM focusing on the recognition of social emotions. Social emotions refer to expressions of more complex states of mind, including the inner thought states of others (Shaw, Bramham, et al., 2005; Shaw et al., 2005). Different measures were used in the mentioned studies and the present study, which may explain the different outcomes. For instance, the ToM test used in the current study does not include a task that measures the recognition of complex states of mind (social emotions).

The ToM test that was used in the current study (Korkman et al., 2007) also does not include items pertaining to certain later-developing (9 to 11 years old) ToM abilities, such as understanding of faux pas. These more advanced ToM abilities were found to be deficient in individuals with early-onset amygdala damage (Shaw et al., 2004). Finally, two adults with LiP were also found to be impaired on oxytocin-sensitive (social) empathy tasks, but performed normally in tasks requiring cognitive empathy (Hurlemann et al., 2010). In the current research, a distinction is not made between empathy and cognitive ToM, and using measures of these different aspects of ToM might have yielded different results.

In conclusion, the children and adolescents with LiP, similar to adults with the disorder, presented with significantly worse scores on measures of recognition of facial emotion compared to typically developing peers. They had significantly more difficulty than their peers had in recognising negative and neutral facial expressions, but showed intact recognition of happiness. These results show that onset of deficits in persons with LiP with regard to recognition of facial emotion can be as early as the pre-school years or

earlier. Whereas it was expected that children and adolescents would specifically find it difficult to recognise fearful facial expressions, only one child with LiP had difficulty recognising fearful facial expressions. The outcomes of the current study strongly support indications in a previous study that the recognition of happiness is intact in children and adolescents with LiP. Although it was suggested that the recognition of happiness could possibly deteriorate with age, this study did not indicate such deterioration. It was hypothesised that such deterioration most likely would occur only during adulthood. The current study further contributed to sparse literature on ToM in individuals with LiP. The children in this study did not obtain significantly different scores compared to typically developing peers on a measure of ToM, but it was hypothesised that certain aspects of ToM that were suggested to be affected negatively in persons with LiP might not have been measured by the specific subtest that was used. Further research should focus on measuring a wider range of ToM functions.

Attention and Executive Function

Executive function cannot always be dissociated discretely from other constructs such as attention, information processing, or memory; therefore, it becomes difficult to interpret and generalise research results (Baron, 2004; Romine, 2004; Rosso, 2004). In the current study, every LiP participant presented with a deficient score on at least one of the attention and executive function measures.

In the current study, the 15- and 17-year-old LiP participants made significantly more errors than the similarly aged average individual in the norm group did in a task that measures processing speed. However, the 15- and 17-year-old control participants also scored above the mean error score of the similarly aged average person in the ARN group, indicating that factors other than LiP might have affected the performance of the participants on the measure of processing speed. In the literature on LiP, mixed results are reported on measures of processing speed among adults with LiP, ranging from intact performance (Hurlemann et al., 2007; Hurlemann et al., 2010) to deficient performance (Thornton et al., 2008). Brand et al. (2007) was the only researcher to describe the performance of an adolescent with LiP on a measure of processing speed. This adolescent (17-year-old) obtained a borderline to low average score on a task that normally is affected by processing speed. Therefore, the findings with regard to processing speed among the

LiP participants in the current study are in line with the results of some adult studies (intact performance when compared to controls), but different from that of a study on an adolescent with LiP who performed less adequately on a measure of processing speed.

Slow processing speed can affect performance, underlie difficulties, or be associated with low scores on measures of memory, attention, executive function, and hyperactive and impulsive behaviour (Marco et al., 2012; Mulder, Pitchford, & Marlow, 2011a, 2011b). Although there was not a way to determine the correlation or association between processing speed, inhibition and hyperactive-impulsive behaviour in the current study, it has to be noted that the same LiP and control participants who presented with worse performance than the average person in the ARN group did on the processing speed measure (15- and 17-year-olds), also presented with worse performance on a measure of inhibition. The mother of the 17-year-old LiP participant also noted hyperactive and impulsive behaviour at home.

It is not clear why the 15- and 17-year-old rural LiP and control participants performed worse (LiP participants performed significantly worse) than the average person in the ARN group did on the measure of processing speed. Differences between the rural and urban participants (gender, language, culture, geo-social environment) do not appear to explain their below-average performance. The processing speed score of the 8-year-old rural, male participants, who came from the same background as the 15- and 17-year-olds, was equivalent to the mean score of the norm group.

In typical development, maturation of white matter tracts (myelination) underlies improvement in processing speed during childhood and adolescence, with prominent development during adolescence (Asato, Terwilliger, Woo, & Luna, 2010; Barnea-Goraly et al., 2005; Giorgio et al., 2010). Therefore, difficulties with processing speed may be especially – although not exclusively – noticeable during adolescence, as rapid improvement would be evident in typically developing adolescents.

Apart from the 17-year-old**,** two other LiP participants (4- and 6-year-olds) presented with significantly elevated scores, compared to typically developing peers, on the Attention Problems scales of the parent or teacher ASEBA checklists. High scores suggest difficulties with attention and behavioural inhibition among these participants. This result is in line with findings of Thornton (2006), who reported that adults with LiP performed

significantly worse than controls did in tests measuring auditory selective attention and working memory. Thornton (2006) also reported that one child with LiP met the MINI+ research criteria for the diagnosis of Attention Deficit Hyperactivity Disorder (Hyperactive type). This child was 12 years old when Thornton (2006) assessed him and was, in fact, the same 17-year-old LiP participant in the current study. In the current study, he also presented with a score in the clinical range on the Attention Problems scale of the CBCL/6-18. Thus, consistency in the rating of his impulsive and hyperactive behaviour since he was 12 years old is evident. Whereas inattention and disinhibition in one child with LiP could have been an incidental finding, results of the current study suggest that inattentive, hyperactive, or impulsive behaviour was also evident among other children with LiP. Hyperactive-impulsive and inattentive behaviour was hypothesised to be associated with response inhibition (Barkley, 1997; Christodoulou, Lewis, Ploubidis, & Frangou, 2006; Gambin & Święcicka, 2009). Therefore, it is interesting to note that the 4- and 17-year-old LiP participants, who obtained significantly higher scores (more attention problems) than their typically developing peers did on the Attention scale of the ASEBA behaviour checklists, also performed significantly worse on a measure of behavioural inhibition (4-year-old) and response inhibition (17-year-old).

Tests of cognitive flexibility were presented to the three older participants (8-, 15- and 17-year-olds). Two of these LiP participants (8- and 15-year-olds) performed significantly worse than their typically developing peers did on one measure of cognitive flexibility (NEPSY-II AS subtest) but not on another measure of the same function (NEPSY-II INS subtest). Different performance on the two measures of cognitive flexibility may be explained by the added component (abstract thinking) on the NEPSY-II AS subtest (grouping cards according to categories). Difficulties with cognitive flexibility and abstract thinking were also reported for some adults with LiP (Brand et al., 2007; Thornton et al., 2008; Tranel & Hyman, 1990). Rule use, rule formation (abstract thinking) and flexible task-switching have been shown to rely primarily on the pre-frontal cortex, although several parietal and subcortical structures also contribute in different ways to flexible rule use and formation (Bunge, 2004; Bunge et al., 2005; Dosenbach et al., 2007; Kim, Johnson, Cilles, & Gold, 2011; Wallis & Miller, 2003). Amygdala lesions in persons with LiP were shown to result in alteration of connected brain regions, specifically the size of the orbitofrontal cortex, the gray-matter morphology of the ventromedial prefrontal cortex and the anterior cingulate and cortical thickness over the latter areas (Boes et al.,

2011; Morgan, personal communication, 28 July, 2009). Therefore, executive function deficits in individuals with LiP and amygdala damage may be explained by these brain changes. Nevertheless, without sufficient information about the nature of the brain pathology of the LiP participants in the current study, it is not possible to reach any conclusion in this regard.

It has to be pointed out that the mean error scores of controls in all three the age groups (8-, 15- and 17-year-olds) on the NEPSY-II AS Total subtest (cognitive flexibility and abstract thinking) are above (worse performance) the mean scores of the average person in the ARN group. Literature indicates that factors associated with poor socio-economic circumstances, such as lower quality of education, have an effect on children's performance on measures of cognitive functions associated with the left/perisylvian/language system and the prefrontal/executive system (Farah et al., 2006; Noble, Norman, & Farah, 2005). Therefore, the socio-economic environments of the rural children and adolescents who participated in the current study might have affected the performance of both the LiP and control participants in a task measuring cognitive flexibility and abstract thinking.

Executive function deficits have implications for social behaviour and adjustment (Riggs, Jahromi, Razza, Dillworth-Bart, & Mueller, 2006; Ross, Zinn, & McCauley, 2000). Executive function deficits in children and adolescents with LiP may contribute to atypical social behaviour, such as overfamiliarity and disinhibition, found among some individuals with LiP (Tranel & Hyman, 1990).

In conclusion, the children and adolescents with LiP, similar to adults with the disorder, presented with significantly worse scores than typically developing peers did on the measures of attention, inhibition, and cognitive flexibility that were used in the current study. Results among the participants varied, but each LiP participant had at least one significantly deficient score (compared to matched controls and the norm group) on a measure of attention or executive function. The results indicate that onset of attention and executive function deficits in LiP can be as early as the pre-school years. Two of the participants who presented with more inattentive, hyperactive and impulsive behaviour than their peers did, also obtained significantly lower scores on a measure of inhibition. Hypothetically, this is in line with literature that implies an association between

inattention, hyperactivity, impulsivity, and inhibition. The results of the current study indicate that particular aspects of executive function, such as abstract thinking, are affected in children and adolescents with LiP.

The current study contributes to the literature by indicating that difficulties with attention, impulsivity, and hyperactivity are evident in more than one child with LiP, and that executive difficulties are evident since a young age in individuals with LiP.

Psychosocial Adjustment

The main findings with respect to adaptive and maladaptive behaviour will be discussed next.

Adaptive Behaviour

The children and adolescents with LiP in the current study did not have severe social impairments (such as autistic behaviour), but compared to typically developing children, three of them presented with significantly lower scores on different scales of social adaptive behaviour. Each child's profile was unique. The 4- and 8-year-old LiP participants, according to their scores on the Vineland-II Adaptive Behaviour Scale, adapted equally well as their peers. The 6-year-old LiP participant has a significantly lower score than healthy peers have on the Play and Leisure subdomain of the Vineland-II Adaptive Behaviour Scale, indicating that she had poor play skills (such as sharing toys and knowing the rules of games). The 15-year-old participant was not as competent as his peers with regard to interpersonal relationship skills (such as keeping a comfortable distance between himself and others in social situations, being careful about sharing personal information). The 17-year-old participant obtained a significantly lower score compared to peers on the Coping Skills scale, indicating poor emotion regulation (such as controlling his anger), adjusting flexibly to different situations and internalising what is construed as good manners (socially acceptable behaviour).

The significantly lower scores on selective adaptive behaviour scales suggest that the LiP participants did not adapt as well as the controls and the similarly aged average person in the ARN group did, but their social adjustment was not affected pervasively. These results seem to be in keeping with those obtained among adults with LiP, who did not present with severe deficits (such as autistic behaviour) in their social interactions (Al-

Ekrish & Al-Sadhan, 2012; Paul et al., 2010; Tranel & Hyman, 1990). For instance, one woman (SM) with LiP presented with intact basic skills in communication and social interaction, but her social interactions were "poorly integrated, somewhat exaggerated, impulsive and inappropriate" (Paul et al., 2010, p. 169). SM was also overly trusting and disinhibited in her interactions. In her real-life situation, she was notably socially isolated and unable to sustain employment, although she lived independently (Paul et al., 2010). The literature also indicates, similar to what is apparent in the current study, that adults with LiP have variable levels of social competence and adjustment. For instance, another woman in the study by Paul et al. (2010) functioned much better socially than SM did. She was well adjusted, had a college education, and worked as a teacher.

The inclusion of interviews and observation in the research by Paul et al. (2010) appears to have been beneficial in identifying subtle forms of atypical social behaviour that would not have been apparent on general adaptive behaviour scales. Although observation and semi-structured interviewing were not employed in this study, the parents and teachers made a few remarks in response to the open-ended questions of the ASEBA scales. These remarks illustrate the kind of information that may be gained by interviews and observation in future studies. Remarks in response to open-ended questions (such as asking to mention any concerns about the child) indicated that both the younger female LiP participants tended to "wander off". The 4-year-old child's mother explained further that her daughter "lives in her own world". The pre-school teacher of the 4-year-old observed that the child "wanders away – on her own little planet." Her teacher further indicated that she had "little fear". The 4-year-old child, who was observed to have little fear, was also found to be less competent than her typically developing peers were in recognising fearful facial expressions. Tranel, Gullickson, Koch, and Adolphs (2006) and Feinstein et al. (2011) describe a woman with LiP (SM) and amygdala damage, who had difficulty in recognising facial expressions of fear. An interview with her revealed that she did not experience a sense of danger, did not show any fear when exposed to live snakes and spiders and scary situations. She also did not report intense experiences of fear or negative feelings related to traumatic experiences in her life. This indicates that SM did not only have difficulty in recognising facial expressions, but also experienced emotions (and especially fear) differently from other individuals and, consequently, she behaved differently in situations where other people would have showed fear. The results in this

study point to a similar lack of overt fear manifestations in combination with poor recognition of facial expressions of fear in a child with LiP.

Inadequate or atypical social behaviour could result from insensitivity to important social cues such as emotional expressions, impaired understanding of social situations and other peoples' intentions, and failure to adjust one's behaviour flexibly in accordance with social rules and demands (Capage & Watson, 2001; Jahromi & Stifter, 2008; Riggs et al., 2006; Spence, 2003). Furthermore, integration of the skills required for social adjustment requires executive function (Spence, 2003). The children and adolescents with LiP in this study were less able to recognise facial emotion expressions and had executive function deficits when compared to peers. These apparent deficits may have contributed to less adequate social competence (compared to peers) among the LiP participants in the current study. For instance, the 17-year-old LiP participant's Coping Skills score on the Vineland-II Adaptive Behaviour Scale is significantly below that of his typically developing peers. A low score on this scale reflects difficulty with flexible adjustment in social situations and controlling one's emotions appropriately.

Deficits in social skills and competence may also be related to specific neuropsychiatric or psychological problems (Barton & North, 2004; Deniz, Öztürk, Turan, & Özyeşil, 2009; Sato & Murai, 2004). It was evident from the remarks made by teachers and parents that the children and adolescents with LiP in this study were teased by peers about their hoarse voices (6-, 8- and 17-year-olds), leading to sadness and withdrawal (8-year-old). Experiences of rejection and teasing may cause embarrassment, self-consciousness, low self-esteem, low mood, anxiety, and social withdrawal and lead to a lack of opportunity to develop social skills (Norton, 2010). The children and adolescents with LiP in the current study presented with a variety of behavioural problems such as attention deficit and hyperactivity, oppositional behaviour, anxiety, and affective disturbance. Poor social skills and adaptive behaviour may be associated with behavioural problems (Motoca, Williams, & Silverman, 2012). For example, inattention and impulsivity can prevent the acquisition of social skills or hinder the performance of appropriate social behaviour in different settings (Barton & North, 2004). Such difficulties may have a detrimental effect on scholastic adjustment and performance.

Only two LiP participants in this study attended school. Results on the TRF (ASEBA behaviour checklist) for these two males indicate that their school performance and their general adjustment in school were similar to those of controls.

Scholastic difficulties in children and adolescents with genetic disorders are often caused by factors such as epilepsy, hospitalisation, social problems, behaviour problems, and cognitive problems (Benjamin et al., 1993; De Vries, Hunt, & Bolton, 2007; Michaud, Suris, & Viner, 2007). In line with this observation, the literature on LiP (Emsley and Paster, 1985) suggests that an 18-year-old South African adolescent with LiP performed poorly in school due to "borderline mental retardation" (Emsley and Paster, 1985, p. 1291). However, no matched controls were included in the study; therefore, it is not clear if the adolescents' intelligence was different from that of her peers. This adolescent's IQ may well have been a manifestation of the normal distribution of intelligence, similar to the general population from which she came.

The two individuals in the current study who attended school presented with significantly worse performance than their typically developing peers did on some neuropsychological measures (such as verbal recognition memory, visual memory, inhibition and abstract thinking), and one of them also had severe behavioural difficulties. The literature indicates that such cognitive and behaviour problems during childhood can have a detrimental effect on the daily life, school learning, and social learning of a child (Anderson et al., 2001; Jambaqué et al., 2006; Larsen, 2012). However, despite the identified cognitive challenges of the LiP participants in the current study, their school adjustment and performance were similar to those of their peers. It is possible that their neuropsychological functioning, although less intact than that of their peers, was not affected to such an extent that it had a detrimental effect on their school learning. Additionally, compensation for certain deficits may take place. The 8- and 15-year-old LiP participants performed better on some memory indices compared to others, and areas of strength may compensate for deficits. For example, a child with an episodic memory deficit may still have an intact semantic memory, even though not optimal (De Haan, 2012). Different types of memory deficits may have different effects on certain aspects of academic performance (De Haan et al., 2006; Larsen, 2012) and this would not be noticed if the person's academic performance were not analysed in greater detail. For example, it is suggested that children with visual memory deficits tend to perform worse in arithmetic

than children without these deficits did, but they do not necessarily perform worse in all aspects of reading and spelling (Kulp, Edwards, & Mitchell, 2002; Larsen, 2012). The school-attending 8- and 15-year-old LiP participants in this study obtained similar scores to their peers on a scale measuring adjustment in school. However, it does not mean that they did not have problems with specific aspects of their adjustment that were not measured on the instrument utilised to measure adjustment in school, such as verbal communication (due to hoarseness). For example, Steenkamp (1997) suggests that young people affected by LiP may need guidance with regard to realistic plans for career choice and further training due to their hoarse voices.

Apart from the performance of the two school-going children with LiP, it is also apparent that the 17-year-old rural male adolescent in this study obtained a Grade 8 education and then left school. Salih et al. (2011) reported that other adolescents with LiP had also left school due to emotional and social difficulties. Leaving school early or failing a grade is not uncommon in the Northern Cape community where the 17-year-old LiP participant came from (Thornton, 2006). Therefore, leaving school early is not necessarily an indication that cognitive or social difficulties prevented him from continuing his education. However, parents of one child with LiP (6-year-old) in the current study, who lived in an urban middle-class area, decided to home school their child due to the reactions of peers to the child's difficulties. This illustrates how social rejection may lead to difficulties with scholastic adjustment. The parents' decision to home-school their child with LiP also indicates how observing a child's social difficulties, may lead to an urge by parents to protect their child. Parents may overprotect their children and thereby prevent them from dealing effectively and independently with difficult situations (Brown et al., 2007; Holmbeck et al., 2002; Kirk et al., 2011).

The effect of having a child with a genetic disorder such as LiP can be stressful and pose certain challenges such as reproductive decisions, feelings of guilt, heightened levels of parental support and medical care (Farmer, Deidrick, Gitteri, Fennell, & Maria, 2006; Read, 2002; Sadek, Shellhaas, Camfield, Camfield, & Burley, 2004; Waisbren, Rones, Read, Marsden, & Levy, 2004). There is no research on the experiences or difficulties of parents of children and adolescents with LiP, but the information obtained by means of the SDH form and the ASEBA behaviour checklists in the current study indicates that the parents of the LiP participants faced certain challenges. The children and adolescents with

LiP had more medical problems and some of them had been hospitalised for complications related to the disorder. Therefore, their parents would be expected to spend more time and energy on their children's medical needs compared to the parents of typically developing children. One of the parents of a LiP participant (17-year-old) in the current study sought the help of a psychologist in managing her child's behaviour. Another parent was worried about the future and how to deal with her child's difficulties. Emotional reactions (such as depression and anxiety) and challenging behaviour of children with a genetic disorder can affect the relationship between parent and child, contributing to psychosocial difficulties (Besier et al., 2011; Farmer et al., 2006). Finally, although not one of the parents in this study reported that they had LiP, they were all carriers of the gene responsible for the symptoms of LiP. It is not known if carriers of the disorder have certain cognitive deficits or social impairments that may affect their parenting style or abilities. Some of these parents might have had LiP (mild symptoms) without being aware of it. Thus, it seems that the psychosocial development of children and adolescents with LiP can be affected by difficulties in parenting.

The findings in the current study suggest variable adaptive behaviours in children and adolescents with LiP. These findings are similar to observations in adults with LiP (Paul et al., 2010; Thornton, 2006; Tranel & Hyman, 1990). Amygdala damage is associated with LiP, and it was hypothesised that compensatory brain mechanisms underlie the subtle and variable social deficits that were observed in some individuals with LiP (Paul et al., 2010; Tranel & Hyman, 1990). Phelps and LeDoux (2005) suggest that subtle social deficits following amygdala lesions may reflect compensatory mechanisms and may not be indicative of the extent of involvement of the amygdala in normal or severely deficient social behaviour. For instance, Becker et al. (2012) hypothesise that the cortical mirror-neuron system (premotor cortex face area and inferior parietal lobule) of one of two monozygotic twin sisters compensated for the pathology of the amygdala (bilateral amygdala damage). The other twin sister was impaired in recognising fearful facial expressions, lacked potentiated responses to fearful faces, and did not show the compensatory brain mechanism observed in her twin sister. Thus, variable levels of brain pathology and plasticity can underlie variable social adaptation in individuals with LiP.

The findings in the current study suggest that social adaptation in LiP can be affected already during childhood and adolescence. Social adjustment was variable among the five

children and adolescents with LiP, with two of them adjusting just as well as their peers. The three LiP participants, who did not adjust well, did not develop the necessary play skills, social skills or emotional control. There is some evidence that children and adolescents with LiP may find it increasingly difficult to adapt socially due to increasing demands for flexibility and emotional control. However, longitudinal data is necessary to explore their social adjustment across the age groups further. Scholastic adjustment, as measured by a behaviour checklist, in the population of children and adolescents with LiP in the current study was adequate. However, only two of the five children attended school and it may be significant that one of the remaining three children with LiP left school early and another participant's parents decided to home-school her due to social difficulties (rejection and teasing by peers). The fifth LiP participant was in pre-school; there was no particular indication of poor social adjustment. Overall, the study raises questions about the association between less adequate social adaptation and factors such as brain pathology, cognitive difficulties (recognition of facial emotion, executive function), parenting, reactions to social rejection and impairment in communication.

Maladaptive Behaviour

Four of the five LiP participants in the current study had significantly higher scores than their typically developing peers had on measures of maladaptive behaviour. Three of the five children and adolescents with LiP (4-, 8- and 17-year-olds) presented with significantly higher Total Problems scores, indicating significantly more total behaviour problems compared to peers. Two of these children and adolescents (8- and 17-year-olds) had significantly higher scores on all the problem scales that were used in this study, indicating a wide range of problem behaviours (total, externalising, internalising and social problems), while the 4-year-old LiP participant had a significantly higher score than typically developing peers had on the Other Problems scale (problematic behaviour that was not identified by factor analysis as belonging to any of the specific problem behaviour scales).

Significantly higher scores compared to typically developing peers on the Externalising Problems scale were obtained by two of the three rural, male participants (8- and 17-year-olds). Externalising problems (anger outbursts or rage attacks, aggression) have also been identified in some adolescents and adults with LiP (Brajac et al., 2004;

Newton et al., 1971; Steenkamp, 1997; Thornton, 2006). In the general literature and the literature on South African children, it was found that more males tend to present with behaviour problems, especially externalising behaviour problems, compared to females (Barbarin, 1999; Bongers, Koot, Van der Ende, & Verhulst, 2004). Therefore, it is interesting to note that only males in this study presented with significantly higher scores than their peers did on the Externalising Problems scale. Although substance abuse is prevalent (especially among males) in the community from which the 8-, 15- and 17-year-old male participants came (Thornton, 2006), none of the participants in the current study were reported to abuse substances. Consequently, substance abuse does not appear to be the underlying cause of the 8- and 17-year-old participants' externalising behaviour problems. Thus, gender differences may explain the variable behavioural difficulties in this population of children and adolescents with LiP, although anger outbursts in women with LiP have also been reported (Gonçalves et al., 2010). It is also apparent that, although the 4- and 6-year-old LiP participants did not obtain significantly higher scores than their peers did on the Externalising Problems scale, both of them presented with significantly higher scores on the ASEBA Attention Problems scale, either at home (6-year-old) or at school (4-year-old). Hyperactivity, impulsivity and attention problems are also viewed as externalising problems and the score on the ASEBA Attention Problems scale is one of the subscales contributing to the overall score on the Externalising Problems scale.

Hyperactivity, impulsivity and attention problems, as well as other externalising problems (oppositional behaviour), were previously described in a child (12-year-old) with LiP (Thornton, 2006). In fact, this 12-year-old child described by Thornton (2006) was the same 17-year-old who participated in the current study. At the age of 12, he was assessed by means of the Mini Neuropsychiatric Interview as part of a different research project. This child eventually dropped out of school and worked as a part-time labourer on a farm. At the age of 12, he was diagnosed (Mini Neuropsychiatric Interview) with ADHD, bipolar affective disorder, conduct disorder, anxiety disorder with panic attacks and a rating of "high risk" on suicidal behaviour (Thornton, 2006). The 17-year-old LiP participant's high scores on the DSM scales of the CBCL/6-18 (Affective Problems, ADHD, Conduct Disorder, Oppositional Defiant Disorder) in the current study, although not directly related to *DSM-IV* categories, suggest that the participant's maladaptive behaviour persisted into adolescence. It is noticeable that the 17-year-old LiP participant's score on the Anxiety

Problems scale of the CBCL/6-18 was not in the clinical range while he presented with panic attacks at the age of 12 years. The DSM scales of the CBCL/6-18 were reported being highly consistent with DSM-IV diagnostic categories. However, the instrument may not be effective in identifying specific anxiety disorders (such as panic disorder). Overall, the 17-year-old LiP participant's maladaptive behaviour appeared to have stayed consistent since the age of 12. It has to be noted, however, that a psychiatrist has never assessed this 17-year-old LiP participant to confirm the diagnoses.

Internalising behaviour problems (including observations of low mood, worry, withdrawn behaviour, and fearfulness) were reported among the 4-, 8- and 17-year-old participants. The 8-year-old LiP participant's score on the Anxiety Problems DSM scale of the CBCL/6-18 is also in the clinical range, suggesting an anxiety disorder (not confirmed by psychiatric evaluation). These results are in line with the findings of other studies, suggesting an increased but variable incidence of depression and anxiety among adults with LiP (Lupo et al., 2005; Thornton et al., 2008; Wiest et al., 2006). Literature on LiP suggest that some children and adolescents with LiP are depressed, have panic attacks and are socially withdrawn (Bahadir et al., 2006; Brajac et al., 2004; Thornton, 2006; Steenkamp, 1997), while others have normal mood and affect and essentially normal emotional development (Wiest et al., 2006). A case study by Claeys et al. (2007) reported recurring episodes of affective disorder (major depressive disorder) since the age of five years in a woman with LiP, culminating in two suicide attempts at the ages of 36 and 38. This gives some indication that psychopathology in children with LiP is likely to continue into adulthood and possibly worsen with age. In line with Claeys and colleagues' (2007) description of the clinical course of their patient's depression, the 17-year-old LiP participant in the current study, who presented with an affective disorder at the age of 12 (Thornton, 2006), again presented with internalising difficulties, including low mood, at the age of 17 years.

However, it has to be mentioned that the woman with LiP described by Claeys et al. (2007) also presented with therapy-resistant epilepsy since a young age, which has strong comorbidity with depression (Epps & Weinshenker, 2013; Kanner et al., 2012). The suggested mechanisms underlying the strong comorbidity between epilepsy and depression include the neurochemistry and function of key brain regions such as the amygdala and hippocampus. The woman described by Claeys et al. (2007) was also treated with several

trials of different anti-convulsants, some of which can cause or exacerbate affective disorders (Miller, Kustra, Vuong, Hammer, & Messenheimer, 2008; Mula & Sander, 2007). This illustrates the complexity of the underlying factors involved in the psychopathology or behavioural difficulties associated with LiP.

The complex pathophysiological mechanisms of a genetic disorder such as LiP may lead to an associated cascade of aberrations in neurodevelopment, resulting in a central nervous system that is suboptimal with respect to structure and function. In turn, structural and functional brain alterations may lead to disruption in emotion, cognition and behaviour (Gothelf, Schaer, & Eliez, 2008; Reiss & Dant, 2003). In LiP, calcifications in the temporal lobe structures have been identified as one of the signs of the disorder. In the general literature, abnormalities in the temporal lobe structures and corticolimbic circuits were suggested to underlie the pathophysiology of internalising and externalising behaviour problems (Caetano et al., 2007; MacMaster & Kusumakar, 2004; Pine, 2007; Rosso et al., 2005). The 8- and 17-year-old LiP participants in the current study presented with partial and complete amygdala damage, and both of them obtained significantly higher scores than typically developing peers did on indices of internalising and externalising problem behaviour, which is in line with the mentioned literature on the role of the amygdala in such behaviour problems.

Threat-related information processing and fear conditioning are associated strongly with the functions of the amygdala and are important with regard to their role in psychopathology (Davis, 2006; Viviani & Stroop, 2008). The children and adolescents with LiP in the current study recognised negative facial expressions (fear, anger, sadness) significantly less well than their typically developing peers did. Individuals may misread different facial emotion expressions as more intense or less intense (such as being more aggressive or as less aggressive) compared to how these expressions appear to the typical individual (Lundh & Ost, 1996). In some cases, misinterpretation or poor perception of social and emotional information may lead to frustration and aggressive or hostile behaviour in social situations, due to inferring anger in ambiguous contexts and attributing hostile intent (Schultz, Izard, & Ackerman, 2000). Misinterpretation of facial expressions may also lead to underreaction (such as a lack of fear) or inappropriate trusting behaviour. Misinterpretation of facial expressions has been noted in an adult with LiP (Adolphs et al., 1998). This woman (SM) with LiP interpreted the negative and unapproachable facial

expressions of strangers as more positive and trustworthy than controls did, and it was hypothesised that this misinterpretation could have explained the woman's overfamiliarity and overly trusting behaviour (Adolphs et al., 1998).

The literature also indicates that psychiatric disorders in children and adults involve difficulties in recognising specific facial expressions or facial expressions in general (Csukly, Czobor, Simon, & Takács, 2008; Rocca, Heuvel, Caetano, & Lafer, 2009). For instance, anxiety disorders in children and adolescents cause them to make more errors in tasks involving recognition of facial emotion, with a greater attentional bias towards angry or fearful faces (Mueller et al., 2012; Waters, Henry, Mogg, Bradley, & Pine, 2010; Waters, Mogg, Bradley, & Pine, 2008). In line with this research, Thornton (2006) found that there was a statistically significant correlation between having an anxiety disorder and obtaining lower scores (worse performance) on a recognition of facial emotion measure. Such a correlation might possibly reflect an attentional bias towards threat, with subsequent erroneous interpretation of non-threatening facial expressions. However, it is not clear to what extent deficits in recognition of facial emotion are either the causes or the results of emotional dysregulation. Research with regard to the relationship between recognition of facial emotion and psychopathology had not been attempted among children and adolescents with LiP.

The results of the current study indicate social problems among the three older LiP participants (8-, 15- and 17-year-olds). The 8- and 17-year-old LiP participants presented with significantly higher scores than the controls and the similarly-aged average person in the norm group did on the Social Problems scale of the CBCL/6-18 and TRF, while the 15-year-old LiP participant has significantly higher scores compared to the controls only. Scrutiny of parent ratings on specific items of the Social Problems scales indicates that the children were teased by peers (8-year-old) and that they were lonely (17-year-old). The CBCL/1.5-5 and C-TRF scales do not include a Social Problems scale; therefore, a measure of social problems was not included in the preschool age group. However, the 6-year-old LiP participant's parents mentioned on the SDH form that she was teased by peers; therefore, it is apparent that she had similar difficulties as the school-going LiP participants. Thus, social problems are apparent across the different age groups among the LiP participants (from pre-school onwards) in the current study. Similar social problems (such as persistent difficulties in relationships with schoolmates, being teased, few or no

friends) have been reported in other children and adolescents with LiP (Juberg et al., 1975; Keipert, 1970). The literature on LiP suggests that these difficulties persist into adulthood, as adults with LiP also have been reported to have social problems (Claeys et al., 2007; Steenkamp, 1997; Thornton, 2006).

The general literature on children with disfiguring conditions indicate that the interaction between the effect of a genetic defect on appearance and the reaction of others may be one of the contributors to maladaptive behaviour in children and adolescents (Dunn, Austin, Harezlak, & Ambrosius, 2003; Jankovic, Vukicevic, Djordjevic, Jankovic, & Marinkovic, 2012; Mosam, Vawda, Gordhan, Nkwanyana, & Aboobaker, 2005). The literature on LiP refers to the negative effect of hoarseness and disfigurement on the mood and level of anxiety of children and adolescents with LiP (Steenkamp, 1997). Therefore, internalising and externalising problem behaviour among the LiP participants in the current study may be explained partially by the experience of social rejection.

Qulitative analysis of the trends in performance on the behaviour checklists, support the hypothesis that socioeconomic circumstances may have contributed to the higher scores of the two rural LiP participants on behaviour problem scales. The two individuals who presented with severe and pervasive problems both came from a rural, impoverished area. The performance trend across the different age groups suggests that the rural controls' scores on the Internalising Problems scale were above the mean scores of the ARN group, while the urban controls (4- and 6-year-olds) had scores below the mean scores of the ARN group on this scale. Therefore, the rural LiP participants' higher scores on the internalising scales of the CBCL cannot be attributed to LiP alone. Literature supports the hypothesis that the elevated scores on the internalising behaviour scales among individuals in the rural area can partially be attributed to their socio-economic circumstances. Literature indicates a higher likelihood of behavioural difficulties in children who are at risk, such as children experiencing socio-economic hardship and children living in communities with high levels of interpersonal violence (Gilman, Kawachi, Fitzmaurice, & Buka, 2003; Schwab-Stone, Koposov, Vermeiren, & Ruchkin, 2012; Tracy, Zimmerman, Galea, McCauley, & Stoep, 2008). Children living in violent communities across different cultures, also in South Africa, were found to have especially high levels of internalising problems, which include behaviour associated with posttraumatic stress disorder (Schwab-Stone et al., 2012; Shields, Nadasen, & Pierce,

2013). This might explain the significantly higher scores of the rural control participants in the current study (compared to the mean score reported for the norm group) on the Internalising Problems scale

Nevertheless, it has to be noted that although the control participants in the current study obtained higher scores than the ARN group on the internalising scales of the CBCL, their scores are still significantly lower than the LiP participants' scores on these scales. This may be explained by the risk factors associated with LiP. It was found that children with chronic conditions (such as children with genetic illnesses) are generally at risk for behaviour problems (Wilmshurst & Brue, 2010). Additional stress can have a "multiplier effect" (accumulating negative effect) on the adjustment of a child who is already at risk (Wilmshurst & Brue, 2010, p. 220). Poor socio-economic circumstances may be associated with increased stress and therefore play a role in the onset or exacerbation of behavioural and emotional difficulties in children who are already at risk (Wilmshurst & Brue, 2010). These multiple risk factors may explain why two of the rural children and adolescents with LiP presented with such pervasive behaviour problems, while the urban LiP participants did not. Therefore, the concept of risk may explain the variable intensity of behavioural difficulties among the LiP participants.

The discussion so far focused on the maladaptive behaviour of four of the five LiP participants in the current study. However, parent and teacher ratings on the same measures suggest that the 15-year-old LiP participant has no behavioural difficulties. Similarly, some adults with LiP were reported to have no psychopathology (Adolphs et al., 1999). One explanation for variable maladaptive behaviour and psychopathology in individuals with LiP might be risk, which was also discussed in the previous paragraph. Reiss and Dant (2003) found that the trajectories of cognitive impairments and behaviour/emotional problems during childhood are complex due to variability in the multiple and complex interplay between genetic, environmental, and biological risk factors. The combination of high-risk child characteristics or genetic risk factors and social risk factors might exponentially multiply or increase the overall risk for persistent behaviour disorders, but would not automatically lead to such difficulties (Brennan, Hall, Bor, & Williams, 2003). For example, a child with a genetic disorder (such as LiP) who finds himself in poor socio-economic circumstances as well as in a stressful home situation, may have a higher risk of developing behaviour problems or psychopathology

compared to another child with different circumstances. One of individual with LiP in the current study (17-year-old) came from a family with divorced parents and had an absent father. These circumstances, in combination with all the difficulties associated with LiP, could have contributed to the noticeable acting out or internalising behavioural problems. Although matched controls came from the same environment, with several risk factors involved (alcohol abuse and domestic violence in families), they did not suffer from a serious genetic disorder. Genetic risk factors combined with social risk factors may exponentially multiply or increase the overall risk for persistent behaviour disorders and/or psychopathology. In line with the discussion of multiple risk factors, Thornton (2006) and Hurlemann et al. (2007) point out that different factors might affect one another in individuals with LiP. These may include interplay between LiP, brain plasticity, epilepsy, medication, mood disorders and cognitive difficulties (mood disorders are often associated with cognitive difficulties).

Overall, the current study contributes to a better understanding of maladaptive behaviour in children and adolescents with LiP. Results indicate maladaptive behaviour in most children and adolescents with LiP. An early onset of internalising and externalising behaviour difficulties is likely. A variety of behavioural difficulties can be evident among these individuals. Literature suggests an interplay between different factors that can potentially explain behavioural difficulties among children and adolescents with LiP. Cognitive factors, environmental factors, physical symptoms, extent and type of brain lesions, and gender factors may all interact to produce maladaptive behaviour patterns. The types of maladaptive behaviour patterns identified in this population of children and adolescents with LiP are similar to the types of emotional and psychiatric difficulties (mood disorders, anxiety disorders, anger outbursts) previously identified among individuals with this disorder. A previous study on LiP identified a child with hyperactivity, impulsivity and attention problems. The current study indicates that such problems are evident also among other children with LiP.

Conclusion

The results of the study were discussed in this chapter. The discussion began with the results obtained on neuropsychological measures and then proceeded to the discussion of results obtained on behaviour checklists. The comparison of the LiP and control

participants with regard to their neuropsychological and psychosocial development yielded results that were similar to those found for adults with the disorder. The main conclusion was that the children and adolescents with LiP in this study, presented with significantly more neuropsychological deficits and psychosocial difficulties than typically developing peers did. These difficulties were noted with regard to certain cognitive functions (memory and learning, attention and executive function, recognition of facial emotion), and with regard to social adaptation and behavioural difficulties. However, variable results were found, and each LiP participant presented with a unique cognitive and psychosocial adjustment profile. The following chapter contains a discussion of the limitations of the study and recommendations for further research.

Chapter 7

Limitations and Recommendations

This chapter provides the conclusion of the research and describes the limitations of the research pertaining to the sample and controls, the constructs, the measuring instruments, extraneous variables and the methodology. The implications of the study for treatment and further research are discussed, and recommendations are made. Finally, the significance of the study is highlighted.

Summary of the Aims and Results of the Study

The aim of the study was to determine whether the neuropsychological and psychosocial functioning of children and adolescents with LiP is different from the neuropsychological and psychosocial functioning of typically developing children. The study also aimed to compare the performance of the LiP and control participants across the different age groups in order to identify developmental trends. All the evaluated children and adolescents diagnosed with LiP performed significantly worse (although sometimes significantly better) compared to the controls and the similarly-aged average individuals whose scores were used to norm the instruments. These findings apply to at least one or more neuropsychological measures in each of the neuropsychological domains (i.e., memory and learning, social perception, and executive function). The results show intact face recognition and ToM in this paediatric LiP population. Moreover, 60% of the children and adolescents with LiP had difficulty with some aspect of adaptive behaviour (e.g., play behaviour, interpersonal relationships, or emotional control). Similarly, 80% of the study participants in this group presented with significantly increased behavioural difficulties compared to typically developing children. Overall, the results indicate variable profiles of cognitive and behavioural difficulties in children and adolescents with LiP.

Limitations of the Research

Sample, Norm Group and Controls

First, the control group was small. A larger group of typically developing controls would have been more representative of the typically developing South African population. While the urban participants that formed the control group for this study were matched to the LiP participants according to FSIQ, one of the rural controls was matched according to PIQ due to his home language (Afrikaans) being different from the test language (English). Another FSIQ score was also not available for this participant. Presence of some potentially confounding cognitive factors (such as a significantly lower VIQ than PIQ and, therefore, worse language skills compared to the PIQ) might have affected the performance of this rural participant.

Second, using a neuropsychiatric interview to screen the participants assigned to the control group probably would have resulted in a more comprehensive assessment, ensuring that the control participants did not suffer from any condition that potentially could have affected their performance or scores on the instruments employed in the study.

The Constructs

First, the CBCL/1.5-5, CBCL/6-18, C-TRF, and TRF Attention Problems scales were used to measure attention. While these scales include items referring to focused and sustained attention, as well as behavioural inhibition (hyperactivity and impulsivity), they do not distinguish clearly between different constructs, such as selective and sustained attention, shifting of attention or inhibition.

Second, The TM subtest of the NEPSY-II focuses on some aspects of ToM, but does not include higher-order ToM abilities that may be associated with amygdala lesions, such as the detection of *faux pas* (Shaw et al., 2004; Stone et al., 2003). Moreover, the test does not make a clear distinction between different components of ToM (such as affective ToM and ToM reasoning) that have been suggested to rely partially on different underlying neural mechanisms (Leopold et al., 2012; Shamay-Tsoory & Aharon-Peretz, 2007; Shamay-Tsoory, Aharon-Peretz, & Perry, 2009). Although the TM subtest of the NEPSY-II is divided into two sections, namely TM and TM Verbal (Korkman et al., 2007a), norms for the two separate sections across the different age groups are not available.

Finally, the recognition of facial emotion measure that was used in this study did not measure verbal categorisation of emotions additional to matching and memory of facial expressions. Also, separate scores for the matching and memory components of the task were not available. The literature indicates that performance on a measure of nonverbal matching of facial emotion expressions reaches a plateau relatively earlier compared to performance on other cognitive measures (Korkman, Lahti-Nuuttila, Laasonen, Kemp, & Holdnack, 2013). It was also shown that nonverbal matching of facial emotion expressions matures earlier than verbal categorisation does (Gagnon, Gosselin, Hudon-ven der Buhs, Larocque, & Milliard, 2010; Gao & Maurer, 2010). Therefore, including a verbal component when measuring facial emotion perception would increase the complexity of the task. A more complex task may show clearer distinctions between the performance of LiP and typically developing children on tasks requiring recognition of facial emotion.

The Measuring Instruments

The use of a control group addressed the effect of socio-economic, language and cultural factors on test results by allowing interpretation of the results in relation to the specific South African context. Similar performance in relation to the North American norms is evident with regard to some subtests (such as ToM), showing that socio-economic and cultural differences did not necessarily affect the performance of the local children and adolescents on all measures. However, the primary difficulty with all the measuring instruments was that they were normed on a North American sample that is different from the local population. Ultimately, the instruments were designed with the North American population in mind; therefore, they may not have measured similar constructs in the local population (validity). For instance, in the face recognition task, photos of children of different racial groups were included, but these might not have been representative of the local context.

Translation and adaptation of instruments is an important factor that could have affected the performance of the participants on the neuropsychological and behavioural instruments. Not all the participants spoke the same language, and they came from different cultural backgrounds. Therefore, it was necessary to translate and adapt the instruments. Translation and adaptation of an instrument may lead to questions concerning the validity of the data. Although every effort was made to ensure a high standard of

adaptation and translation, the instruments were not standardised in relation to the local population groups. Although everyone who participated in the translation and adaptation of the instruments was bilingual (Afrikaans and English), not one of these individuals lived in the rural area where the Afrikaans LiP participants resided. A particular dialect of Afrikaans is spoken in this area, and the cultural background of these individuals differs from that of the researcher and the translators. This may have affected the appropriateness of the translation of the instruments for the particular population and may have disadvantaged them.

Owing to differences in level of education and language preference of parents, they could not respond to the behaviour checklists in a uniform manner. Some parents completed the checklists themselves, while the instrument was administered to other parents in an interview format. This could have affected the reliability of results.

Although the NEPSY-II proved to be a very suitable instrument for assessing neuropsychological functioning in the current study, especially as it allowed for the assessment of functions across a wide age range, a few disadvantages could also be identified. One of the drawbacks includes the questionable reliability and validity of some of the subtests. Adequate reliability of most of the subtests of the NEPSY-II has been suggested by psychometric data published in the *NEPSY-II Clinical and Interpretive Manual* (Korkman et al., 2007b). However, reliability of a few specific subtests may be questionable in specific age groups (such as Memory for Faces Total score in three of the age groups and Narrative Memory Recall in the 9- to 10-year-old age group). Practice effects were assumed to be the cause of the low test-retest reliability of memory measures; therefore, the tests were employed in the study despite this. Unsatisfactory reliability coefficients for the total score on the subtest measuring recognition of facial emotion were reported. Possibly, a different general measure of recognition of facial emotion should be included in future research. The validity of certain subtests of the NEPSY-II was reported being less favourable than others were (Brooks et al., 2010). In some cases, current data on the psychometric properties of the NEPSY-II are missing (such as for the NM Recognition subtest) or not comprehensive enough to reach conclusions in this regard. Another drawback of using the NEPSY-II was that some of the subtests of this measure could not be used in the current study. Translation of some subtests evidently requires more specialised input (such as word list interference), the age range of the List Learning

subtest is too narrow (ages 7 to 12 years) and the Auditory Attention and Response Set subtest require the use of a recording, which is available only in English. Consequently, some constructs, such as verbal learning, working memory and attention, could not be assessed in the current study by means of the NEPSY-II.

The use of norms for 16-year-olds to interpret and compare the data of the 17-year-old LiP and control participants on the NEPSY-II in the study is a limitation. Owing to the ceiling effect – the scores individuals obtain on a certain measure are approaching their possible maximum (Cramer & Howitt, 2004) – the NEPSY-II subtests might not be sensitive enough to detect differences in performance between the LiP and control participants in the 17-year-old age group.

In this study, parent ratings of behaviour were used to measure adaptive and maladaptive behaviour. Parent ratings and teacher ratings of behaviour often differ due to several factors such as parent characteristics and situation specificity (Berg-Nielsen, Solheim, Belsky, & Wichstrom, 2012; Gagnon, Nagle, & Nickerson, 2007; Nickerson & Nagle, 2001). Observation of the child or adolescent's behaviour in two settings (such as school and home) usually provides a more realistic picture of the child or adolescent's behaviour (Berg-Nielsen et al., 2012; Gagnon et al., 2007). One LiP participant did not attend school; therefore; it was impossible to obtain ratings of his behaviour in more than one setting. Therefore, information about his behavioural difficulties was incomplete.

Although valuable information was obtained by means of the ASEBA scales with regard to inattentive, hyperactive and impulsive behaviour of the children and adolescents with LiP in the current study, the validity of rating scales as cognitive measures of attention and executive function has been questioned (Anderson et al., 2002). There is some evidence of correlations of scores on behaviour rating scales with measures of sustained and selective auditory attention (Fahey, 2006). The CBCL/1.5-5 (parent rating scale) was also reported being less reliable than the C-TRF (teacher rating scale) was for rating attention in the pre-school developmental period due to inattentive behaviour being more noticeable at school than at home (Achenbach & Rescorla, 2000). Therefore, it is recommended that an additional measure of attention, such as Digits Forward and Backwards, be employed in future research.

Extraneous Variables

First, research participants were tested in different settings such as the participants' homes, community clinics, at pre-schools or in the researcher's office. Participants might react differently at home than in a formal setting. Variable levels of distraction might have been present in the different circumstances, although an attempt was made to limit disturbances.

Second, as signs of LiP are very noticeable (hoarse voice, skin lesions) and the group of participants was small, it was impossible for the researcher not to be familiar with the research participants' group status. This might have unintentionally affected the research results due to certain expectations based on the literature.

Methodological Limitations

Research on adults with LiP often consists of studies using a single case or small group design (Adolphs, 2007; Siebert et al., 2003; Strange et al., 2003), raising questions about the validity of the results and conclusions. However, the small group of children and adolescents with LiP involved in the current research represented the entire population of children and adolescents known to have LiP in South Africa. Therefore, the usual concerns about reliability and validity associated with small group studies (Bates & Appelbaum, 1994) did not apply. The conclusions regarding the performance of children and adolescents with LiP in South Africa were definitive. However, other difficulties were associated with being forced to use a small group design. Owing to the small number of participants in each age group, test scores obtained by individuals in one age group could not statistically be compared to the test scores obtained by individuals in another age group. Therefore, conclusions made with regard to age-related changes in performance were based purely on observing trends in performance across the different age groups, as depicted in the graphs.

Another limitation of the study is that a group of children with different pathology (such as children with a different neurocutaneous disorder) were not included in the study. This would have controlled for the effect of having a severe or disfiguring genetic or neurological disorder on psychosocial adjustment and development.

Finally, unfortunately, brain imaging results were not available for all the participants. Brain imaging was also not done on the control participants, so that correlations between the extent and type of brain lesions and the results of the neuropsychological and behavioural measures could not be determined.

Implications of the Findings

Implications for Treatment and Counselling

Given that children and adolescents with LiP present with deficits in recognising facial emotion expressions, training of these skills may prove to be helpful. Intervention programmes developed for children and adolescents with autistic spectrum disorders, such as the Mind Reading programme of Golan and Baron-Cohen (2006), may be successful. The programme designed by Golan and Baron-Cohen (2006) aims to use strong abilities to facilitate improvement in areas of weakness (such as recognition of facial emotion). The programme aims to improve the recognition of a range of emotions across different modalities. Despite limited generalisation, the authors observed improvement in emotion recognition skills across a range of complex emotions and different modalities in the individuals with autism spectrum disorders included in their programme (Golan & Baron-Cohen, 2006). Golan et al. (2010) also designed an animated series (The Transporters) to enhance emotion comprehension in children with autism spectrum conditions. It is anticipated that such a series would equally benefit any child (such as a child with LiP) who presents with emotion recognition or comprehension difficulties.

Cognitive rehabilitation and behavioural therapy resources aimed at individuals with brain injury might be helpful for work with children and adolescents with LiP. An example of such a resource is a DVD version of Stallard's (2002) cognitive behaviour therapy programme recommended by Tonks et al. (2008) for children with brain injury and impulsive behaviour. Initially, the programme was developed to address impulsivity in older children with ADHD. Stallard's (2002) DVD was developed for therapist-guided individual work with learners with brain injuries. The programme and DVD focus on the relationship between feelings and thoughts and learning how to interpret physical signs as clues to emotional states (Stallard, 2002; Tonks et al., 2008). Tonks et al. (2008) found "Stop and Think" programmes useful in training children to take more time to process and understand their emotional states before responding. The authors recommend that frequent

sessions with the opportunity to rehearse real-world situations are helpful to contextualise learning. Developmental programmes designed specifically for children and adolescents have an advantage over adult-oriented programmes in that they incorporate age-appropriate skills training. However, the effectiveness of these recommended interventions for children and adolescents with acquired brain injury has not been evaluated yet.

The use of stimulant medication to treat ADHD in other genetic disorders such as Neurofibromatosis seems to have a positive effect and lead to improvement in cognitive, academic, and social functioning (Mautner, Kluwe, Thakker, & Leark, 2002). This might also be true for children and adolescents with LiP, who present with attention deficit, impulsiveness and hyperactivity. Therefore, psychiatric assessment and management could be standard recommendations for children with LiP.

Research suggests that interactive and contextual approaches to interventions in the case of children with neuropsychiatric or neurocognitive difficulties are most successful (Wade, Carey, & Wolfe, 2006; Wade, Michaud, & Brown, 2006; Yeates et al., 2007). Therefore, including the parents and family in any intervention programme aimed at children and adolescents with LiP is of great importance. The current research provides information with regard to the challenges that children and adolescents with LiP face. This information can be helpful when counselling or educating parents of children and adolescents with LiP. They can be told that the research results indicate that all children with LiP included in the study presented with some kind of behavioural or emotional challenge. Every child and adolescent with LiP presented with cognitive deficits, although no uniform cognitive profile was evident and normal functioning in several areas of cognitive functioning was identified. Academic deficits were not evident, but academic functioning has been monitored only in a limited number of children with LiP. Normal social interaction is a possible outcome, but difficulties with regard to some aspects of their interpersonal relationships and emotional control may be evident. Teasing by peers can affect children and adolescents with LiP, emotionally and socially.

As all children and adolescents with LiP in the study population presented with cognitive and behavioural difficulties, psycho-educational assessment should be advised. Owing to possible interpersonal and emotional difficulties, children and adolescents with

LiP may benefit from psychotherapy (if available in the particular community). Cognitive rehabilitation or training in compensatory techniques may be necessary to support these children. Monitoring their progress and follow-up assessments would be good practice to ensure that problems are addressed when necessary. Early intervention and rehabilitation may prevent negative or destructive cycles from occurring.

Implications for Research

The current research provides a baseline indication of the neuropsychological and psychosocial development of children and adolescents with LiP. The results stimulate further questions with regard to the possible relationship between the brain and behaviour in this disorder. Deterioration in functioning does not appear to be evident in the group of children and adolescents that took part in the current study, but longitudinal research is necessary to determine the trajectory of neuropsychological and psychosocial functioning in this population. Research on the trajectory of cognitive and psychosocial functioning in LiP should be extended into adulthood, as deterioration in functioning may possibly commence only in adulthood.

The areas of difficulty highlighted in the current research may stimulate further thinking and provide pointers to the areas of neuropsychological and behavioural functioning that may be relevant in future research. An example of this is the deficits in memory function that are pointed out in the current research. This outcome may be an indication that research on memory in children and adolescents with LiP should be extended. The literature suggests that adults with LiP may have deficits in emotional memory (Adolphs et al., 1997) and this aspect of memory, as opposed to non-emotional declarative memory, may be worthwhile to explore in the future. Another area of research that was suggested to be relevant is recognition of facial emotion. Atkinson, Heberlein, and Adolphs (2007) and Birmingham, Cerf, and Adolphs (2011) conducted neuroscience research with regard to recognition of facial emotion in an adult with LiP, and this type of research in the paediatric population may provide insights into the brain mechanisms underlying these skills.

Intact and elevated scores on neuropsychological measures and behaviour checklists raise questions about the mechanisms contributing to areas of intact functioning (such as ToM) as opposed to areas of weaknesses. Neuroimaging should be included in research on

children and adolescents with LiP to explore the effect of age of onset of amygdala lesions and the effect of plasticity on the development of cognitive functions in individuals with LiP.

Elevated scores with regard to internalising and externalising problems and indications of possible mood, anxiety, conduct, social and attention deficit disorders on behaviour checklists raise questions with regard to the role of amygdala pathology in these disorders. Descriptions of the behaviour of the children and adolescents with LiP (such as lack of fear in certain situations) provide an impetus for further research on their social behaviour and psychopathology.

Observations with regard to possible correlations between socio-economic factors and performance on certain neuropsychological measures provide pointers for further exploration of these issues in populations of typically developing children. The apparent differences in performance of children and adolescents from different cultural and socio-economic backgrounds highlight the lack of standardised and appropriate measures for the various groups in the country. Therefore, the current research accentuates the importance of the standardisation of existing instruments or the development of new instruments that are appropriate for the diverse groups in South Africa.

Recommendations for Further Research

Matching participants according to FSIQ proved to be important to control for the effect of differences in intelligence and verbal ability. It is advisable to use a local measure of intelligence or a test that has been formally translated and standardised on the South African population that can be administered in the participant's home language and that also includes measurement of verbal abilities.

Several cognitive functions that are affected in adults with LiP and individuals with amygdala damage have not been studied in the paediatric LiP population. These skills include emotional memory and learning (Adolphs et al., 2005; LaBar & Cabeza, 2006), moral reasoning (Raine, 2006), social attention (Spezio, Huang, Castelli, & Adolphs, 2007) and decision making (Bechara, Damasio, & Damasio, 2003). These gaps in extant knowledge could be addressed by further social cognition and neuroscience research. One such study could compare learning of associations of pairs of emotional faces to

associating pairs of neutral faces. Using comprehensive measures of social cognition would expand the current research and provide detailed understanding of these functions in children and adolescents with LiP. For instance, although no significant differences in ToM scores between the LiP participants and those attained by their typically developing peers were noted in the current study, using a measure of more advanced ToM skills can extend the current findings on ToM in LiP patients. Including surprised facial expressions in the set used in the recognition of facial emotion task would provide more information with regard to the recognition of positive facial expressions in children and adolescents with LiP. It would also be beneficial to interview the patients diagnosed with LiP about their emotional experiences, as this would facilitate assessment of whether the children perceive the surprised faces as a good surprise or a frightening surprise. These findings would help determine how they view the valence of the stimulus (as positive or negative). Adding a verbal component to the facial recognition measure would provide more in-depth understanding of the recognition of facial emotion abilities of children and adolescents with LiP.

Although the NEPSY-II measures a wide range of neuropsychological functions, it is recommended that additional neuropsychological measures be employed to assess constructs that could not be evaluated by means of the NEPSY-II in the current study (such as attention and autobiographical memory).

Longitudinal research is essential for enhancing the current understanding of the neuropsychological and psychosocial development of children and adolescents with LiP. Studies of age-related features of cognitive and behavioural deficits make it possible to draw inferences about the relationship between development and cognitive ability as the child ages (Fisch et al., 2007). Longitudinal research would also increase understanding of the psychosocial variables, such as self-worth, self-esteem, maternal adjustment or family stress, and support that may mediate the expression of LiP across the lifespan. It is recommended that longitudinal research (and repeated scanning) should also be extended to the adult and older adult age groups, as it is possible that deterioration in function occurs only during adulthood. Results of the current study indicate that longitudinal research on the progress of recognition of facial emotion across the lifespan in individuals with LiP may yield interesting results. Another focus of such research can be changes in intelligence scores of individuals with LiP across the lifespan. Data from the current study

on the WASI can be combined with data from a previous study (the WASI was used among adults with LiP in the Northern Cape) to explore the changes (if any) in intelligence scores across the lifespan. It would also be important to match this to norms and follow it up longitudinally.

Another suggestion for further research among children and adults with LiP is to compare the performance and functioning of males versus females. There are hormonal, structural and functional differences in the brains of males and females (Berenbaum, Bryk, & Beltz, 2012; Darlington, 2009; Keller & Menon, 2009; Lenroot & Giedd, 2010; Suzuki et al., 2005) also with regard to amygdala functioning and development (Hamann, 2005). Structural differences in the brain were suggested to be related to differences in cognitive and emotional processing of males versus females, such as differences in recognition of facial emotion, emotion processing and emotional memory (Hamann, 2005; Hampson, Van Anders, & Mullin, 2006; Stevens & Hamann, 2012). Therefore, comparing male and female performance in tasks measuring constructs that are relevant to LiP would provide further insight into the relationship between the brain and behaviour/cognition in persons with LiP.

Future research would be more powerful than the current research if it were possible to interpret neuropsychological test results in the context of information obtained by means of brain imaging. Comparing the neuropsychological and brain imaging data of children and adolescents with LiP to that of children with other neurocutaneous (such as neurofibromatosis) and neurological disorders may present interesting differences in cognitive functioning related to the differences in underlying brain pathology. Furthermore, comparison of the neuropsychological and psychosocial functioning of LiP children and adolescents to a group of children with another neurocutaneous or skin disorder may provide valuable insights into the role of disfigurement in the psychosocial adjustment of these children.

Although neuropsychological assessments and ratings of children's behaviour can provide important information about their neuropsychological and psychosocial functioning and behaviour, neuropsychological tests and rating scales are restricted and do not provide a deeper understanding of children's real-life interactions and problems. In order to explore and understand the effect of social-cognitive deficits on the social skills

and interaction of children and adolescents, observation of their behaviour in a real-life or experimental context or ratings of their social skills need to be included (Steinberg, 2005). Additionally, qualitative studies can provide new insight and rich information about the psychosocial adjustment of children and adolescents with genetic disorders across different age groups (Holland, Whittington, & Butler, 2002; Lagrou et al., 1998; Quittner, Modi, & Roux, 2004; Sutton et al., 2005). Obtaining clinic and hospital records as well as school reports as part of the data can provide more information about their development.

Significance of the Study

The current study contributes to an understanding of the neuropsychological and psychosocial difficulties of individuals with LiP, and specifically extends the focus of research to children and adolescents with LiP. The study not only provides an understanding of the difficulties of individuals with LiP, but also shows possible areas of strength. Some understanding of the possible deficits prevalent in children and adolescents with LiP provides pointers for the focus of further research on paediatric LiP. The results of the study have implications for genetic, individual and family counselling, as they provide knowledge about the possible problems that children and adolescents with LiP may have and the consequent action that parents can take with regard to supporting their children and optimising their development.

The study provides a baseline assessment for future longitudinal or developmental research on LiP and thereby contributes to the understanding of the progression of the illness. Two of the participants in this study presented with amygdala lesions, which may have been associated with certain deficits. This possibility can be substantiated only by further research that includes the imaging of controls. Relative normal functioning in some children and adolescents with LiP raises the question of plasticity effects, but more research on the relation between lesion size, progression of the lesion and severity of problems is necessary to clarify these effects. Overall, the study can be regarded as a pilot study. Subsequent studies will increase the power and significance of the results.

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Appendix A

English and Afrikaans Information and Consent Documents

Information and Informed Consent Document

Version 2

(May 2007)

Title of the Research Project:

The Neuropsychiatry and Neuropsychology of Lipoid Proteinosis

Project Number:

2002/C103

Principal Investigator:

Dr Helena Thornton

Department of Psychiatry and Mental Health, University of Cape Town
Groote Schuur Hospital
Observatory, 7925
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Patient Information and Consent Form

Study title: The Neuropsychiatry and Neuropsychology of Lipoid Proteinosis

Investigators:	Dr Helena	Prof Dan Stein
	Prof Thornton	Dr Tinus Brink
	Dr Jonathan Carr	Dr BarakMorgan
	Dr Jack van Honk	Dr Paul
	James Warwick	Carey
	Prof Kit Vaughan	Dr Ernesta Meinjtes
	Dr Kevin Thomas	Dr Greetje de Jong
	Susan Malcolm-Smith	
Collaborators:	Prof Ralph Adolphs	Prof Michele Ramsay
	Dr James Butler	

Dear volunteer

You are being asked to participate in a research study. Please read the following information carefully and do not hesitate to ask questions now or at any time during the study. Your participation in the study is entirely voluntary.

Description and Purpose of the Study

You are being invited to take part in a study carried out by the University of Stellenbosch. The purpose of this study is to understand some of the symptoms of Lipoid Proteinosis (LP). This illness may cause no problems at all, or it may cause difficulties with memory or feelings (e.g. anxiety) or thinking. We want to assess all people living with LP in South Africa, (and controls, who are people without LP from the same areas) to study memory, thinking, feelings and behaviour. One other person who has daily contact with you (e.g. family member or other caregiver) will be asked to answer questions about your memory and feelings and behaviour. We hope to understand the way LP works by studying people who may have symptoms and people who do not have symptoms. The study will take place at your community clinic and at Tygerberg Hospital (the Faculty of Health Sciences of the University of Stellenbosch), and will be conducted according to the Declaration of Helsinki and the guidelines for Good Clinical Practice (ICH). The Research Ethics Committee of the University of Stellenbosch has approved the study. If you are invited to Cape Town to participate in further LP research, all your transport and accommodation will be provided free of charge. If necessary, we shall arrange with your employer to give you time off work. You will stay in Tygerberg Hospital or in a nearby hotel or hotel-like accommodation near the hospital belonging to the University of Stellenbosch. Visits to Cape Town may last three to five days, and over the years, you may be invited for further research visits. All the research activities are described in this document.

Medical Examination

As a participant in this study, you will be given a full medical examination by a doctor experienced in LP. Depending upon the findings, you may be referred to specialists in the hospital for particular problems you may have (eg. skin, breathing or voice problems or epilepsy).

SPECT, MRI and fMRI Scans

If you are invited to come to Cape Town, you may have a type of brain scan, called a SPECT scan, which analyses blood flow in the brain. This scan will require a radioactive dye to be injected into you. The amount of radiation you will be exposed to is very small and is considered safe, but you will have some radiation exposure. (This investigation is frequently used in diagnostic procedures and is an acceptable, standard investigative procedure.) You may also have another brain scan called an MRI. With this scan, there are no injections. MRI uses magnets to make pictures of the inside of the body. People with any of the following may not have an MRI: implanted medical devices such as aneurysm clips in the brain, heart pacemakers, and cochlear (inner ear) implants; lead-based tattoos; or pieces of metal close to or in an important organ (such as the eye). To be sure about his, your doctor will ask you all the necessary questions about these things before you have the MRI scan. The scan will require you to lie on your back on a table that will move into the scanning machine, which is open at both ends. The scan will take about 45 minutes. You will be asked to stay as still as possible while pictures are being taken. The MRI scan itself does not hurt, and many people in the hospital use it every day. During some of this time, you will simply lie still with your eyes closed and rest. If you have an fMRI scan, then it means that during the scan you will be asked to look at a screen and in some cases respond to questions about what you see or how the pictures make you feel.

EEG, ECG and Skin Conductance Level

Research EEG. The EEG machine is used to record brainwaves. A rubber cap resembling a swimming cap is placed on your head to hold the sensors in place. Four sensors will also be placed on your face around your eyes. At the same time, your heart rate will also be measured by three electrodes – one placed on each of your shoulders and one on your lower back. Another sensor will measure changes in the electrical resistance of the skin on the palm of your hand (SCL or skin conductance level). EEG recordings will last for approximately 10 minutes, during which time you will be asked to sit in a comfortable chair and assume a relaxed resting state. You will be asked to open or close your eyes at 2 minutes intervals.

Clinical EEG. Some subjects may be required to stay in hospital for a sleep EEG to diagnose suspected epilepsy. This involves sleeping with EEG sensors attached to your head. A video camera is there to record any epileptic movements of your body that may occur while you are asleep. EEGs are painless and completely safe procedures.

Saliva and 24-hour Urine Sampling for Hormonal Measurement and DNA Blood Sampling

You will be asked to provide a sample of saliva every hour for a day by holding a soft dental roll in your mouth for 3 minutes. In addition, you will be asked to provide saliva in a plastic tube four times during the day: One sample will be taken in the morning, two in the afternoon and one in the evening. You will also be asked to provide a sample of all your urine over a 24-hour period.

If you have not already been tested for LP, then a test tube of blood will be taken to check for the LP gene. The blood will be analysed for the LP gene and, if you want, you will receive genetic counselling and can be told the results of the blood test. The blood sample

may be stored indefinitely with the Health Sciences Faculty of the University of Stellenbosch for future research in this field and for research purposes only, and any information from such research will remain confidential. Any new research study will be submitted to the Research Ethics Committee for approval.

Discomfort Associated with the Study

If you come to Cape Town for the hospital-based work, you will be away from home for 3 to 5 days.

You might experience some discomfort when the injections for the SPECT scan are given. When giving a blood sample, there is sometimes some discomfort with the needle and there may be minor bruising. With the EEGs, the only inconvenience will be the small amounts of gel applied to your scalp, which is easily washed out with water and shampoo.

During the MRI neuroimaging assessment, certain metal objects such as watches, credit cards, hairpins and writing pens may be damaged by the MRI scanner or pulled away from the body by the magnet. For these reasons, you will be asked to remove these objects before entering the scanner. When the scanner makes the pictures, the bed may vibrate and you will hear loud banging noises. You will be given earplugs and/or headphones to protect your ears. Also, some people feel nervous in a small, closed space such as when they are in the scanner. You will be able to see out of the scanner at all times, and we will not start the procedure until you tell us that you are comfortable. You will be able to stop the procedure at any time by squeezing a ball that you will hold in one hand, and you can talk to us using an intercom that is built into the scanner.

Potential Benefits

Although this study may not benefit you now, it may benefit you and other patients in the future. This study may help clinicians to understand your condition and develop new treatments for patients with a similar condition.

The doctor can make sure that any treatment you get for LP symptoms is correct, and it may benefit your family planning decisions to know your LP carrier status. If you do not have the LP gene, there is no danger of any of your children having LP. If you are an LP gene carrier, you and your partner should consider genetic counselling.

Compensation for Study Participation

Tests and examinations required as part of the study will be provided at no cost to you or your medical aid.

While you will not be paid to take part in the study, your travelling costs will be reimbursed if necessary. If you come to Cape Town, then transport to and from Tygerberg Hospital, and all your meals and accommodation needs will be provided free of charge (including caregivers and controls) throughout the duration of the study. Someone on the research team will be responsible for ensuring that all your basic needs are catered for.

Compensation for Possible Injury or Disability

You will be referred for medical treatment, should this be necessary. Therefore, you must follow your doctor's instructions at all times, and you must immediately report any injury to the doctor conducting the study. In case of an emergency that involves this trial, please contact Helena Thornton on 084 690 2288.

Confidentiality

Your participation is regarded as strictly confidential. The results of the study will be published in professional literature and made available to Subcommittee C of the Research Committee, but your identity will not be revealed in any way.

The Right to Ask Questions and/or to Withdraw from the Study

You have the right to ask questions about any aspect of the study at any time.

Your participation in the study is entirely voluntary. You have the right to withdraw at any time. If you decide to withdraw from the study, this will have no influence on your future treatment, and will not jeopardize you in any way. You are entitled to a signed copy of this document.

I have read and understood these pages, and have had the opportunity to ask questions.

Signed on:_____at: _____

Patient's signature:_____

Witness: _____

If you agree to take part, please complete the following section:

Informed Consent Document for a Research Project Compiled According to Guidelines Provided by the Ethics Committee of the Faculty of Healthy Sciences of the University of Stellenbosch

The Neuropsychiatry and Neuropsychology of Lipoid Proteinosis

Declaration by Patient/Control:

I, the undersigned_____(ID:_____)

(address)_____

A: hereby declare the following:

The Department of Psychiatry of the University of Stellenbosch invites me (or my child) to participate in the above-mentioned research project.

It has been explained to me that psychometric (paper and pen and computer) tests will be performed on me / my child. One other person who has daily contact with me (e.g. family member or other caregiver), will be asked to answer questions about my / my child's memory and feelings and behaviour. If I come to Cape Town, I understand it will be for 3 to 5 days.

If I / my child come to the Medical School of the University of Stellenbosch, I / my child will be examined by a doctor, and blood, urine and saliva samples may be taken. My blood will be checked for the LP gene and I can know my LP status if I want. I may have research and sleep EEGs and may be monitored by video. My heart and skin reactions will also be measured. If I have brain scans, I will lie with my eyes closed in a darkened room. A doctor will then inject me with a medication that will help the machine to take a picture of my brain. This medication has some radioactivity, so that it is like having an X-ray. A doctor will check if it is safe for me to have MRI or fMRI scans of the brain – then I will lie in a noisy machine and may be asked to respond to questions or lie still.

This testing will not affect my / my child's treatment in any way.

I have been informed that I / my child may refuse participation in this project and that such refusal will not affect my / my child's current and future treatment at this institution. Participation in this project will not lead to any extra costs for me. There is no special advantage or disadvantage in participating in this project.

I have been informed that all information will be treated as confidential, but that it will be used in a thesis or publication in a medical journal. My name will not appear in the publication and it will not be possible to identify me in this publication. Although the results will be computed at a later stage, I will have access to all my / my child's clinical results if I want.

The information above has been explained to me in English. I have not been forced to participate in this project, and I can stop my participation at any moment without any consequences.

B: I hereby give voluntary permission for me / my child to participate in the above-mentioned project.

Signed at_____on_____20_____

Patient's / Guardian's Signature: _____

Witness:_____

Declaration by / on behalf of the Researcher

I,_____, declare that I

explained the information contained in this document to _____;

he / she was requested to put questions to me in the event of any misunderstanding; and I

conducted this conversation in English.

Signed at: _____ on _____20_____

Researcher / Representative:_____

Witness:_____

Inligting- en Ingeligte Toestemmingsdokument
Weergawe 2

(Mei 2007)

Titel van Navorsingsprojek

Die Neuropsigiatrie en Neurosielkunde van Lipoïed-Proteïnose.

Projeknommer

2002/C103

Hoofnavorser

Dr Helena Thornton

Departement Psigiatrie en Geestesgesondheid
Universiteit van Kaapstad
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Observatory, 7925
Suid-Afrika
Telefoon: (021) 404-3185
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Inligting- en Toestemmingsvorm vir Pasiënt

Titel van Studie: Die Neuropsigiatrie en Neurosielkunde van Lipoïed-Proteïnose

Navorsers:	Dr Helena Thornton	Prof Dan Stein
	Prof Jonathan Carr	Dr Tinus Brink
	Dr Jack van Honk	Dr Barak Morgan
	Dr James Warwick	Dr Paul Carey
	Prof Kit Vaughan	Dr Ernesta Meinjtes
	Dr Kevin Thomas	Dr Greetje de Jong
	Susan Malcolm-Smith	
Medewerkers:	Prof Ralph Adolphs	Prof Michele Ramsay
	Dr James Butler	

Inleiding

Geagte Vrywilliger

U word uitgenooi om aan ’n navorsingstudie deel te neem. Lees asseblief die volgende inligting sorgvuldig deur en moenie huiwer om nou of enige tyd gedurende die studie vrae te vra nie. U deelname aan die studie is heeltemal vrywillig.

Beskrywing en Doel van die Studie

U word uitgenooi om deel te neem aan ’n studie wat deur die Universiteit Stellenbosch uitgevoer word. Die doel van hierdie studie is om meer duidelikheid oor die simptome van Lipoïed-Proteïnose (LP) te verkry. Hierdie siekte kan óf geen probleme veroorsaak nie, óf u kan moontlik probleme ervaar met u geheue, gevoelens (bv. angstigheid) of denkpatrone. Ons wil graag alle persone met LP in Suid-Afrika evalueer (en Kontrole-deelnemers wat mense is sonder LP wat in dieselfde gebiede woon) om geheue, denkpatrone, gevoelens en gedrag te bestudeer. Een ander persoon wat daagliks met u kontak het (soos ’n familielid of ander versorger) sal gevra word om vrae oor u geheue, gevoelens en gedrag te beantwoord. Ons hoop om meer te verstaan oor hoe LP werk deur die persone wat simptome ervaar, asook diegene wat nie simptome het nie, te bestudeer. Die studie sal plaasvind by u gemeenskapskliniek en by die Tygerberg Hospitaal (die Fakulteit Gesondheidswetenskappe van die Universiteit Stellenbosch) en word uitgevoer volgens die Deklarasie van Helsinki en die riglyne van “Good Clinical Practice” (ICH). Die studie is deur die Navorsingsetiekkomitee van die Universiteit Stellenbosch goedgekeur.

Indien u uitgenooi word om vir verdere LP-navorsing na Kaapstad te kom, sal alle vervoer en verblyf gratis aan u voorsien word. Indien nodig, sal ons reëlings met u werkgewer tref om verlof aan u toe te staan. U sal in Tygerberg Hospitaal of ’n nabygeleë hotel of iets soortgelyks wat aan die Universiteit Stellenbosch behoort, tuisgaan. Besoeke aan Kaapstad kan drie tot vyf dae duur en oor jare strek; u kan dalk vir verdere navorsingsbesoeke uitgenooi word. Al die navorsingsaktiwiteite word in hierdie dokument beskryf.

Mediese Ondersoek

As 'n deelnemer aan hierdie studie sal ’n dokter wat ervaring van LP het, u volledig ondersoek. Afhangende van die bevindings, kan u verwys word na spesialiste in die hospitaal vir bepaalde probleme wat u kan ondervind (soos vel-, asemhaling- of stemprobleme of epilepsie).

SPECT-, MRI- en fMRI-Skanderings

Indien u na Kaapstad uitgenooi word, sal u moontlik ’n tipe breinskandering ondergaan, naamlik ’n SPECT-skandering wat die bloedvloei in die brein analiseer. Hierdie skandering behels dat u met ’n radioaktiewe kleurstof ingespuit sal word. Die hoeveelheid bestraling waaraan u blootgestel sal word, is baie klein en word as veilig bestempel, maar u sal wel aan bestraling blootgestel word. (Hierdie ondersoek word gereeld in diagnostiese prosedures gebruik en is ’n aanvaarbare, standaard ondersoekprosedure.) U kan ook ’n ander breinskandering, naamlik ’n MRI, ondergaan. Hierdie skandering behels geen inspuitings nie. Die MRI-skandering gebruik magnete om foto’s van die binnekant van die liggaam te neem. Hierdie skandering is nie vir mense met die volgende geskik nie: ingeplante mediese toestelle soos aneurisme-plaatjies in die brein, hartpasaangeërs en kogleêre (binne-oor-) inplantings; loodbasistatoeëermerke; of metaalstukkies naby aan of binne-in ’n belangrike orgaan (soos die oog). Om seker te maak hiervan, sal u dokter u al die nodige vrae hieroor vra alvorens u ’n MRI-skandering ondergaan. Die skandering vereis dat u op u rug lê op ’n tafel wat in die skanderingsmasjien inbeweeg. Die masjien is oop aan weerskante. Die skandering sal ongeveer 45 minute duur. U sal versoek word om so stil moontlik te lê terwyl foto’s geneem word. Die MRI-skandering is nie seer nie en word elke dag deur baie mense in die hospitaal gebruik. Vir ’n gedeelte van die tyd sal u bloot stil en met geslote oë lê en rus. Indien u ’n fMRI-skandering ondergaan, beteken dit dat u gedurende die skandering gevra sal word om na die skerm te kyk en in sommige gevalle op vrae te reageer oor wat u sien en hoe die prentjies u laat voel.

EEG, EKG en Velkonduktansievlak

Navorsing-EEG: Die EEG-masjien word gebruik om breingolwe op te neem. ’n Rubberpet wat soos ’n swempet lyk, word op u kop geplaas om die sensors in plek te hou. Vier sensors sal ook op u gesig rondom u oë geplaas word. Terselfdertyd sal u hartslag deur drie elektrodes gemeet word – een op elke skouer en een op u lae rug. Nog ’n sensor sal veranderings in die elektriese weerstand van die vel op u handpalm meet (SCL of velkonduktansievlak).

EEG-opnames sal vir ongeveer tien minute duur waartydens u gevra sal word om in ’n gemaklike stoel te sit en ’n ontspanne, rustende houding in te neem. U sal gevra word om u oë met intervalle van twee minute oop en toe te maak.

Kliniese EEG: Sommige persone kan gevra word om in die hospitaal te bly vir ’n slaap-EEG om sodoende ’n diagnose te maak as epilepsie vermoed word. Dit behels dat u met EEG-sensors wat aan u kop geheg is, sal slaap. ’n Videokamera sal enige epileptiese bewegings van u liggaam wat gedurende u slaap kan plaasvind, opneem. ’n EEG-prosedure is pynloos en heeltemal veilig.

Speeksel- en 24-Uur-Urienmonster vir Hormoonmeting en DNA-Bloedtoets

U sal versoek word om ’n speekselmonster elke uur vir ’n dag lank te voorsien deur ’n sagte tanderolletjie vir drie minute in u mond te hou. Daarby sal u gevra word om vier maal per dag speeksel in ’n plastiekbuisie te voorsien: een monster in die oggend, twee in die middag en een in die aand. U sal ook gevra word om ’n monster van al u urien oor ’n 24 uur-periode te voorsien. U sal ’n spesiale houer vir hierdie doel ontvang.

Indien u nog nie vir LP getoets is nie, sal ’n toetsbuisie bloed getrek word om te kyk of die LP-geen teenwoordig is. Die bloed sal geanaliseer word en, indien u wil, sal u genetiese berading ontvang en die uitslae van die bloedtoets kan aan u bekend gemaak word. Die bloedmonster kan vir ’n onbeperkte tyd by die Universiteit Stellenbosch se Fakulteit Gesondheidswetenskappe vir latere navorsing in hierdie navorsingsrigting en vir navorsingsdoeleindes alleenlik geberg word. Enige inligting wat uit hierdie navorsing spruit, sal vertroulik bly. Enige nuwe navorsingstudie wat hieruit voortspruit sal vir goedkeuring aan die etiese komitee voorgelê word.

Ongemak wat met hierdie Studie Geassosieer word

Indien u na Kaapstad kom vir die hospitaalgebaseerde werk, sal u vir drie tot vyf dae weg van die huis wees.

U kan dalk effense ongemak ervaar met die toediening van die inspuitings vir die SPECT-skandering. Wanneer ’n bloedmonster geneem word, is daar soms effense ongemak met die naald en u kan effens gekneus word. Met die EEG’s is die enigste ongemak die klein hoeveelhede jel wat aan u kopvel toegedien word, maar wat maklik met water en sjampoe uitgewas word.

Gedurende die MRI-neurobeeldassessering kan sekere metaalvoorwerpe soos horlosies, kredietkaarte, haarnaalde en skryfpenne deur die MRI-skandeerder beskadig word of deur die magneet van die liggaam weggetrek word. Om hierdie rede sal u versoek word om dié voorwerpe te verwyder alvorens u die skandeerder betree. Wanneer die skandeerder die foto’s neem, kan die bed vibreer, en u sal harde stampgeluide hoor. U sal oorpluisies en/of oorfone ontvang om u ore te beskerm. Voorts voel party mense senuagtig wanneer hulle hul in ’n klein, afgeslote spasie soos binne-in die skandeerder bevind. U sal deurentyd uit die skandeerder kan sien, en ons sal nie die prosedure begin alvorens u ons verseker dat u gemaklik is nie. U sal die prosedure enige tyd kan stop deur ’n bal te druk wat u in een hand hou, en u kan met ons praat met behulp van ’n interkom wat in die skandeerder ingebou is.

Potensiële Voordele

Hoewel hierdie studie moontlik nie nou vir u tot voordeel strek nie, kan u en ander pasiënte in die toekoms daarby baat vind. Die studie kan klinici help om u toestand beter te begryp en nuwe behandelings vir pasiënte met soortgelyke toestande te ontwikkel.

Die dokter kan seker maak dat enige behandeling wat u vir LP-simptome ontvang, korrek is, en dit kan tot voordeel wees vir u gesinsbeplanningsbesluite om te weet van u LP-draerstatus. Indien u nie die LP-geen het nie, is daar geen gevaar dat enige van u kinders LP sal hê nie. Indien u ’n LP-geendraer is, behoort u en u maat genetiese berading te oorweeg.

Vergoeding vir Deelname aan die Studie

Toetse en ondersoeke wat deel van hierdie studie uitmaak, sal kosteloos aan u en u mediese fonds voorsien word.

Hoewel u nie betaal sal word om aan die studie deel te neem nie, sal u reiskoste aan u terugbetaal word, indien nodig. Indien u na Kaapstad kom, sal vervoer na en van Tygerberg Hospitaal, asook al u etes en verblyf vir die duur van die studie gratis aan u voorsien word (insluitende versorgers en kontrolepersone). 'n Lid van die navorsingspan sal verantwoordelik wees om toe te sien dat daar in al u basiese behoeftes voorsien word.

Vergoeding vir Moontlike Besering of Ongeskiktheid

U sal vir mediese behandeling verwys word, indien nodig. U moet dus u dokter se instruksies te alle tye goed navolg, en u moet enige beserings onmiddellik rapporteer aan die dokter wat die studie uitvoer. In geval van nood gedurende die proeftydperk, skakel Helena Thornton by 084 690 2288.

Vertroulikheid

U deelname word as streng vertroulik beskou. Die resultate van die studie sal in die professionele literatuur gepubliseer word en aan Subkomitee C van die Navorsingskomitee beskikbaar gestel word, maar u identiteit sal op geen manier bekend gemaak word nie.

Die Reg om Vrae te Vra / om aan die Studie te Onttrek

U het te alle tye die reg om oor enige aspek van die studie vrae te vra.

U deelname aan die studie is heeltemal vrywillig. U het die reg om enige tyd aan die studie te onttrek. Indien u besluit om te onttrek, sal dit geen invloed op u toekomstige behandeling hê nie, en dit sal u in geen mate benadeel nie. U is geregtig op 'n ondertekende afskrif van hierdie dokument.

Ek het hierdie bladsye gelees en verstaan en het die geleentheid gehad om vrae te vra.

Geteken: _____ op _____20_____

Pasiënt:_____

Getuie: _____

Indien u instem om deel te neem, vul asseblief die onderstaande in:

Ingeligte Toestemmingsdokument vir ’n Navorsingsprojek Saamgestel volgens Riglyne Voorsien deur die Etiese Komitee van die Universiteit Stellenbosch se Fakulteit Gesondheidswetenskappe

Die Neuropsigiatrie en Neurosielkunde van Lipoïed-Proteïnose

Verklaring deur Pasiënt/Kontrole

Ek, die ondergetekende……..……(ID)……...

van adres…….....……

A. verklaar hiermee soos volg:

Die Departement Psigiatrie van die Universiteit Stellenbosch het my of my kind genooi om aan die bogenoemde projek deel te neem.

Dit is aan my verduidelik dat psigometriese (papier-en-pen en rekenaar-) toetse op my of my kind uitgevoer sal word. ’n Ander persoon wat daaglikse kontak met my het (soos ’n familielid of ander versorger) sal gevra word om vrae oor my / my kind se geheue, gevoelens en gedrag te beantwoord. Indien ek na Kaapstad kom, verstaan ek dat dit vir drie tot vyf dae sal wees.

Indien ek / my kind na die Mediese Skool van die Universiteit Stellenbosch kom, sal ek deur ’n dokter ondersoek word, en bloed- en urienmonsters kan moontlik geneem word. My bloed sal vir die LP-geen ondersoek word, en ek mag my LP-status weet as ek wil. Ek kan moontlik navorsing- en slaap-EEG’s ondergaan en moontlik deur middel van ’n video-opname gemonitor word. My hart- en velreaksies sal ook gemeet word. Indien ek breinskanderings ondergaan, sal ek met toe oë in ’n donker kamer lê. ’n Dokter sal my dan inspuit met medikasie wat die masjien sal help om ’n foto van my brein te neem. Hierdie medikasie bevat effense radioaktiwiteit soos wanneer ’n X-straal geneem word. ’n Dokter sal seker maak dat dit vir my veilig is om MRI- of fMRI-breinskanderings te ondergaan. In hierdie geval sal ek in ’n raserige masjien lê en kan gevra word om vrae te beantwoord of stil te lê.

Hierdie toetse sal nie my / my kind se behandeling op enige manier beïnvloed nie. Ek is in kennis gestel dat ek mag weier om aan hierdie projek deel te neem en dat weiering nie my huidige of toekomstige behandeling by hierdie instansie sal beïnvloed nie. Deelname aan hierdie projek sal geen koste vir my inhou nie. Deelname aan hierdie projek hou geen spesiale voordeel of nadeel in nie.

Ek is in kennis gestel dat alle inligting as vertroulik hanteer sal word, maar in ’n mediese vaktydskrif gepubliseer sal word. My naam sal nie in die publikasie verskyn nie, en dit sal nie moontlik wees om my in hierdie publikasie te identifiseer nie. Hoewel die resultate in ’n later stadium bereken sal word, sal ek toegang tot al my / my kind se kliniese resultate hê as ek sou wou.

Die inligting hierbo is in Afrikaans aan my verduidelik. Ek / my kind is nie gedwing om aan hierdie projek deel te neem nie en ek kan enige tyd my deelname sonder enige nagevolge beëindig.

B Ek gee hiermee my vrywillige toestemming dat ek / my kind aan die bogenoemde projek deelneem.

Geteken te……op ……20……

Pasiënt / Voog se Handtekening:_____

Getuie:_____

Verklaring deur/namens Navorser

Ek, _____, verklaar dat ek

die inligting vervat in hierdie dokument verduidelik het aan_____;

hom / haar versoek het om vrae aan my te vra sodat enige onduidelikhede opgeklaar kan word; en

hierdie gesprek in Afrikaans gevoer het.

Geteken te: _____ op _____20____

Navorser/Verteenwoordiger:_____

Getuie: _____

Appendix B

English and Afrikaans Letters to the Headmaster regarding the Completion of the C-TRF and TRF

9D Sandown Road
Blouberg Sands
7441
Tel. (021) 554 0081
Fax 086 716 1521

August 2008

The headmaster

_____

Dear Sir/Madam

Re:
_____

I am currently completing a PhD study in Child Psychology at the University of the Free State. The title of the study is "The neuropsychological and psychosocial development of children and adolescents with Lipoid Proteinosis." I have already obtained permission from the parents of all the children and adolescents with this genetic illness, as well as a group of "normal" children to include them in the study. I now need an indication of all these children's functioning in school to form a complete picture of their development.

I would appreciate it if the class teacher of the above-mentioned learner could complete the included behaviour checklist with regard to his / her behaviour. The checklist is called the Teacher's Report Form, and will take approximately ten to fifteen minutes to complete. The instructions are written clearly on the checklist. Once finished, please place the checklist back in the envelope provided so that I can collect it from school or fax it.

All parents or guardians signed this letter to give permission with regard to participation in this project and for you to be able to provide this information to me.

Thank you very much for you cooperation. Please do not hesitate to call if anything is unclear. I trust I can be of service to you in return.

Erika Steenberg
Clinical Psychologist

I,_____, hereby give permission to the

teacher of my child, _____, to complete a behaviour checklist and to make this information available to Erika Steenberg as part of the above-mentioned research project.

Parent's Signature_____

9D Sandown Road
Blouberg Sands
7441
Tel. (021) 554 0081
Fax 086 716 1521

Augustus 2008

Die hoof

_____

Geagte Mnr / Mev

Aangaande:_____
_

Ek is tans besig met 'n PhD studie in Kindersielkunde aan die Universiteit van die Vrystaat. Die titel van die studie is: “The neuropsychological and psychosocial development of children and adolescents with Lipoid Proteinosis.” Ek het reeds toestemming gekry van al die ouers van die kinders en adolessente met hierdie genetiese siekte, sowel as 'n groep “normale” kinders, sodat hulle in my navorsing ingesluit kan word. As deel van my studie wil ek graag verstaan hoe hierdie kinders in die skool aanpas.

Ek sal dit waardeer as die klasonderwyser / onderwyseres die aangehegte gedragsvraelsy kan invul. The gedragsvraelys word *Die Onderwyser Verslagvorm* genoem en sal ongeveer 10-15 minute neem om te voltooi. Die instruksies word duidelik op die vraelys beskryf.

Alle ouers of voogde het hierdie brief onderteken om toestemming te gee dat informasie omtrent hul kinders se gedrag en prestasie by die skool aan my bekend gemaak kan word. Wanneer die vraelys voltooi is, plaas dit asseblief terug in die koevert sodat ek dit by die skool kan afhaal, of faks dit na die bogenoemde faksnommer.

Baie dankie vir u samewerking. Skakel gerus as enigiets onduidelik is. Ek hoop ek kan u ook in die toekoms van diens wees.

Erika Steenberg
Clinical Psychologist

Ek,_____, gee hiermee toestemming dat my kind, _____ , se onderwyser / onderwyseres die gedragsvraelys voltooi en informasie omtrent my kind aan Erika Steenberg as deel van die bogenoemde navorsingsprojek bekend maak.

Ouer / voog se handtekening_____

Appendix C

Afrikaans Translation of Structured Developmental History Form

Gestruktureerde Ontwikkelingsgeskiedenis(SDH)

BASC-2

Gedragsassesseringsisteem vir Kinders, Tweede Uitgawe

Cecil R. Reynolds, PhD, en Randy W. Kamphaus, PhD

Voltooiingsformaat:	Vraelys ☐	Onderhoud ☐	
Naam van Onderhoudvoerder/Kliënt:			Datum:
Naam van Kind			Geslag: F ☐ M ☐
Adres:			Telefoon:
			Geboortedatum:
Skool:			Ouderdom:
Onderwyser			Graad:
Wat is die kind se primêre taal?			Is hierdie verwysing verwant aan enige tipe regs- of hofprosedure? Ja/Nee
Wat is die kind se sekondêre taal?			

Aanwysings: Voltooi asseblief al die vrae na die beste van u vermoë, selfs al kom dit voor asof sommige vrae nie van toepassing is nie. Indien u 'n item nie verstaan nie, vra asseblief die persoon by wie u die vraelys gekry het om u te help.

NOTAS:

PERSOON WAT VRAE BEANTWOORD

Naam:	
Verwantskap aan die kind:	
Adres:	
Huistelefoon:	Werktelefoon:

VERWYSINGSINFORMASIE

Waarom soek u hulp vir hierdie kind?
Wie het u na ons diens verwys?
Watter tipe diens verwag u vir die kind (byvoorbeeld, skoolverandering, skoolplasing, terapie, sielkundige toetsing, evaluering vir voogskap, ens.)?

OUERS		NOTAS:
Naam van moeder:	Stiefmoeder? Ja/Nee	
Adres:	Ouderdom:	
Huistelefoon:	Werktelefoon:	
Beroep:	Werkgewer:	
Hoe lank werk u by u huidige werkgewer?	Hoogste graadkwalifikasie voltooi:	
Primêre Taal:	Sekondêre Taal:	
Naam van Vader:	Stiefvader? Ja/Nee	
Adres	Ouderdom	
Huistelefoon	Werktelefoon	
Beroep	Werkgewer	
Hoe lank is u al by die huidige werkgewer?	Hoogste kwalifikasie voltooi?	
Primêre Taal	Sekondêre Taal	
Het hierdie kind ander /'n ander ouer(s)/stiefouer(s)? Ja/Nee		
Indien wel, verskaf asseblief die volgende inligting:		
Naam	Ouderdom	
Verwantskap aan kind	Huistelefoon	
Adres		
Naam	Ouderdom	
Verwantskap aan die kind	Huistelefoon	
Adres		
PRIMÊRE VERSORGERS		
By watter ouer(s) bly die kind?		
Hoe lank is die kind in die huidige situasie?		
Verskaf asseblief die volgende inligting rakende die kind se primêre versorgers, indien u dit nie voorheen gegee het nie.		
Naam	Verwantskap aan Kind	
Adres	Ouderdom	
Huistelefoon	Werktelefoon	
Beroep	Werkgewer	
Hoe lank by huidige werkgewer?	Hoogste graad voltooi	
Primêre Taal	Sekondêre Taal	
Naam	Verwantskap aan kind	
Address	Ouderdom	
Huistelefoon	Werktelefoon	
Beroep	Werkgewer	
Hoe lank by huidige werkgewer?	Hoogste graad voltooi	
Primêre Taal	Sekondêre Taal	

KINDERVERSORGING	NOTAS:
Indien die primêre versorgers uithuisig werk, voorsien asseblief die volgende inligting:	
Wie versorg hierdie kind indien die versorgers weg is?	
Hoeveel uur per dag is hierdie kind in 'n kinderversorgings opset?	
Hoeveel verskillende mense sorg vir die kind?	

FAMILIEGESKIEDENIS
Is hierdie kind nader aan een van die twee ouers? Ja/Nee Indien ja, watter ouer?
Het hierdie kind al ooit enige skeiding, egskeiding of dood van die ouers ervaar? Ja/Nee Indien ja, wanneer?
Hoe oud was die kind op daardie stadium?
Beskryf asseblief die omstandighede
Indien ouers vervreem of geskei is, wie het toesig oor die kind?
Hoe dikwels sien die ander ouer hierdie kind? (merk een) Weekliks of Meer Gereeld ☐ Een of tweemaal per maand ☐ 'n Paar keer per jaar ☐ Nooit ☐

BROERS/SUSTERS			
Maak asseblief 'n lys van al die broers en susters, asook enige ander kinders wat saam met die gesin bly.			
Ouderdom	Geslag	Verhouding met hierdie kind	Bly by die huis?
Hoe kom hierdie kind oor die weg met ander broer(s) en/of suster(s)?			

BLYPLEK VAN KIND (kies een)			
Woonstel ☐	Enkelhuis ☐	Ander ☐	Hoe lank by die huidige adres?

GESINSVERHOUDINGE				NOTAS:
Merk die aktiwiteite waaraan die kind saam met die gesin deelneem:				
Flieks	Etes	Gesprekke	Kuier by familie	Kerk
Speletjies	Sport	Uitstappies	Televisie	Ander
Taal wat in die huis gepraat word				
Hoe gereeld sien hierdie kind die grootouers? (*merk een*)				
Weeksliks of Meer gereeld	Een of Twee maal per Maand	'n Paar Keer per Jaar		
Nooit	Geen van die grootouers leef meer nie.			
Wat geniet u die meeste van hierdie kind?				
Wat vind u die moeilikste omtrent die opvoeding van hierdie kind?				
Wat sal u graag wil hê moet hierdie kind wees wanneer hy/sy groot is?				
Watter vlak van onderwys hoop u dat hierdie kind sal voltooi? (*merk een*)				
Hoërskool	Technikon of handelskool	Kollege	Regte, Medies, Ander gevorderde studies	
Wie is hoofsaaklik in beheer van dissipline by die huis?				
Stem al die versorgers ooreen ten opsigte van dissipline?				
Beskryf dissiplinetegnieke				
SWANGERSKAP				
Was hierdie kind 'n beplande swangerskap Ja/Nee				
Was die moeder onder versorging van die dokter Ja/Nee				
Hoeveelheid Vorige Swangerskappe/Misgeboortes				
Merk enige van die volgende komplikasies wat plaasgevind het gedurende die swangerskap				
Probleme met konsepsie	Vergiftiging	Abnormale hoeveelheid Gewig Opgetel		
Masels	Oormatige Braking	Duitse Masels		
Oormatige Opswelling	Emosionele Probleme	Vaginale Bloeding		
Verkoue	Griep	Hoë Bloeddruk		
Ander (Rh pasbaarheid, ens.):				
Beserings van Moeder: Beskryf:				
Hospitalisasie Gedurende Swangerskap: Rede				
X-Strale Gedurende Swangerskap: Watter maand?				
Drank Gebruik Gedurende Swangerskap: Hoe gereeld?				
Sigarette Gebruik Gedurende Swangerskap: Hoe gereeld?				

Ander Middels of Medikasie Gebruik Gedurende Swangerskap?			
Tipe	Hoe gereeld?	Voorskrif	
		Nee	Ja
		Nee	Ja
		Nee	Ja

NOTAS:

GEBOORTE

Hoe oud was die moeder met hierdie kind se geboorte?
Ouderdom van Vader?

Moeder se ouderdom met die geboorte van eerste kind?

Is hierdie kind in 'n hospitaal gebore? Ja/Nee
Indien nie, waar?

Lengte van die Swangerskap: weke	Geboortegewig: kg
Lengte van Kraam:	Apgartelling:

Kind se Toestand Tydens Geboorte:

Moeders se Toestand tydens Geboorte:

Merk indien enige van die volgende kondisies tydens geboorte aanwesig was:

☐ Tang Gebruik	☐ Bruggeboorte	☐ Induksie	☐ Keisersnee

☐ Ander geboortekomplikasies: Beskryf

☐ Broeikas: Hoe lank?

☐ Geelsug: Bilirubin ligte? Ja/Nee
Indien Ja, Hoe lank?

☐ Asemhalingsprobleme net na Geboorte: Beskryf

☐ Suurstofaanvulling Ja/Nee
Indien ja, hoe lank?

Is narkose gegee gedurende die geboorte? Ja/Nee
Indien ja, watter tipe?

Lengte van verblyf in hospitaal: Moeder_____dae Kind: _____dae

ONTWIKKELING

Op watter ouderdom het hierdie kind die volgende gedoen? Dui asseblief die ouderdom in jare/maande aan.

	Rol om		Loop met trappe af
	Sit alleen		Toon belangstelling in/ aangetrokkenheid tot klank
	Kruip		Verstaan eerste woorde
	Staan alleen		Sê eerste woorde
	Loop alleen		Praat in sinne
	Loop met trappe op		

Is hierdie kind geborsvoed? Ja/Nee Wanneer gespeen?

Het hierdie kind bottel gedrink? Ja/Nee Wanneer opgehou met bottel?

Wanneer was hierdie kind van die doeke af? Dae:_____
Nagte:_____

Het die kind bed natgemaak nadat hy/sy van die doeke af is? Ja/Nee Indien ja, tot op watter ouderdom?

Het hierdie kind sy bed vuilgemaak nadat hy/sy van die doeke af is? Ja/Nee
Indien ja, tot op watter ouderdom?

Was daar enige mediese redes vir bed natmaak of vuilmaak? Ja/Nee Indien ja, beskryf asseblief.		NOTAS:
Het hierdie kind enige van die volgende probleme ondervind? Indien wel, beskryf:		
Loopprobleme Ja/Nee		
Onduidelike Spraak Ja/Nee		
Voedingsprobleme Ja/Nee		
Ondergewigprobleem Ja/Nee		
Oorgewigprobleem Ja/Nee		
Koliek Ja/Nee		
Slaapprobleem Ja/Nee		
Eetprobleem Ja/Nee		
Probleem om te Leer fietsry Ja/Nee		
Probleem om te Leer Spring Ja/Nee		
Probleem om te Leer Vang of Gooi Ja/Nee		
Is enige van die volgende spesifieke probleme opgemerk tydens die eerste vier jaar van hierdie kind se lewe? Indien wel, beskryf asseblief.		
Eet te min of te veel Ja/Nee		
Motoriese Vaardighede Ja/Nee		
Te veel Slaap Ja/Nee		
Woede-uitbarstings (Tantrums) Ja/Nee		
Te min Slaap Ja/Nee		
Groei nie (Failure to Thrive) Ja/Nee		
Skeidingsangs (Skeiding van Ouers) Ja/Nee		
Oormatige Huil Ja/Nee		
Watter hand gebruik hierdie kind om te skryf of teken?		
Eet?	Ander (gooi ens.)?	
Is hierdie kind geforseer om handvoorkeur te verander? Ja/Nee		
MEDIESE GESKIEDENIS		
Kindersiektes/Beserings		
Merk asseblief siektes wat hierdie kind gehad het en dui die ouderdom aan (jaar/maand)		
Masels	Rumatiekkoors	
Duitse masels	Difterie	
Pampoentjies	Meningitis	
Waterpokkies	Enkefalitis	
Tuberkulose	Anemie	
Kinkhoes	Koors bo 104°	
Skarlakenkoors	Gebreekte bene	
Hoofbesering: Beskryf		
Koma of enige bewussynsverlies: Beskryf		
Volgehoue hoë koors: Beskryf		
Beskryf asseblief ander ernstige siektes en operasies:		
Siekte/Operasie	Ouderdom	
Was hierdie kind ooit op enige medikasie vir 6 maande of langer? Ja/Nee Indien ja, wanneer? Watter soort?		

Dui asseblief aan of hierdie kind tans enige van die volgende probleme ondervind. Indien wel, beskryf hoe gereeld.			NOTAS:
Asemhaling			
Gereelde verkoue	Ja/Nee		
Kroniese hoes	Ja/Nee		
Asma	Ja/Nee		
Hooikoors	Ja/Nee		
Sinuskondisie	Ja/Nee		
Kardiovaskulêre probleme			
Kortasem of Duiseligheid tydens Fisiese Oefening	Ja/Nee		
Beperking van Aktiwiteit as gevolg van Hartkondisie	Ja/Nee		
Hartgeruis	Ja/Nee		
Gastro-intestinale probleme			
Oormatige braking	Ja/Nee		
Gereelde diaree	Ja/Nee		
Hardlywigheid	Ja/Nee		
Maagpyn	Ja/Nee		
Genito-urinêre stelsel			
Urinering in broek/bed	Ja/Nee		
Pyn gedurende urinering	Ja/Nee		
Oormatige urinering	Ja/Nee		
Sterk reuk van urine	Ja/Nee		
Spier- of Skeletstelsel			
Spierpyn	Ja/Nee	*Wanneer?* *Waar?*	
Loop lomp?	Ja/Nee		
Swak postuur	Ja/Nee		
Ander spierprobleme	Ja/Nee	*Indien ja, beskryf*	
Vel			
Gereelde uitslag	Ja/Nee		
Kneus maklik	Ja/Nee		
Sere	Ja/Nee	*Indien ja, beskryf*	
Erge aknee	Ja/Nee		
Jeukerige vel	Ja/Nee		
Neurologiese probleme			
Epileptiese aanvalle/konvulsies	Ja/Nee		
Spraakdefekte	Ja/Nee		
Geneig tot ongelukke	Ja/Nee		
Byt naels	Ja/Nee		
Duimsuig	Ja/Nee		
Kners op tande	Ja/Nee		
Het spiertrekkings	Ja/Nee		
Stamp kop	Ja/Nee		
Wieg vorentoe en agtertoe	Ja/Nee		
Opelyf in broek/bed	Ja/Nee		

Het hierdie kind al ooit medikasie gebruik om aktiwiteit te verhoog? Ja/Nee			NOTAS:
Indien wel, wanneer?	Watter medikasie?		
Het hierdie kind al ooit sederende medikasie gebruik? Ja/Nee			
Indien wel, wanneer?	Watter medikasie?		
Het hierdie kind al ooit medikasie vir ADD, ADHD, of soortgelyke probleme geneem? Ja/Nee			
Indien wel, wanneer?	Watter medikasie?		
Allergieë			
Allergies vir medikasie	Ja/Nee	Indien ja, beskryf	
Allergies vir voedsel	Ja/Nee	Indien ja, beskryf	
Ander allergieë	Ja/Nee	Indien ja, beskryf	
Spraak			
Hakkel	Ja/Nee		
Onduidelike spraak	Ja/Nee		
Ander spraakprobleme	Ja/Nee		
Datum van mees onlangse spraakevaluering:			
Gehoor			
Oorontsteking	Ja/Nee		
Gehoorprobleme	Ja/Nee		
Oorbuisies	Ja/Nee		
Datum van mees onlangse gehoorevaluering			
Visie			
Visieprobleme	Ja/Nee		
Dra bril of kontaklense	Ja/Nee		
Datum van mees onlangse oogtoets			
Mediese sorg			
Kind se Mediese Dokter		Telefoon	
Hoe gereeld sien hierdie kind 'n dokter?		Datum van laaste besoek	
Is hierdie kind tans op medikasie?		Ja/Nee	
	Indien ja, noem asseblief die tipe en rede		
Is hierdie kind ooit fisies of seksueel mishandel? Ja/Nee			
	Indien ja, bespreek asseblief die aangeleentheid met die persoon by wie u hierdie vorm gekry het.		
Het hierdie kind ooit sielkundige berading of terapie ontvang? Ja/Nee			
	Indien ja, naam van die sielkundige/berader		
	Adres		
	Telefoon		
	Tipe berading		
	Wanneer?		
Is hierdie kind ooit neurologies geëvalueer? Ja/Nee			
Indien ja, naam van neuroloog			
	Stad	Datum van evaluasie	
	Rede vir neurologiese ondersoek		
Is hierdie kind ooit sielkundig of psigiatries geëvalueer? Ja/Nee			
	Indien ja, naam van dokter		
	Stad	Datum van evaluasie	
	Rede vir evaluasie		

FAMILIEGESONDHEID		NOTAS:
Het enige familielede enige van die volgende siektetoestande of gedrag? Indien ja, spesifiseer asseblief die familielid se verwantskap aan hierdie kind. Indien die kind nie by biologiese ouers bly nie, sluit asseblief inligting rakende die biologiese ouers se gesondheid in, indien bekend.		
☐ Kanker	☐ Hoë bloeddruk	
☐ Sistiese fibrose	☐ Niersiekte	
☐ Diabetes	☐ Migraine hoofpyne	
☐ Hartsiekte	☐ Veelvuldige sklerose	
☐ Fisiese gestremdheid	☐ Alkohol/dwelmmisbruik	
☐ Beroerte	☐ Gedragsversteuring	
☐ Tuberkulose	☐ Emosionele versteuring	
☐ Alzheimer se siekte	☐ Geestessiekte	
☐ Hemofilie	☐ Verstandelike vertraging	
☐ Huntington se siekte	☐ Senuagtigheid	
☐ Spierdistrofie	☐ Konvulsies of epilepsie	
☐ Parkinson se siekte	☐ Leesprobleem	
☐ Sekelsel-anemie	☐ Ander leergestremdhede	
☐ Tay-Sachs-siekte	☐ Spraak- en taalprobleem	
☐ Tourette-sindroom	☐ Voedselallergieë	
☐ Geboortedefek	☐ Erge hoofbesering	
☐ Serebrale verlamming	☐ Lipoïed- proteïnose	
	☐ Ander: Beskryf	
Bekryf vader se huidige gesondheid		
Beskryf moeder se huidige gesondheid		
Was enige een in die familie ooit in spesiale onderwys? Ja/Nee		
Indien ja, wie?		
Watter tipe spesiale klas?		
VRIENDSKAPPE		
Het probleme om met ander kinders oor die weg te kom of te speel Ja/Nee		
Indien ja, beskryf		
Baklei gereeld met Speelmaats Ja/Nee		
Verkies om met Jonger Kinders te Speel Ja/Nee		
Vind dit Moeilik om Vriende te Maak Ja/Nee		
Verkies om Alleen te Speel Ja/Nee		
Is daar kinders in die buurt met wie hierdie kind kan speel? Ja/Nee		
Watter rol speel hierdie kind in sy/haar ouderdomsgroep se speletjies (byvoorbeeld, leier, volgeling, ens.)?		
Noem asseblief of enige van hierdie kind se vriende betrokke is by enige van die volgende gedrag		
Sigaretrook Ja/Nee	Kou Tabak Ja/Nee	
Snuif Giftige Middels (bv. verf) Ja/Nee	Drink bier, wyn of alkohol Ja/Nee	
Gebruik Onwettige Dwelms (bv. marijuana, kokaïene) Ja/Nee		

ONTSPANNING/BELANGSTELLINGS		NOTAS:
Watter aktiwiteite geniet hierdie kind?		
	Sport:	
	Stokpertjies:	
	Ander:	
Het hierdie kind se belangstelling in spesifieke aktiwiteite onlangs afgeneem? Ja/Nee		
	Indien ja, beskryf	
GEDRAG/TEMPERAMENT		
Dui asseblief aan of hierdie kind enige van die volgende gedrag toon:		
Word maklik oorgestimuleer tydens spel Ja/Nee	Kom buitengewoon energiek voor gedurende spel Ja/Nee	
Het 'n kort aandagspan Ja/Nee	Kom impulsief voor Ja/Nee	
Gebrek aan selfbeheersing Ja/Nee	Oorreageer wanneer gekonfronteer met 'n probleem Ja/Nee	
Kom meeste van die tyd ongelukkig voor Ja/Nee	Kom ongemaklik voor wanneer hy/sy nuwe mense ontmoet. Ja/Nee	
Wys nie emosie en aangetrokkenheid nie Ja/Nee	Vereis baie aandag van die ouer Ja/Nee	
Steek gevoelens weg Ja/Nee	Kan nie kalmeer nie Ja/Nee	
Het vrese Ja/Nee		
	Indien ja, beskryf	
Wat maak hierdie kind kwaad?		
ONDERWYSGESKIEDENIS		
Voorskool en Dagsorg		
Woon hierdie kind tans voorskool/dagsorg by of het hierdie kind voorheen voorskool/dagsorg bygewoon? Ja/Nee		
	Op watter ouderdomme?	
	Hoeveelheid Tyd per Dag	
	Dae per Week	
	Enige probleme by die voorskool? Ja/Nee	
	Indien ja, beskryf	
Woon hierdie kind kleuterskool by/ het hierdie kind kleuterskool bygewoon? Ja/Nee		
	Enige probleme by die kleuterskool? Ja/Nee	
	Indien ja, beskryf	
Laer/Hoërskool		
Toon asseblief aan of hierdie kind enige van die volgende skoolervarings het/gehad het:		
Het van skool verander vir ander rede as normale akademiese vooruitgang? Ja/Nee		
	Indien ja, wanneer en waarom?	
Is teruggehou tydens 'n graad op skool? Ja/Nee		
	Indien ja, wanneer en waarom?	

Het 'n graad op skool oorgeslaan Ja/Nee		NOTAS:
	Indien ja, wanneer en waarom?	
Het leesprobleme? Ja/Nee		
	Indien ja, beskryf	
Het probleme met Wiskunde Ja/Nee		
	Indien ja, beskryf	
Kry swak punte Ja/Nee		
	Beskryf mees onlangse rapportuitslae	
Is getoets vir spesiale onderwys Ja/Nee		
	Indien ja, wanneer?	
Is tans in spesiale-onderwysklas geplaas Ja/Nee		
	Indien ja, watter tipe klas?	
	Ure per dag	
Hou nie daarvan om skool toe te gaan nie? Ja/Nee		
Is gereeld afwesig van skool Ja/Nee		
	Indien ja, waarom?	
Indien op hoërskool, wanneer sal hierdie kind matrikuleer?		
Het u enige bekommernis oor die kwaliteit van hierdie kind se skool of onderwysers? Ja/Nee		
	Indien ja, beskryf	
ADDISIONELE OPMERKINGS		

Appendix D

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The University of Vermont
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Research Center for Children, Youth & Families, INC.
A Non-Profit Corporation
1 South Prospect Street, St Joseph's Wing (Room #3207), Burlington, VT 05401
Telephone: (802)656-5130 / Fax: (802)656-5131
Email: mail@aseba.org / Website: http://www.aseba.org

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LICENSOR:
Thomas M. Achenbach, Ph.D.

Signature: Thomas M Achenbach

Title: Professor

Date: January 10, 2008

For License # 266-1-7-08

Accepted and Agreed to:

LICENSEE:
Erika Steenberg

Signature: Steenberg

Print name: Erika Steenberg

Title: Ms.

Address: 9 Mast Mews Blouberg sands, 7441, South-Africa

Date: 9 January 2008