THE USE OF NEUROPSYCHOLOGICAL ASSESSMENT IN THE DIAGNOSIS OF CEREBRAL LESIONS

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This thesis is submitted to fulfil the requirements of the degree M.Soc.Sc. (Psychology) in the Faculty of Social Sciences, Department of Psychology, University of the Free State. It is submitted in the form of two articles as permitted in the regulations of this institution.

As in the general situation where two articles is written by the same author, there inevitably will be overlapping. In this case the overlapping was mainly restricted to the method as the same instruments, participants and statistical methods were used.

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I declare that the thesis hereby submitted by me for the M.Soc.Sc. (Psychology) degree at the University of the Free State is my own independent work and has not previously been submitted by me at another university/faculty.

For Dan.

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NEUROPSYCHOLOGICAL ASSESSMENT VERSUS NEURO-IMAGING IN THE DIAGNOSIS OF CEREBRAL LESIONS: AN EXPLORATIVE STUDY

ABSTRACT

Certain authors emphasise that, as neuro-imaging techniques seem to be significantly superior, psychological assessment techniques have no place in neurological assessment, and that the reliability and validity of these techniques, regarding the presence and localisation of cerebral damage, are questionable. The purpose of the study was to determine the relative effectiveness of neuropsychological assessment in the diagnosis and localisation of cerebral lesions, compared to magnetic resonance imaging (MRI). An availability sample of patients was taken from patients whom neurologists and neurosurgeons had seen and who had either a normal MRI or a MRI with localised lesions. They were then assessed by means of the South African Wechsler Adult Intelligence Scale, the Folstein's Mini Mental State Examination, the Bender Gestalt Test, and the Grassi Block Substitution Test. The test results were interpreted blindly. The findings are discussed, shortcomings of the study mentioned and recommendations made.

Neuropsychology; neuro-imaging; cerebral lesions; diagnosis; presence; lesion localization; South African Wechsler Intelligence Scale; Folstein's Mini Mental State Examination; Bender Gestalt Test; Grassi Block Substitution Test.

SAMEVATTING

Sekere outeurs beklemtoon die superioriteit van radiologiese beeldingstegnieke bo dié van sielkundige toetse in die neurologiese evaluasie van pasiënte. Die betroubaarheid en geldigheid van sielkundige toetse rakende die diagnosering en lokalisering van breinskade word ook bevraagteken. Die doel van hierdie verkennende studie was om die effektiwiteit van neurosielkundige assessering in die diagnose en lokalisering van breinletsels met dié van die MR te vergelyk. 'n

Beskikbaarheidsteekproef is getrek van pasiënte met óf 'n normale MR óf 'n MR wat dui op gelokaliseerde breinletsels. Die proefpersone is evalueer met die Suid-Afrikaanse Wechsler Intelligensieskaal vir Volwassenes, die Folstein Mini Mental State Examination, die Bender Gestalttoets en die Grassi Blokvervangingstoets. Die toetsresultate is blind geïnterpreteer. Die bevindinge word bespreek, tekortkominge van die studie word aangetoon en aanbevelings word gemaak.

Neurosielkunde; neurologiese beelding; breinletsels; diagnose; teenwoordigheid; letsel lokalisering; Suid-Afrikaanse Wechsler Intelligensie Skaal; Folstein Mini Mental State Examination; Bender Gestalttoets; Grassi Blokvervangingstoets.

INTRODUCTION

Prior to the 1970s, the only way for medical and psychological clinicians to localise brain lesions was by combining their knowledge of anatomy and pathology by means of clinical examinations and results obtained by means of neuropsychological testing. However, with the development of neuro-imaging techniques such as computerised axial tomography (CT or CAT) and magnetic resonance imaging (MR or MRI), the situation changed dramatically. These techniques have made it possible to obtain clear images of not only specific brain structures, but also their functioning, for example positron emission tomography (PET) and single photon emission computed tomography (SPECT). The specific applicability and even necessity of neuropsychological tests have therefore become debatable. In this regard Plug[1] states that "the question is not whether testing is perfect (which it obviously is not), but rather how it compares to alternative techniques of assessment and whether, when used in combination with other processes, it leads to a more reliable, valid, fair and cost effective result".

As there has been no agreement on what constitutes an injury sufficient enough to affect the brain, it has proved difficult to obtain reliable estimates of the frequency of closed-head injuries. However, according to Casson et al.,[2] Kolb and Whishaw,[3] Lishman[4] and Vanderploeg,[5] cerebral trauma is the most common form of brain damage in people under the age of 40, ranging from about 300-450 per 100 000 of the population per year in industrialised countries.

Certain authors emphasise that, as neuro-imaging techniques seem to be significantly superior, psychological assessment techniques have no place in neurological assessment, and that the reliability and validity of these techniques regarding presence and localisation of cerebral damage are questionable.[4] For example, the ability of the CAT scan to detect variations in soft-tissue density is significantly higher than that of any psychological test, while the reliability of several neuropsychological tests leaves much to be desired.[6 7] In this context the testimony of neuropsychologists in insurance claims have been ruled inadmissible in certain cases (e.g. Turkington[8]). The basis of this ruling was that, without using medical methods, a psychologist could not provide an expert evaluation in cases where brain damage is suspected.

However, authors such as Murphy and Davidshofer[9] hold the view that, although neuropsychological assessment cannot replace medical techniques of assessing brain damage, such tests should not be totally discarded. "Psychological tests are less risky, less invasive, and often more cost-effective than medical tests. The optimal use of medical and non-medical techniques in diagnosing brain damage has yet to be determined" (p. 415).

Against this background, the purpose of the study was to determine the relative effectiveness of neuropsychological assessment and neuro-imaging. More specifically, to determine:

1. the agreement between the diagnosis of cerebral lesions with the MRI and the diagnosis of cerebral lesions by means of neuropsychological assessment;
2. the agreement in localisation of cerebral lesions between MRI and neuropsychological assessment; and
3. the correlation of different subscales of the psychometric tests with the MRI diagnosis.

The results will hopefully indicate to what extent neuropsychological tests still have a function in determining the nature and localisation of cerebral injuries. Such a study is especially important in the South African context where almost no research has been done in this regard.

UNDERSTANDING OF THE BRAIN THOUGH THE AGES

Evidence shows that people have long been aware of brain-behaviour relationships:[10 11] Archaeologists have retrieved thousands of skulls with evidence of having undergone trephination - an ancient surgical operation to relieve pressure related to brain edema after trauma. Classical Greeks wrote the first accounts of brain-behaviour relationships. Pythagoras (580-500 B.C.) described the so-called brain hypothesis, namely that the brain is the source of all reasoning and behaviour. Hippocrates (460-377 B.C.), the father of modern medicine, was the first to recognise that paralysis occurs contra-lateral to the side of brain injury. In ancient Egypt, what is known as the "ventricular localisation hypothesis" or "cell doctrine" was developed. This was an erroneous suggestion that the ventricles contain spirits responsible for mental faculties and movement. This notion endured for almost 2000 years. Galen (A.D. 130-201), a Roman anatomist and physician, believed that all physical functions depend on the balance of bodily fluids or humours, specifically blood, mucus, and yellow and black bile. He suggested that the brain is a large clot of phlegm from which a pump forces the psychic pneuma out into the nerves. Vesalius (1514-1564), through the first systematic dissections of human beings in Europe, demonstrated that Galen's views were inaccurate. By the 17th century, René Descartes (1596-1650) hypothesised that the mind and body are separate, but interact with each other. He believed that mental processes are localised in the pineal gland. Giovanni Lancisi (1654-1720) viewed the corpus callosum as the seat of mental functions. Beaumont[12] mentioned that early investigators were preoccupied with identifying the specific part of the brain that was the seat of the mind, but that their discussions were based primarily on speculation and that they had conducted relatively little experimentation.

The first global theory concerning brain functioning was the phrenological theory of Gall and Spurzheim. In the 19th century Gall (1758-1828) postulated that the brain consists of a number of different areas, each responsible for different psychological attributes. By assigning specific functions to certain areas in the cerebral cortex, the localisation theory of brain function was born. Scientific evidence supporting this localisation theory was first provided by Broca's (1824-1880) studies on aphasia. He proved that the motor area for speech was located in the postero-inferior region of the left frontal lobe. A few years later Wernicke (1848-1904) followed by proving that the area for understanding speech is located in the postero-superior area of the temporal lobe. Flourens (1794-1867) was one of the first researchers to suggest an alternative to the localisation theory. He viewed all cerebral matter as being equipotential, that is, if sufficient cortical matter remains intact, it will take over the functions of any lost brain tissue. According to the equipotential theory, sensory input may be localised, but perception involves the whole brain. The effects of brain lesions thus do not depend on their location, but on their extent.[7]

By means of various experiments with dogs, Goltz (1834-1902) proved that decortication does not eliminate any function, though it seems to reduce all functions to some extent. This was a strong argument against the localisation of function.[3] Jackson (1835-1911) suggested a third alternative. He believed that behaviour results from interactions among all the areas of the brain and that certain areas are therefore not uniquely associated with specific functions. This is known as the hierarchical organisation concept of brain function or the interactionist theory, according to which each successively higher level controls more complex aspects of behaviour, but does so through the lower levels.[13]

Luria integrated these previous theories (1902-1977) in his theory of pluripotentiality, which states that any given area in the brain can be involved in relatively few or relatively many behaviours. Luria's hypothesis is particularly attractive to clinical neuropsychologists, because it can account theoretically for most observations of brain-injured patients. The theory also explains the observation that certain lesions generally result in consistent deficits. In addition, through the concept of reorganisation, Luria's theory can account for individuals who recover from brain trauma. Finally, the theory suggests ways of establishing rehabilitation and treatment programmes for the brain-injured patient and provides a strong theoretical basis for understanding clinical neuropsychology.[7]

NEUROPSYCHOLOGICAL ASSESSMENT

Psychological testing developed from two important lines of enquiry, namely the measurement of individual differences (based on the work of Darwin, Galton and Cattell) and psychophysics (based on the work of Herbart, Weber, Fechner and Wundt). An important breakthrough regarding the creation of modern tests arrived at the beginning of the 20th century when the French started to study ways of identifying intellectually subnormal individuals in order to provide them with special education. The first intelligence test, known as the Binet-Simon Scale, followed in 1905. With the onset of World War I, the testing movement grew enormously and group tests and standardised achievement tests were developed. In 1916 the well-known Afrikaans poet and author, C. Louis Leipoldt, played a key roll in the standardisation of South Africa's first intelligence test, based on the

Binet-Simon Scale, commonly known as the Moll-Leipoldt Scale.[14] During 1920 to 1940 personality tests began to blossom: first structured tests and later the projective tests such as the Rorschach test. However, during the 1950s a sharp decline in the use of testing followed, due to the attacks on, for example, testing's intrusive nature and the possibility of misuse. This persisted into the 1970s. [3 14]

Although there have been endless arguments over the virtues, limitations and utility of clinical psychological testing during the past two decades, psychological testing once again moved to the foreground with the emergence of speciality areas such as neuro-, health, forensic and child psychology. All of these areas depend heavily on the use of tests.[15 16]

The origin of clinical neuropsychology can be traced to studies by Broca in 1861 and Wernicke in 1874. They recognised that certain functions, such as the recognition of speech, are localised in the left hemisphere of the brain.[3] In 1935 Halstead founded a laboratory to study the impact of impairments in brain functioning on a wide range of abilities. Reitan joined him in 1944 and thus the Halstead-Reitan Neuropsychological Battery was developed. Performance on specific subtests of the battery was correlated with injury in different hemispheres of the brain. Later studies by Reitan and Wolfson also indicated the ability of the battery to localise lesions as left- or right-hemispheric and anteriorly or posteriorly located.[10]

Luria[17] had a different approach. He saw the brain as a functional system where various areas interact in certain behaviours. If one area is damaged, various functions will be affected to different extents. He also introduced the concept of pluripotentiality where any one centre in the brain can be involved in several different functional systems. The test he developed became known as the Luria-Nebraska Neuropsychological Battery. Golden[18] summarised a variety of studies that demonstrated that the Luria-Nebraska Neuropsychological Battery is able to make fine distinctions in respect of neuropsychological function such as hemispheric localisation of tumours.

Since the 1990s psychologists have had various tests to choose from for neuropsychological assessment. On the one end of the spectrum there are set test batteries, such as the Halsteid-Reitan Battery. At the other end there are individually tailored batteries that psychologists individualise depending on the patient and circumstances. Somewhere in between are clusters of tests that are used together because of their availability and practicality. Examples of such clusters are the South African Wechsler Adult Intelligence Scale (SAWAIS), the Bender Gestalt and Grassi Block

Design tests and the Mini Mental State Examination that are widely used in private practice and institutions to assess the presence and localisation of brain damage. Nell[19] also suggested a "core" battery where certain subtests of, for instance, the WAIS, are used, combined to suit the individuals' case requirements.

Incagnoli[20] feels that, in the light of recent neuro-imaging innovations such as CT scans, it is clear that the focus of the clinical neuropsychologists shifted from lesion localisation to precise specification of deficits in functioning. She also mentioned that neuropsychologists would continue to have a role in the pre-operative localisation of lesions in focal epilepsy, as positive signs are often absent in certain radio- and neurological tests. Casson et al.[2] found that neuropsychological testing is a highly sensitive and accurate means of detecting brain injury. The overall pattern of test results showed a high correlation with abnormal findings on CT scan and/or EEG and "is an excellent predictor of brain damage" (p. 2667). This view is supported by Zilmer and Spiers[7] who postulate that neuropsychological evaluations are a precursor or complementary to more in-depth neurological or neuro-imaging procedures that can establish the exact medical or neurological diagnosis. It has become less important for neuropsychologists to act as lesion detectors and more important to document the precise effects of brain dysfunction on behaviour for purposes of remediation and treatment.[19]

NEURO-IMAGING

Risberg[21] rightly points out that the gross anatomy of the brain has been depicted accurately since the Renaissance, but that it took centuries for physicians to be able to see the living brain.

Since 1895 doctors have been able to take skull X-rays, though these could only show the bones. Pneumoencephalography (x-rays of the fluid containing structures of the brain by removing cerebrospinal fluid and replacing it with air, oxygen or helium) and angiography were developed. This resulted in the ability to delineate both intra- and extra cranial vessels accurately by intra-arterial injection of contrast and imaging directly by X-ray or by digital subtraction.[22] Electroencephalography (EEG) was developed in the 1930s and is still widely used. By means of scalp electrodes it examines the spontaneous electrical activity of the brain, but it has very little localising value.[23]

In the 1970s, the development of computerised axial tomography (CAT) scanning was a great leap forward, allowing physicians to produce pictures of slices of the brain through a non-invasive procedure. A pencil beam of X-ray traverses the patient's head and a diametrically opposed detector measures the extent of its absorption. Reconstruction of these differential absorption values on a two-dimensional display provides the characteristic CAT scan appearance. For routine scanning slices are 5-10 mm wide, but with high definition imaging views may consist of slices of only 1 mm thick.[24]

Approximately 20 years later, magnetic resonance imaging (MRI) was developed, in which large-bore homogenous magnets and computer-assisted imaging are used to map hydrogen nuclei densities and their effect on the surrounding molecules in vivo. These densities differ among different types of tissue, and enables far more detailed images of the soft tissue.[25]

Radio nucleotide imaging is a new technique, which makes it possible to obtain information about the functioning of the brain. Both single photon emission computed tomography (SPECT) and positron emission tomography (PET) rely on the correlation between local changes in neuronal activity during mental activities and local changes in metabolism and blood flow to generate pictures of the brain.[26]

Regarding the compatibility of neuro-imaging and neuropsychology, Zilmer and Spiers[7] suggest "we are now in an era in which data should be used routinely with that of neuropsychology information. Note that even though modern imaging technology has had spectacular success in depicting the brain's anatomy, neuropsychological findings appear more sensitive to the progression of degenerative diseases than either CT or MRI".

It is thus clear that neuro-imaging currently plays the dominant role in clinical diagnosis, but that neuropsychological evaluation is mandatory to complete clinical assessment.

METHODS

The methodology will be discussed under the headings participants, measuring instruments and statistical analysis.

Participants

An availability sample was taken from patients seen by neurologists and neurosurgeons, practicing in Bloemfontein, between October 2001 and February 2002.

Inclusion criteria were the following:

- A normal MRI.

- An abnormal MRI with localised lesions.
- A minimum age of 18 years.

Exclusion criteria were the following:

- Participant not contactable.
- Participant not able to be assessed in Bloemfontein.
- Participant refused to participate in the study.
- The participant participated in the study, but the assessment was incomplete.
- Participant factors, such as severe lack of concentration, that led to the participant being unfit for evaluation.

Although the aim was a much higher number of participants, because of the exclusion criteria and other practical problems, 48 patients were included. Informed consent was obtained from all participants or their legal guardians. They were then assessed blindly and the psychological tests were marked and checked. An independent expert, who was blind to the diagnosis, interpreted the tests.

Measuring instruments

The following measuring instruments were used:

- Magnetic resonance imaging

  The MRI provides superior 3-D images of the brain without exposing the patient to ionising radiation.[27] This is currently the gold standard in structural neuro-imaging to which all other assessments (medical and psychological) are compared (C.S. de Vries, personal communication, 17 October 2002). The MRI slices are composed of voxels (the smallest computer-addressable volume in a three-dimensional object, equal to $3mm^3$). The image is then composed of pixels (picture elements) of which the intensity is proportionate to the signal intensity of the contents of the corresponding voxel.[28 29] It is clear that a lesion smaller than 3 mm in diameter will be missed. It is also interpreted by clinicians and is therefore subject to human error.

- Psychological tests

  The following psychological tests were used:

- *The South African Wechsler Adult Intelligence Scale*: "The Wechsler tests continue to be the most widely used in neuropsychogical practice, and have generated a large body of quantitative and process-oriented studies with both adults and children" (p171).[19] However, although the psychometric properties of the American version of the Wechsler are satisfactory,[30 10] the South African edition has been criticised on various grounds.[31 19] Regardless of this criticism, the South African edition is still widely used, also for neuropsychological assessment.
- *The Folstein's Mini Mental State Examination (MMSE)*: This is a brief instrument designed to assess cognitive function.[32] The test-retest reliability is high (0.827 - 0.887) and sensitivity is reported from 0.57 and specificity from 0.63. It is, however, affected by various factors such as educational level, literacy, cultural differences, linguistic ability and the presence of psychopathology such as depression.[33] The validity of this test was also found to be very high for differentiating dementia from schizophrenia and depression, and for monitoring the improvement of clinical conditions such as head trauma and delirium. Results on the MMSE have a significant correlation with intelligence level, but this does not interfere with its ability to differentiate between organic states and functional syndrome.[34] Because of these properties, the test was also included in the assessment of the patients.
- *The Bender Gestalt Test*: This test is widely used in the diagnosis of organicity and for assessing intellectual and visual-motor functioning.[35] Despite a vast amount of criticism, the Bender Gestalt Test continues to be ranked among the top 10 assessment instruments in terms of use.[36 37] A test-retest reliability coefficient of 0.79 is reported for total scores, with a concordance rate of 86% for the occurrence of particular types of errors, and a 93% agreement rate for the diagnosis of organicity. Test-retest reliability of up to 0.9 and interscorer reliability of 0.90 - 0.92 were found.[35] Using five copying errors as a cut-off score, it was found that the Bender Gestalt Test rules out organicity with 92% accuracy and detected organicity with 67% accuracy.[38]
- *The Grassi Block Substitute Test (GBST):* This instrument was developed to demonstrate early and late mental changes due to organic pathology, as well as impairment due to functional pathology.[39] It evaluates simple and complex concrete performance, as well as simple and complex abstract performance.

The test-retest reliability is estimated at 0.85. The GBST has a sensitivity of 83%, but 25% of patients test false negative and 30% false positive.[40]

Testing was done in either Afrikaans or English, depending on the participant's preference. Translating into an African language was done in four of the cases.

Statistical analysis

In order to realise the first two goals of the article, the measure of agreement was determined by means of the *Kappa (κ)–coefficient.* This coefficient is known as Cohen's Kappa and it measures interrater agreement,[41] which presents us with information on the reliability of the results. The higher the coefficient, the greater the agreement between the two measures.

The *Point-biserial correlation* (r_{pb}) was used to realise the third goal of the article. This coefficient is used when the relationship between dichotomic and continuous variables is being established. In this case the results of the MRI was dichotomic (absent/present), while the scores on the psychometrical tests were continuous.

Arbitrary assignment of 0 (zero) to the group without a diagnosis of cerebral lesions (absent) and 1 (one) to the group with a diagnosis of cerebral lesions (present) took place. Because of the arbitrary assignment of the codes, the sign of the correlation coefficient can be ignored. A negative correlation only indicates that the average of the group with Code 1 is smaller than that of the group with Code 0, while a positive correlation indicates the opposite.

To determine the practical significance of statistical significant results, effect size was determined. The following guidelines by Cohen[42] were used to interpret the effect size:

P = 0.1: small effect

P = 0.3: medium effect

P = 0.5: big effect

The effect size was only determined if statistical significant results were found (on the 1%- or 5% level).

RESULTS AND DISCUSSION

In discussing the results the focus will fall on the biographical data of the participants, the agreement between the diagnosis and localisation of cerebral lesions with the MRI and neuropsychological tests, and the correlation of different subscales of the psychometric tests with the MRI.

Biographical data of the participants

Biographical information regarding the experimental (abnormal MRIs) and control group (normal MRIs) is highlighted in Table 1.

Table 1: Biographical information of the experimental group and control group

BIOGRAPHICAL VARIABLES	Experimental group		Control group	
	N = 23	%	N = 25	%
Gender				
Male	17	73.9	22	88.0
Female	6	26.1	3	12.0
Age				
20- 35	11	47.8	14	56.0
36- 55	8	34.8	8	32.0
56 or older	4	17.4	3	12.0
Mother tongue				
Afrikaans	11	47.8	8	32.0
English	1	4.3	0	0.0
Sotho	7	30.4	13	52.0
Portuguese	1	4.3	0	0.0
Zulu	0	0.0	2	8.0
Xhosa	0	0.0	1	4.0
Tswana	3	13.0	1	4.0
Test language				
Afrikaans	19	82.6	17	68.0
English	4	17.4	8	32.0
Educational level*				
None	2	8.7	4	16.0
Primary school	5	21.7	7	28.0
Secondary school	10	43.5	12	48.0
Tertiary education	3	13.0	2	8.0
Employment status#				
Employed	8	34.8	14	28.0
Unemployed	10	43.5	5	20.0
Pension	5	21.7	2	8.0
Co-morbidity				
None	8	34.8	3	12.0
Medical disorders	7	30.4	7	28.0
Psychiatric disorders	7	30.4	12	48.0
Mental retardation	1	4.3	3	12.0
Time elapsed since injury/scan				
1- 6 months	11	47.8	7	28.0
More than 6 months since injury/ MRI	12	52.1	18	72.0
Type of lesion				
None	0	0.0	13	52.0
Trauma	6	26.1	6	24.0
Tumour	3	13.0	1	4.0
Stroke	4	17.4	1	4.0
Other	10	43.5	4	16.0

* Three unknown in the experimental group
#Four unknown in the control group

Motor-vehicle accidents were the most common cause of trauma in the participants, followed by interpersonal violence. Specifically, younger male participants were more prone to injury. This confirms the observation by Zilmer and Spiers.[7] Other causes of lesions were cerebral infections, epilepsy and vasculitis. Although there were no abnormalities on the MRIs of the participants in the control group, they did have neurological symptoms and signs that led the neurologist/neurosurgeon to request a MRI. Unemployment was higher in the experimental group. This could be as a result of the injuries, though the current situation in the country is also reflected. Though there were no deliberate pairing of control and experimental participants, it is clear that the two groups are comparable.

The incidence of medical disorders in the participants is depicted in Diagram 1.

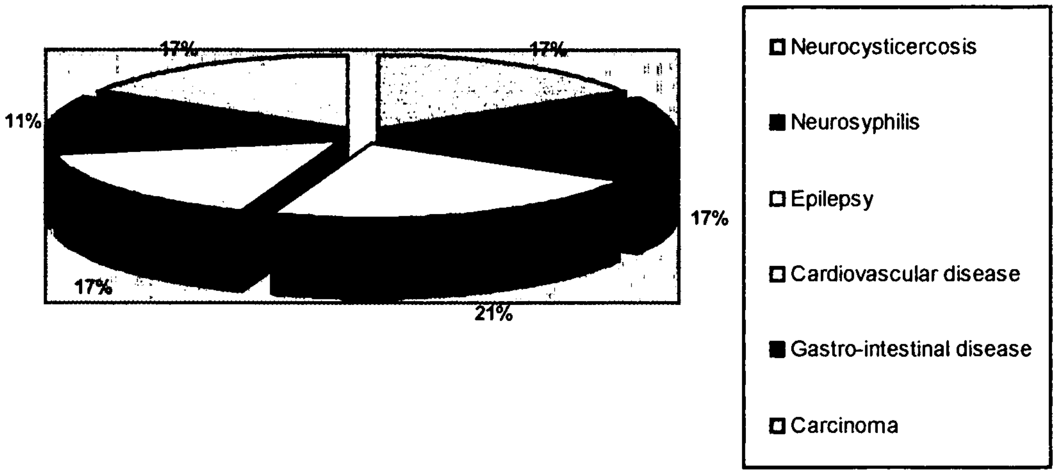

Diagram 1: Medical disorders in the participants

It is clear that the group of central nervous system infections represented the most frequent co-morbid problem in the participants, followed by epilepsy. It should be kept in mind that epilepsy can lead to cognitive impairment and thus influence an individual's scholastic performance, which can also have an influence on the mentioned unemployment rate.

Diagram 2 represents the distribution of psychiatric diagnosis (Axis I or Axis II of the DSM-IV) in the participants.

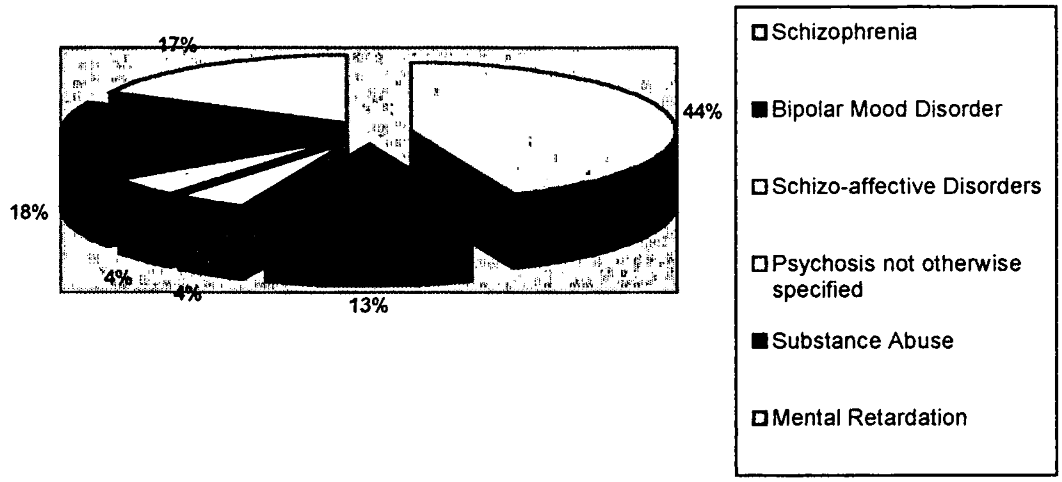

Diagram 2: Psychiatric diagnosis in the participants

Although a variety of psychotic disorders were diagnosed, none of the participants was psychotic at the time of psychometric evaluation. All the mentally retarded participants fell in the "mild" category and were fit for evaluation. Concerning substances abuse, alcohol, cannabis and analgesics were the main substances.

The agreement between the diagnosis of cerebral lesions with the MRI and by means of neuropsychological assessment

The results regarding the agreement between the diagnosis of cerebral lesions with MRI (absent/present) and by means of neuropsychological assessment are reflected in Table 2.

Table 2: Interrater agreement regarding cerebral lesions

	Diagnosis: Neuropsychological assessment		
Diagnosis: MRI	No lesion	Lesion	**Total**
No lesion	1 **(2.08)**	24	25
Lesion	3	20 **(21.08)**	23
Total	4	44	48

(κ) – coefficient = -0.09; effect size = small

The results in Table 2 show that 24 (96%) of the 25 participants with no lesion present on the MRI were diagnosed as having lesions when psychometry was used. Twenty (20 = 87%) of the 23 participants who had lesions present on the MRI were diagnosed as such by the neuropsychological assessment. As only 4% of participants without lesions were identified as such by psychometry, it seems that neuropsychological assessment is reasonably successful in diagnosing cerebral lesions when present, while it does not succeed in excluding participants without cerebral lesions. According to the Kappa *(κ)–coefficient* is clear that there was only a 9% agreement between the diagnoses of cerebral lesions by MRI and neuropsychological assessment after correcting for chance. This indicates a low congruity between the two diagnoses. However, it is important to bear in mind that psychometrical tests may be able to demonstrate functional abnormalities in the absence of visible structural abnormalities on the MRI, as MRI may not reveal microscopic shearing of axons. Casson et al.[2] found neuropsychological testing highly sensitive and accurate in detecting brain injury. This can explain the many false positive findings of cerebral lesions in the participants. Another problem may be to differentiate between psychiatric and organic brain dysfunction. For example, schizophrenia may result in impairment on tasks measuring frontal lobe functioning, on processing speed and on naming. Such patients may thus be wrongly classified as having cerebral lesions.[5] It can be concluded that the present results support the findings of Kesler, Adam and Bigler[43] who found a modest relationship between the clinical observations of the MRI and neuropsychological assessment.

The agreement regarding localisation of cerebral lesions with the MRI and by means of neuropsychological assessment

The 20 participants with a corresponding diagnosis of cerebral lesions by both MRI and psychometry were then examined regarding the congruence between the localisation of the lesion according to the MRI and the localisation according to the neuropsychological testing. This was done for the separate localisations (left frontal, right frontal, left temporal, right temporal, left parietal and right parietal). A participant may have had a lesion in more than one area. The results are depicted in Table 3.

As far as the left frontal lobe is concerned, 15 of the 20 participants had no lesion according to the MRI. Fourteen (93.3%) of these 15 participants were diagnosed as having lesions by the psychometric tests. Of the five participants that did have lesions according to the MRI, four (80%) were diagnosed as such with the psychometric tests. The *(κ)–coefficient* shows a 7% agreement between the diagnoses of left frontal lesions after correcting for chance.

Table 3: Interrater agreement regarding localisation of cerebral lesions

Localisation	Diagnosis: MRI	Diagnosis: Neuro-psychological testing		Total
		No Lesion	Lesion	
Left frontal (κ) = -0.07	No lesion	1 **(1.5)**	14	15
	Lesion	1	4 **(4.5)**	5
	Total	2	18	20
Right frontal (κ) = -0.17	No lesion	2 (3.2)	14	16
	Lesion	2	2 **(3.2)**	4
	Total	4	16	20
Left temporal (κ) = 0.02	No lesion	2 **(1.8)**	16	18
	Lesion	0	2 **(1.8)**	2
	Total	2	18	20
Right temporal (κ) = 0.03	No lesion	3 **(2.8)**	11	14
	Lesion	1	5 **(4.8)**	6
	Total	4	16	20
Left parietal (κ) = -0.13	No lesion	2 **(2.8)**	12	14
	Lesion	2	4 **(4.8)**	6
	Total	4	16	20
Right parietal (κ) = -0.13	No lesion	2 **(2.8)**	12	14
	Lesion	2	4 **(4.8)**	6
	Total	4	16	20

Regarding the right frontal lobe, 16 of the 20 participants had a normal MRI. Of these 16, 14 (87.5%) were diagnosed as having lesions by the psychometric tests. Two (50%) of the 4 participants with lesions according to the MRI were diagnosed as such by the psychometric tests. The *(κ)–coefficient* shows a 17% agreement between the two diagnoses of right frontal lesions with exclusion of the chance factor.

As far as the left parietal lobe is concerned, 18 of the 20 participants had no lesion according to the MRI. Sixteen (88.9%) of these 18 participants were diagnosed as having lesions by the psychometric tests. Both participants (100%) with lesions according to the MRI were diagnosed as such by the psychometric tests. The *(κ)–coefficient* shows a 2% agreement between the diagnoses of left temporal lesions after correcting for chance.

Regarding the right temporal lobe, 14 of the 20 participants had no lesion according to the MRI. Of the 14, 11 (78.6%) participants were diagnosed by psychometry as having lesions. Of the 6 participants with lesions according to the MRI, five (83.3%) were also identified as having lesions by the psychometric tests. The *(κ)–coefficient* shows a 3% agreement between the diagnoses of right temporal lesions with exclusion of coincidence.

With regard to the left and right parietal lobes, the MRI diagnosed 14 of the 20 participants as not having lesions. In both cases, 12 (85.7%) of the 14 participants without lesions according to the MRI were diagnosed as having lesions by the psychometric tests. In both instances four (66.7%) of the six participants with lesions according to the MRI were diagnosed as such by the psychometric tests. The *(κ)–coefficient* shows a 13% agreement between the diagnoses of parietal lesions after correcting for chance.

All the Kappa-coefficients determined are very low and it can be accepted that there is no congruence between the localisation of the lesions diagnosed by MRI and those diagnosed by means of neuropsychological testing. It therefore seems as if the psychometrical tests are able to diagnose lesions when they are present (according to the MRI), but that the tests do not succeed in excluding lesions in the absence thereof. However, the small sample size, the cultural diversity, as well as the use of a single independent rater may have affected the results adversely.

The correlation of different subscales of the psychometric tests with the MRI diagnosis

The *Point-biserial correlation* (r_{pb}) was determined in assessing the correlation of the different subscales of the psychometric tests with the MRI diagnosis. The results are depicted in Table 4.

Table 4: Correlation coefficients between MRI diagnosis and subscales of the different psychometrical tests

Folstein's Mini Mental State Examination	MRI	Bender Gestalt Test	MRI	Grassi Block Substitute Test	MRI	South African Wechsler Intelligence Scale for Adults	MRI
Orientation	0.06	Perseveration	0.17	Accuracy	0.10	General information	0.12
Registration	0.01	Rotation	0.09	Behavior	0.31*	General comprehension	0.03
Recall	0.04	Transformation	0.10	Total	0.15	Arithmetic	0.02
Attention and calculation	0.02	Added angles	0.15			Digit repetition	0.10
Confrontation naming	0.22	Separation	0.27			Similarities	0.13
Writing	0.21	Integration	0.28*			Picture completion	0.18
Repetition	0.03	Distortions	0.09			Object assembly	0.08
Comprehension	0.10	Additions	0.39**			Block patterns	0.14
Construction	0.05	Partial rotation	0.15			Digit/ symbols	0.02
Total	0.02	Deletions	0.23			Picture arrangement	0.30*
		Decreases	0.09			Verbal IQ	0.07
		Gaps	0.05			Practical IQ	0.10
		Absence of erasing	0.03			Total IQ	0.01
		Closure	0.04			Vocabulary	0.02
		Contact	0.19				
		Total	0.01				

* $p <= 0.01$ ** $p <= 0.05$

As mentioned earlier, the sign of the coefficient can be ignored because the codes 0 and 1 were assigned arbitrarily. From Table 4 it is clear that only four of the subscales of the four psychological tests show a correlation with the MRI diagnosis. These subscales are integration and additions of the Bender Gestalt Test, behaviour of the Grassi Block Substitute Test and picture arrangement of the South African Wechsler Adult Intelligence Scale. The correlation is significant on the 1% level for additions (Bender Gestalt Test), while the correlation of the other three subscales is significant on the 5% level. According to Cohen,[44] these four coefficients have medium to large effect sizes. The picture arrangement subtest of the South African Wechsler Adult Intelligence Scale requires a subject to notice details and to plan adequately.[10] This taps on frontal lobe functions such as judgment, planning and insight. It also assesses the ability of a patient to interpret a social situation correctly. Picture arrangement was also identified by Hirt and Cook[45] as one of the subscales with the highest correlation with the presence of brain lesions as determined by the Grassi Block Substitute Test (p = 0.61), only second to the block design subtest. Kolb and Whishaw,[3] however, found the performance tests to be less predictive of the side of the lesion, except in the case of right parietal injury where there is a significant impairment on block design and picture arrangement. Kesler, Adams and Bigler[43] also found a significant correlation between the memory and intellectual impairment of patients with traumatic brain injuries and the extent of structural damage. Clinical MRI abnormalities were specifically related to verbal and general memory, verbal, non-verbal and total IQ. These changes were more severe in patients with more severe frontal and temporal damage.

The lack of a high correlation between the results of the Folstein's Mini Mental State Examination with the presence of lesions on the MRI does not concur with previous studies. In the present study participants with mild mental retardation as well as a number of participants without any formal schooling or with only primary school education were included. As the Folstein's Mini Mental State Examination, as well as the South African Wechsler Adult Intelligence Scale, are influenced significantly by educational and intelligence level,[38] this may have led to false positive diagnoses and a resulting poor correlation between the subscales and the MRI.

The Bender Gestalt Test's superiority in diagnosing cerebral lesions, as found by other researchers, [9 37] is confirmed by the results of the present study. A possible explanation for this finding is that the Bender Gestalt Test was the most culture-fair of the tests used in this study. None of the culturally diverse participants was therefore discriminated against.

CONCLUSION

The significance of the finding that neuropsychological tests are able to diagnose lesions when they are present (according to the MRI), but do not succeed in excluding lesions in the absence thereof, should be interpreted with caution. It could be that neuropsychological tests are highly sensitive for functional impairment, but it could also be that psychometry has a low positive predictive value (the percentage of all positive tests that are true positives). The MRI also seems to be superior to psychometry concerning the localisation of lesions, though neuropsychological tests do have potential in the localisation of left-frontal, left-temporal and right-temporal lesions. In this regard, the only subscales that show a significant correlation with the MRI diagnosis are addition and integration of the Bender Gestalt Test, behaviour on the Grassi Block Substitute Test and picture arrangement of the South African Wechsler Adult Intelligence Scale. However, the findings of this study should be interpreted with care:

- A larger sample size may have led to more reliable and valid results.
- The same applies to the present skewness of the sample regarding gender and cultural representation.
- The fact that speakers of African languages were not assessed in their native tongue and the questionable culture-fairness of the psychological tests may have been a contaminating factor.
- The use of only one independent interpreter, who had to interpret the results of the psychological tests blindly, may have influenced the results. A team of say three interpreters may have yielded more reliable and valid results, especially if allowed in a "real life" situation with personal access to the patient.

This study should therefore be regarded as an exploratory study in the use of neuropsychological assessment in the diagnosis of cerebral lesions. It is therefore strongly recommended that a larger and more comprehensive study should be conducted to determine what the true place of psychometry is in the diagnosis of cerebral lesions. Professionals who use psychometry - especially exclusively - for the diagnosis of cerebral lesions should handle their results with the utmost caution and should confirm their diagnosis with MRI or other neuro-imaging techniques.

At the same time it is strongly recommended that only professionals with the necessary training (especially from the South African Clinical Neuropsychology Association) should be involved in the use of psychological tests for neurological diagnosis. However, it seems that even experienced neuropsychologists with the necessary training should rather use it as an adjunctive evaluation with emphasis on the patient's functioning and planning of rehabilitation.

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MODERATOR VARIABLES IN NEUROPSYCHOLOGICAL ASSESSMENT

ABSTRACT

Controversy reigns over the virtues, limitations and utility of clinical psychological testing. Certain test, patient and lesion variables also influence the results of neuropsychological assessment. The purpose of the study was to determine the effect of moderator variables on the results obtained through neuropsychological assessment versus those obtained by MRI. An availability sample was taken from patients seen by neurologists and neurosurgeons, with either a normal or an abnormal MRI with localised lesions. They were then assessed by means of the South African Wechsler Adult Intelligence Scale, the Folstein's Mini Mental State Examination, the Bender Gestalt Test, and the Grassi Block Substitution Test. The findings are discussed, shortcomings mentioned and recommendations made.

Neuropsychological assessment; neuro-imaging; cerebral lesions; moderator variables; South African Wechsler Intelligence Scale; Folstein's Mini Mental State Examination; Bender Gestalt Test; Grassi Block Substitution Test.

SAMEVATTING

Die doeltreffendheid, beperkings en bruikbaarheid van sielkundige toetse is kontroversieel. Sekere toets-, pasiënt- en letselveranderlikes kan die resultate van neurosielkundige assessering beïnvloed. Hierdie verkennende studie poog om die effek van sekere steuringsveranderlikes op neurosielkundige toetse te bepaal. 'n Beskikbaarheidsteekproef is getrek van pasiënte met óf 'n normale MR óf 'n MR wat gelokaliseerde breinletsels toon. Die proefpersone is evalueer met die Suid-Afrikaanse Wechsler Intelligensieskaal vir Volwassenes, die Folstein Mini Mental State

Examination, die Bender Gestalttoets en die Grassi Blokvervangingstoets. Die toetsresultate is blind geïnterpreteer. Die bevindinge van die studie word bespreek, terwyl tekortkominge uitgewys en aanbevelings gemaak word.

Neurosielkunde; neurologiese beelding; breinletsels; steuringsveranderlikes; Suid-Afrikaanse Wechsler Intelligensie Skaal; Folstein Mini Mental State Examination; Bender Gestalttoets; Grassi Blokvervangingstoets.

INTRODUCTION

Controversy reigns over the virtues, limitations and utility of clinical psychological testing (Cohen, Swerdlik & Smith, 1991; Korchin & Schuldberg, 1981). Previously, the interest in neuropsychology and specifically assessment reflected a need to expand the clinical understanding of behaviour to include the effects of brain dysfunction on behaviour. The role of the neuropsychologist changed from being a mere "lesion-detector" to a more comprehensive function. A shift took place from a neurological-locationist tradition to a behavioural-descriptive frame.

Lezak (1995) suggests that neuropsychological assessment characteristically focuses on identifying and measuring cognitive deficits. She indicates that it is primarily in deficiencies and dysfunctional alteration of cognition, emotionality, self-direction and management that brain damage manifests behaviourally. According to Zilmer and Spiers (2001) and Murphy and Davidshofer (1991) the neuropsychological evaluation has a number of advantages that many standard neurodiagnostic techniques do not share, for example, non-invasiveness, cost-effectiveness and the provision of descriptive information about the patient.

Over 50% of neuropsychological evaluations still have a diagnostic purpose. In many cases with obvious pathology, for example brain tumours, neuropsychological tests are a precursor to or complementary to more in-depth neurological or neuroimaging procedures. However, the main purpose of neuropsychological evaluations is to provide descriptions of cognitive functioning, current adaptation and future prognosis (Nell, 2000).

The objective and comprehensive nature of the evaluation of cognitive and behavioural functioning makes the neuropsychological evaluation very valuable. The findings are integrated with intellectual and personality assessments and evaluated within the context of computed axial tomography (CT or CAT scan) and magnetic resonance imaging (MRI or MR). This leads to a thorough description of abilities and deficits and recommendations for rehabilitation and treatment. According to Zilmer and Spiers (2001, p. 442) clinical neuropsychologists are principally interested in "identifying, quantifying and describing changes in behaviour that relate to the cognitive integrity of the brain".

Developments in neuroscience over the last three decades have seen neuropsychology develop from a purely diagnostic area to where neuropsychological assessment forms an integral part of treatment evaluation and research (Anderson, 2001). Neuropsychological testing will and should not replace neuroimaging techniques. The optimal use of neuroimaging and neuropsychological assessment in diagnosing brain damage has yet to be determined. It is likely that the application of the principles of psychological testing will play an increasingly important role in clinical neuropsychology (Murphy & Davidshofer, 1994).

The results obtained through neuropsychological testing are influenced by test, patient and lesion variables.

(a) Test variables

For any psychological test to be useful, it must be reliable, valid, objective and interpreted according to norms (Louw, 1997).

- Reliability refers to the degree to which test scores are free of measurement errors. More specifically, the essential notion is consistency, i.e. the extent to which the measuring instrument yields the same approximate results when utilised repeatedly under similar conditions (Reber & Reber, 2001).
- Validity refers to the ability of a test to measure what it is supposed to measure (Plug, Louw, Gouws & Meyer, 1997). In a meta-analysis, Meyer *et al.* (2001) found that both psychological and medical tests have varying degrees of validity, ranging

from tests that are essentially uninformative for a given criterion, to tests that are strongly predictive of appropriate criteria (e.g. neuropsychological tests that differentiate dementia from normal cognitive functioning and computed tomography's ability to detect metastases in the head and neck regions). Validity coefficients for many psychological tests (0.35-0.45) are also indistinguishable from those of CT scans (0.32-0.41) and MRIs (0.43).

- Objectivity refers to the comparability of results when various competent scorers score a test (Louw, 1997). This implies that the scoring and interpretation of the test should not be influenced by personal and subjective variables.
- A norm is a value or series of values reflecting the normal or average performance of a group of people (Stratton & Hayes, 1994). For test results to be meaningful, examiners must be able to compare the initial score to some form of derived score based upon comparison to a standardisation or norm group (Gregory, 1992).

It is therefore clear that these test variables should be taken into consideration when interpreting test results.

(b) *Patient variables*

A fundamental problem in diagnostic neuropsychological testing is the considerable variance in cognitive performance associated with variables such as the following (Anderson, 2001; Meyer *et al*, 2001; Mortensen & Gade, 1993):

- *Age*. According to Francel and Snell (1999) children with brain injuries often have better outcomes than adults. Older people do less well on neuropsychological tests, specifically on those requiring flexible problem-solving skills and procedures that require perceptual and attention skills. However, the decline in motor speed and strength with increasing age does not seem to have a significant effect on motor tests (Zilmer & Spiers, 2001). Older people often have pre-existing medical conditions that make them more prone to the development of intra-cranial haemorrhages following traumatic brain injuries (Lannoo & Vingerhoets, 1997). Mortensen and Gade (1993) found that verbal IQ declines substantially only above the age of 60. Low IQ subjects showed much less age-related decline in performance than the high IQ subjects. Age differences are more pronounced for nonverbal subtests. Verbal skills and well-learned information hold up best over time while perceptual-integrative and psychomotor skills decline the most with advancing age. The age-related effects are thus more applicable when referring to fluid intelligence, whereas crystallised intelligence is more stable (Heaton, Ryan, Grant & Matthews, 1996).

- *Gender.* There is increasing evidence to suggest that cerebral organisation is different in men and women. Women are less likely than men to be asymmetrically organised for language than men. They perform better than men on tasks requiring verbal skills, but men have a visual-spatial advantage (Lannoo & Vingerhoets, 1997; Zilmer & Spiers, 2001). Men tend to do better on tests that involve manipulating spatial relationships, quantitative skills, physical strength and simple motor speed, whereas females show advantages on tests of certain verbal abilities (Heaton, Ryan, Grant & Matthews, 1996). Herring and Reitan (1992) also found that there is some evidence of female superiority in verbal functioning, but neither sex performed better than the other on any single dependent variable. Unilateral lesions do not affect the two sexes differentially. The differences in verbal functioning are of little practical significance, particularly as far as clinical neuropsychological evaluation following brain injury is involved. Among groups of neurologically similar males and females, no support for either differential cerebral lateralisation or differential vulnerability could be found. With the exception of motor functioning, the sexes produced similar neuropsychological profiles, suggesting that need for gender-specific norms on these particular measures is limited to lower-level skills and not higher aspects of neuropsychological functions. Research on gender differences in ability has also found no significant differences in general intelligences between the genders (Heaton, Ryan, Grant & Matthews, 1996).
- *Education and socio-economic status.* Lower pre-injury ability, as reflected in educational status, is a risk factor for greater intellectual compromise following injury (Bigler, Johnson & Blatter, 1999). The educational level of non-brain damaged individuals has a striking effect on Wechsler Scale scores, but exerted less influence on tests that are generally more sensitive to brain damage. The tests that were influenced by education depend heavily on auditory-verbal and language

requirements and have a minimal dependence on immediate problem-solving skills. Educational level accounts for a substantial proportion of the variance in performance on all neuropsychological tests, favouring subjects with a higher educational level. Intellectual impairment may be over-diagnosed in old low-education patients and under-diagnosed in young high-education patients (Lannoo & Vingerhoets, 1997; Mortensen & Gade, 1993; Reitan & Wolfson, 1995). Education effects are attenuated in individuals who are still actively participating in the educational system. However, the effects of brain damage may produce sufficient decreases in performance to "wash out" the effects of education. Reitan and Wolfson (1995) mention that when brain damage is present, the attribute variables of age and education have only a minor influence on an individual's overall neuropsychological performance.

- *Dominance.* Dominance is associated with the cerebral organisation of speech. The traditional idea that language skills are located in the left, and visual-spatial perception in the right hemisphere is currently being refuted (Herring & Reitan, 1992). Zilmer and Spiers (2001) stated that though verbal abilities such as speech and reading are located in the left hemisphere of right-handed people, they are not necessarily completely lateralised to the right hemisphere in left-handed people. Left-sided lesions are thus prone to damage verbal abilities, despite cerebral and hand dominance.
- *Past illnesses and co-morbidity.* Functioning can be affected negatively by birth trauma, fever, infections, seizures, head trauma (including nature of the trauma, length of time of unconsciousness, length of post-traumatic amnesia and sequelae), family history, alcoholism or other psychiatric disorders (Beaumont, 1988; Girard *et al*, 1996; Peach, 1982). When interpreting test results, it is important to keep the baseline functioning of the patient in mind.
- *Current motivation and attitude.* In interpreting neuropsychological test data, the interpreter assumes that the testee performed optimally. However, this is not always the case and can lead to the test data being an inaccurate measure of cognitive functioning. Non-optimal test performance can be due to a poor level of co-operation (as in simulation or dissimulation), decreased arousal (as in fatigue that affects speedy information processing and new learning adversely) and medication (that

interferes with both motivation and arousal). If a patient shows more fatigue on a particular test, it might reflect the underlying disorder. Medication should be discontinued, if possible, in order to obtain an accurate picture of the individual's performance and, if possible, testing should be deferred (Lloyd, 2000).

- *Culture*. A culturally sensitive assessment has been described as "one that balances the application of general population norms with culture-specific norms" (Heaton, Ryan, Grant & Matthews, 1996, p. 156). Not only is ethnicity important in language- and knowledge-based tests, but the patient's level of acculturation must also be taken into consideration (Fouad & Chan, 1999). Unfortunately there is not yet sufficient data available to determine the exact extent of the influence of culture and language on tests.

These patient variables can have a profound influence on the significance of test results.

(c) Lesion variables

No two brains are identical in anatomy, size and location of area boundaries. This, together with the absence of neat boundaries for lesion damage, may hamper the assignment of functional significance to the damaged area. Loss of function in one area also leads to immediate alteration in the function of others, a function called plasticity (Lloyd, 2000).

- *Size*. Voller *et al.* (1999) reviewed a clinical homogeneous patient group (N=12) with very mild traumatic brain injury and found that the most sensitive method for detecting brain damage was the neuropsychological examination. They found that verbal memory in particular was affected. The reaction time also lengthened and arithmetic tests were also negatively affected, though non-verbal memory tests were not affected. Mortensen and Gade (1993) mentioned that the mean observed verbal IQ in a group of neurological patients with diffuse cerebral atrophy was about 7 IQ points lower than could be expected from the age and educational level of the group. Diffuse lesions therefore tend to lead to a more severe impairment of test functioning.

- *Acuteness*. There is a very poor correlation between CT scans and functional behaviour with increased time after the trauma, the reason being that nerve shearing injuries are often microscopic in nature and visible only on autopsy. Brain haemorrhages may also clear up with time so that the structure of the brain appears normal, but functioning is impaired. The opposite is also true: where structural abnormalities are present, the individual may be able to function remarkably well because of the plasticity of the brain. A better correlation can be obtained through the use of MRI. It gives a much better resolution of brain structures and it is also sensitive to certain biochemical changes in the brain (Kay & Lezak, 1990).
- *Mechanism of injury*. Unlike tumours, strokes and penetrating head injuries, closed head injuries usually result in diffuse brain damage with multiple impairments ensuing. In addition to the primary insult to the brain, secondary mechanisms of injury, such as haematomas and brain swelling with a resultant increase in intracranial pressure leads to herniation, anoxia and neuronal death. Surgery to relief these complications may also cause additional trauma to brain tissue. When secondary injury occurs, it can lead to functional impairment way beyond the expected primary damage (Kay & Lezak, 1990). In neuropsychological testing diffuse impairment can thus be found, even though the initial insult was localised.
- *Severity*. The duration of post-traumatic amnesia is one of the best indicators of the severity of a traumatic brain injury (Nell, 2000). Signs of poor outcome include lengthy coma and acute subdural haematoma (Francel & Snell, 1999). The extent and severity of primary impairments (that is fronto-temporal concussion, diffuse axonal injury and coup-contracoup injuries) will depend on the severity of the injury, as well as the region involved. This is especially true in the case of diffuse axonal injury with resultant brain-stem damage and extended periods of coma. However, brief loss of consciousness does not exclude the possibility of significant mental impairment (Kay & Lezak, 1990).
- *Focal or diffuse*. A variety of pathological processes may result in case of a diffuse pattern of lesions throughout the brain, or more or less localised or focal lesions. The lesions may be progressive or static and may also be the result of a single pathological event such as in trauma. Lesions affect different hemispheres or lobes and this results in different effects on the patient's functioning (Beaumont,

1988). The majority of cerebral lesions due to motor-vehicle accidents, assaults and falls are diffuse. Goodglass (1986) gives detailed information on the manifestations of focal and diffuse deficits. Some areas of deficit in cognitive functioning are not selectively associated with a focal lesion in any area of the brain, but are present, no matter where the lesion is. These include a reduction in the speed of mental operation during the maintenance of a simple response set, memory impairment and the impairment of abstract thinking. Fontaine *et al* (1999) also include alteration in personality. It is thus virtually impossible to state that certain findings on neuropsychological testing are patognomonic of a specific lesion.

- *Lateralisation.* Herring and Reitan (1992) emphasised that right-hemispheric lesions produce more profound contralateral as well as ipsilateral sensor motor deficits than do lesions of the left hemisphere. Other functions are more commonly present with damage to certain areas of the brain. Constructional apraxia occurs in patients with right-brain injury, whereas limb and facial apraxia are more common in left-brain injury. In extreme disorganisation of visual-spatial performance, the right parietal lobe is almost always involved. Unilateral neglect of details on the opposite side of the lesion is common in right-hemisphere injury, as well as dissociation between the ability to draw by copy and to draw by command. Language disorders and aphasia imply left-hemispheric injury (Goodglass, 1986). Verbal memory and attention/ executive function tasks are strongly correlated with left-hemispheric damage, whereas visual memory tasks are more bilaterally distributed (Fontaine *et al*, 1999). Persons with right-sided lesions tend to be more impaired on neuropsychological testing.
- *Localisation of function within the four major lobes of each cerebral hemisphere.*

Frontal: A wide range of behavioural abnormalities may occur with damage to these lobes, such as executive dysfunction, disinhibition and abulia. The dorsal lateral frontal cortex is the main role player in executive function, which refers to the ability to organise attention, memory, sensory information, and motor function into purposeful, goal-directed behaviour (Filley *et al*, 1999), while the prefrontal cortex is associated with specific verbal abilities, some perceptual functions and some limited aspects of memory. Lesions in the orbital cortex may lead to changes in personality and social behaviour (Gregory, 1992).

Temporal. The temporal lobe is particularly vulnerable to trauma due to its location in the middle intracranial fossa. The temporal lobes play the key role in auditory perception, higher aspects of visual perception and in the receptive aspects of language. They also contribute to the affective, emotional and personal experiences, with resultant changes in personality and sexual behaviour following trauma (Gregory, 1992). Bigler, Johnson and Blatter (1999) found that lower psychometric intelligence post-injury might be associated with more temporal lobe atrophy. Long-term memory storage is also a key function and bilateral lesions lead to severe anterograde amnesia, where almost all capacity for long-term memory and learning is lost.

Parietal. The anterior part of the parietal lobes is important in somatosensory perception, tactile perception and body sense. Damage in these areas leads to agnosia. The posterior region of the parietal lobes contains the association areas for the integration of sensory information. It is important in language, spatial orientation, symbolic synthesis, cross-modal matching, and memory. (Beaumont, 1988). Right-sided lesions lead to the loss of the Gestalt in drawings, while left-sided lesions lead to impoverished drawings (Gregory, 1992).

Occipital. Because the occipital lobes contain only cortex concerning vision, they are almost exclusively associated with visual sensation and perception (Gregory, 1992). However, this area was not included in the present study.

Against this background, the purpose of the study was to determine the effect of moderator variables on the results obtained through neuropsychological assessment versus those obtained by means of MRI. More specifically, the aim was to determine:

- whether there is a difference in the agreement between the diagnosis made by MRI or psychometry for different biographical subgroups, and
- which of the subscales of the psychological tests, for different biographical subgroups, have a higher correlation with the MRI diagnosis.

METHODOLOGY

The methodology will be discussed under the headings participants, measuring instruments and statistical analysis.

(a) Participants

An availability sample was taken from patients seen by neurologists and neurosurgeons, practising in Bloemfontein between October 2001 and February 2002.

Inclusion criteria were the following:

- A normal MRI. (Although there were no abnormalities on the MRIs of the participants in the control group, they did have neurological symptoms and signs that led the neurologist/ neurosurgeon to request an MRI.)
- An abnormal MRI with localised lesions.
- A minimum age of 18 years.

Exclusion criteria were the following:

- Participant not contactable.
- Participant not able to be assessed in Bloemfontein.
- Participant refused to participate in the study.
- The participant participated in the study, but the assessment was incomplete.
- Participant factors, such as severe lack of concentration, that led to the participant being unfit for evaluation.

Although the aim was a much higher number of participants, because of the exclusion criteria and other practical problems, 48 patients were included. Informed consent was obtained from all participants or their legal guardians. They were then assessed blindly and the psychological tests were marked and checked. An independent expert, who was blind to the diagnosis, interpreted the tests.

(b) Measuring instruments

The following measuring instruments were used:

- *Magnetic Resonance Imaging.* The MRI provides superior 3-D images of the brain without exposing the patient to ionizing radiation (Spraycar, 1995). This is currently the gold standard in structural neuro-imaging to which all other assessments (medical and psychological) are compared (C.S. de Vries, personal communication, 17 October 2002). The MRI slices are composed of voxels (the smallest computer- addressable volume in a three-dimensional object, equal to $3mm^3$). The image is then composed of pixels (picture elements) of which the intensity is proportionate to the signal intensity of the contents of the corresponding voxel (Hornak, 2002; Walker, 1995). It is clear that a lesion smaller than 3 mm in diameter will be missed. It is also interpreted by clinicians and is therefore subject to human error.
- *Psychological tests.* The following psychological tests were used:
  - *South African Wechsler Adult Intelligence Scale.* "The Wechsler tests continue to be the most widely used in neuropsychogical practice, and have generated a large body of quantitative and process-oriented studies with both adults and children" (Nell, 2000, p171). However, although the psychometric properties of the American version of the Wechsler are satisfactory (Gregory, 1992; Kaplan & Saccuzzo, 2001), the South African edition has been criticised on various grounds (Pieters & Louw, 1987; Nell, 2000). Regardless of this criticism, the South African edition is still widely used, also for neuropsychological assessment.
  - *The Folstein's Mini Mental State Examination.* This is a brief instrument designed to assess cognitive function (Mitrushina & Fuld, 1996). The test-retest reliability is high (0.827 – 0.887) and sensitivity is reported from 0.57 and specificity from 0.63. It is, however, affected by various factors such as educational level, literacy, cultural differences, linguistic ability and the presence of psychopathology such as depression (Klimidis & Tokgoz, n.d.). Validity of this test were also found to be very high for differentiating dementia from schizophrenia and depression and for monitoring the clinical improvement

of conditions such as head trauma and delirium. Results on the MMSE have a significant correlation with intelligence level, but this does not interfere with its ability to differentiate between organic states and functional syndrome (The Mini Mental State Examination, n.d.). Because of these properties, the test was also included in the assessment of the patients.

- *The Bender Gestalt Test.* This test is widely used in the diagnosis of organicity and for assessing intellectual and visual-motor functioning (Broadhurst & Phillips, 1969). Despite a vast amount of criticism, the Bender Gestalt Test continues to be ranked among the top 10 assessment instruments in terms of use (Lubin & Sands, 1992; Piotrowski, 1995). A test-retest reliability coefficient of 0.79 is reported for total scores, with a concordance rate of 86% for the occurrence of particular types of errors, and a 93% agreement rate for the diagnosis of organicity. Test-retest reliability of up to 0.9 and interscorer reliability of 0.90 – 0.92 were found (Broadhurst & Phillips, 1969). Using five copying errors as a cut-off score, it was found that the Bender Gestalt Test ruled out organicity with 92% accuracy and detected organicity with 67% accuracy (Keller & Manschreck, 1981).
- *The Grassi Block Substitute Test.* This instrument was developed to demonstrate early and late mental changes due to organic pathology, as well as impairment due to functional pathology (Grassi, 1970). It evaluates simple and complex concrete performance, as well as simple and complex abstract performance. The test-retest reliability is estimated at 0.85. The GBST has a sensitivity of 83%, but 25% of patients test false negative and 30% false positive (Ptacek & Young, 1954).

Testing was done in either Afrikaans or English, depending on the participant's preference. Translating into an African language was done in four of the cases.

(c) Statistical analysis

In order to examine the first goal of the article, the measure of agreement was determined by means of the *Kappa* (κ)*-coefficient*. This coefficient is known as Cohen's Kappa and it measures interrater agreement (Howell, 2002), which presents us with information on the reliability of the results. The higher the coefficient, the greater the agreement between the two measures.

The *Point-biserial correlation* (r_{pb}) was used to examine the second goal of the article. This coefficient is used when the relationship between dichotomic and continuous variables is being established. In this case the results of the MRI was dichotomic (absent/ present), while the scores on the psychometric tests were continuous.

Arbitrary assignment of 0 (zero) to the group without a diagnosis of cerebral lesions (absent) and 1 (one) to the group with a diagnosis of cerebral lesions (present) took place. Because of the arbitrary assignment of the codes, the sign of the correlation coefficient can be ignored. A negative correlation only indicates that the average of the group with Code 1 (one) is smaller than that of the group with Code 0 (zero), while a positive correlation indicates the opposite.

To determine the *practical significance* of statistically significant results, effect size was determined. The following guidelines by Cohen (1988) can be used to interpret the effect size:

$P = 0.1$: small effect

$P = 0.3$: medium effect

$P = 0.5$: big effect

The effect size was only determined if statistical significant results were found (on the 1%- or 5% level).

RESULTS

The results, regarding the biographical data of the participants, the difference in agreement between psychometry and MRI diagnosis for different biographical subgroups, and the correlation of different subscales of psychological tests and the MRI in different biographical subgroups will be presented next, followed by a discussion of the findings.

(a) Biographical data of the participants

Biographical information regarding the experimental (abnormal MRIs) and control groups (normal MRIs) is highlighted in Table 1.

The main biographical characteristics of the two groups were as follows:

- There were more male than female participants in both the experimental and control groups.
- Approximately half of the participants were between the ages of 20 and 35 years.
- More than 90% of the participants were either Afrikaans-speaking or speakers of an indigenous language.
- The vast majority of the participants were tested in Afrikaans.

Table 1: Biographical information of the experimental group and control group

BIOGRAPHICAL VARIABLES	Experimental group		Control group	
Gender				
Male	17	73.9	22	88.0
Female	6	26.1	3	12.0
Age				
20- 35	11	47.8	14	56.0
36- 55	8	34.8	8	32.0
56 or older	4	17.4	3	12.0
Mother tongue				
Afrikaans	11	47.8	8	32.0
Indigenous Language	10	43.5	17	68.0
Other (English, Portuguese)	2	8.6	0	0.0
Test language				
Afrikaans	19	82.6	17	68.0
English	4	17.4	8	32.0
Educational level*				
None	2	8.7	4	16.0
Primary school	5	21.7	7	28.0
Secondary school	10	43.5	12	48.0
Tertiary education	3	13.0	2	8.0
Co-morbidity				
None	8	34.8	3	12.0
Medical disorders	7	30.4	7	28.0
Psychiatric disorders	7	30.4	12	48.0
Mild mental retardation	1	4.3	3	12.0
Time lapsed since injury/scan				
1- 6 months	11	47.8	7	28.0
More than 6 months since injury/ MRI	12	52.1	18	72.0
Type of lesion				
None	0	0.0	13	52.0
Trauma (motor vehicle accident, interpersonal violence)	6	26.1	6	24.0
Tumour	3	13.0	1	4.0
Stroke	4	17.4	1	4.0
Other (central nervous system infections, epilepsy, auto-immune disorders)	10	43.5	4	16.0

* Three unknown in experimental group

- Very few participants (10.42%) had tertiary education, although the majority did have secondary school education.
- Psychiatric problems were the most frequent co-morbid condition. DSM-IV diagnoses included schizophrenia, schizo-affective disorder, bipolar mood disorder, psychosis not otherwise specified and substance abuse (mainly dagga, alcohol and analgesics). None of the participants was psychotic at the time of psychometric testing.
- Only a third of patients were evaluated psychometrically within the first six months after a diagnosis of a cerebral lesion was made or an MRI done.
- If the specific "mechanism of injury" is taken into consideration, all subgroups regarding type of lesion were represented more or less equally.

Though there was no deliberate pairing of control and experimental participants, it is clear that the two groups are comparable.

(b) The agreement between the diagnoses made by MRI versus those made by means of psychometry for different biographical subgroups

The results regarding the agreement between the diagnoses of cerebral lesions made by the MRI (absent/present) versus those made by psychometry (absent/present) are depicted according to biographical subgroups in Table 2. No statistical significant agreement between the diagnoses of cerebral lesions with MRI and psychometry were found for subgroups of participants above 55 years, native-tongue speakers, those with none or only primary school education, the group with a co-morbid psychiatric diagnosis and the groups of participants where the mechanism of injury was a stroke or due to miscellaneous factors as discussed. These groups were omitted in the table and will not be discussed further.

The following agreements *((κ)–coefficients)* between the MRI and psychometry diagnoses regarding the presence of cerebral lesions (after correcting for change) were found in the various subgroups. However, these agreements do not necessarily imply practical significance, i.e. where statistical significance refers to the ability of a result to be ascribed to chance or a sample variable. Practical significance refers to the true usefulness of the result (Steyn, 1999):

- In the case of female participants psychometry yielded more accurate results.
- Age did not have a significant influence on the results.

Table 2: Interrater agreement in different biographical subgroups.

	Diagnosis: MRI	Diagnosis: Psychometry		
Biographical subgroup		No Lesion	Lesion	**Total**
Gender				
	No Lesion	1 **(1.7)**	21	22
Male	Lesion	2	15 **(15.7)**	17
(κ) = -0.06	**Total**	3	36	**39**
	No Lesion	0 **(3.2)**	3	3
Female	Lesion	1	5 **(3.2)**	6
(κ) = -0.20	**Total**	1	8	**9**
Age				
20- 35 years	No Lesion	1 **(1.7)**	13	14
(κ) = -0.10	Lesion	2	9 **(9.7)**	11
	Total	3	22	**25**
36- 55 years	No Lesion	0 **(0.5)**	8	8
(κ) = -0.13	Lesion	1	7 **(7.5)**	8
	Total	1	15	**16**
Mother tongue				
Afrikaans	No Lesion	1 **(1.3)**	7	8
(κ) = -0.07	Lesion	2	9 **(9.3)**	11
	Total	3	16	**19**
Test language				
Afrikaans	No Lesion	1 **(1.4)**	16	17
(κ) = -0.05	Lesion	2	17 **(7.4)**	19
	Total	3	33	**36**
English	No Lesion	0 **(0.7)**	8	8
(κ) = -0.18	Lesion	1	3 **(3.7)**	4
	Total	1	11	**12**
Educational level				
Secondary school	No Lesion	1 (1.6)	11	12
(κ) = -0.10	Lesion	2	8 (8.6)	10
	Total	3	19	**22**
Tertiary education	No Lesion	0 **(0.4)**	2	2
(κ) = -0.36	Lesion	1	2 **(2.4)**	3
	Total	1	4	**5**
Co-morbidity				
None	No Lesion	0 **(0.8)**	3	3
(κ) = -0.29	Lesion	3	5 **(5.8)**	8
	Total	3	8	**11**
Medical	No Lesion	1 **(0.5)**	6	7
(κ) = 0.14	Lesion	0	7 **(6.5)**	7
	Total	1	13	**14**
Time period				
1- 6 months	No Lesion	0 **(1.8)**	7	7
(κ) = -0.21	Lesion	2	9 **(9.8)**	11
	Total	2	16	**18**
> 6 months	No Lesion	**1 (1.2)**	17	18
(κ) = -0.02	Lesion	1	**11 (11.2)**	12
	Total	2	28	**30**
Type of lesion				
None	No Lesion	1 **(0.85)**	10	11
(κ) = 0.03	Lesion	0	2 **(1.85)**	2
	Total	1	12	**13**
Trauma	No Lesion	0 **(1.0)**	6	6
(κ) = -0.33	Lesion	2	4 **(5.0)**	6
	Total	2	10	**12**
Stroke	No Lesion	0 **(0.2)**	1	1
(κ) = -0.25	Lesion	1	3 **(3.2)**	4
	Total	1	4	**5**

- In Afrikaans-speaking participants a slight agreement was found between diagnoses made by means of psychometry and MRI.
- Assessment in English was more than three times as accurate as assessment in Afrikaans.
- Tertiary education also had a positive influence on the accuracy of assessment by means of psychometry.
- Co-morbidity clearly affected the agreement between psychometric and MRI diagnoses adversely.
- A time lapse of less than 6 months between MRI diagnosis and psychometrical assessment improved the agreement between the two diagnoses significantly.
- The type of lesion (when present) did not have a significant influence on the results.

(c) Correlation between psychological test subscales and the MRI diagnoses in different participant subgroups

The subscales of the four psychological tests with a significant correlation on the 1% and 5% levels with the MRI diagnosis, for the different subgroups of participants (as discussed in b), are depicted in Table 3. Subtests with no statistical significant correlation will not be discussed further.

The main findings for the different subscales were as follows:

- The South African Wechsler Adult Intelligence Scale practical subscales seem more applicable in the diagnoses of cerebral lesions, especially *digit/symbol* coding.
- The Folstein's Mini Mental State Examination also had a very high correlation with MRI diagnoses in the presence of tertiary education and when no lesions were present.
- The Bender Gestalt Test continuously revealed high correlation with the MRI diagnoses through all subgroups. The correlation with education, though, is conspicuous.
- The Grassi Block Substitute Test behaviour score seems more accurate in the presence of strokes than trauma.

Table 3: Correlation of psychological test subscales with the MRI diagnosis in different participant subgroups.

Biographical group	Subscale	MRI		Subscale	MRI
Gender			Co-morbidity		
Male	Bender Gestalt: integration	0.34	None	Bender Gestalt: gaps	0.77*
	Bender Gestalt: additions	0.34	Medical	Grassi: behaviour	0.62
Female	Bender Gestalt: gaps	0.76	Psychiatric	Mini Mental: total	0.48
Age				Bender Gestalt: gaps	0.49
20 – 35	Grassi: behaviour	0.40		Bender Gestalt: contact	0.50
36- 55	Mini Mental: recall	0.52		Wechsler: general comprehension	0.52
55 or older	Bender Gestalt: gaps	0.75		Wechsler: digit/symbol	0.51
Cultural group			Time interval		
Afrikaans	Bender Gestalt: separation	0.55	1- 6 months	Bender Gestalt: separation	0.37
	Bender Gestalt: additions	0.70*		Bender Gestalt: integration	0.37
	Bender Gestalt: absence erase	0.57		Bender gestalt: additions	0.42
	Wechsler: picture arrangement	0.47	Mechanism of injury		
Indigenous	Grassi: behaviour	0.40	None	Mini Mental: comprehension	0.77*
	Wechsler: digit/symbol	0.47	Trauma	Bender Gestalt: separation	0.68
Test Language				Bender Gestalt: integration	0.64
Afrikaans	Bender Gestalt: separation	0.42		Bender Gestalt: decreases	0.68
	Bender Gestalt: additions	0.37		Bender Gestalt: deletions	0.68
	Wechsler: picture arrangement	0.34		Bender Gestalt: gaps	0.57
English	Bender Gestalt: closure	0.63		Bender Gestalt: additions	0.71*
Education			Stroke	Grassi: behaviour	0.99*
None	Mini mental: recall	0.87			
	Bender Gestalt: transformation	0.99*			
	Bender Gestalt: absence erasing	0.99*			
Tertiary	Mini Mental: comprehension	0.92			
	Bender Gestalt: separation	0.99*			
	Bender Gestalt: additions	0.99*			

* p <= 0.01   p <= 0.05

DISCUSSION

No statistically significant agreement between the diagnoses of cerebral lesions with MRI and psychometry were found for subgroups of participants above 55 years, though the sensitive subscales differed among age groups. Concerning participants above the age of 55 years, there was a significant correlation between the Bender Gestalt Test and the MRI. As visual acuity is important in this test, poor vision might have had a confounding influence. The lack of correlation of injuries in older participants with verbal subscales supports the findings of previous researchers such as Heaton, Ryan, Grant & Matthews (1996). Female participants also had a better agreement between MRI and psychometry diagnoses, although due to the small sample size no definitive conclusion can be drawn. Afrikaans as mother tongue also seems to be a positive, but still weak, predictor of accuracy of findings. The strong correlation between the use of English as test language and the MRI diagnoses may be due to the small subgroup of participants tested in English. The practical subscales of the South African Wechsler Adult Intelligence Scale are less sensitive to cultural influences. The influence of educational level was marked for the group with no and the group with tertiary education. This supports the findings of Lannoo and Vingerhoets (1997) and Reitan and Wolfson (1995). Again the standardisation of the tests used has to be taken into consideration. Certain baseline scholastic skills, e.g. writing and copying of designs, are necessary for the successful completion of the psychological tests used. It is also clear that co-morbidity is a significant confounding factor in respect of test accuracy that can affect functioning negatively (Girard *et al.*, 1996).

Though it seems that the mechanism of injury did not play a significant role in the agreement between MRI and psychometric diagnosis, the groups did differ, e.g. the group with strokes showed a stronger correlation with the Grassi Block Substitute Test, while those with trauma showed a significant correlation with the Bender Gestalt Test. This might be due to the different localisation of injuries, as the group with traumatic lesions were more prone to frontal and temporal lobe injuries. While this group therefore made more mistakes on the Bender Gestalt Test, they tended to be less aware of their problems and therefore scored lower on the Grassi Behavioural Subscale, e.g. due to asking for less repetition of instructions and reassurance. It is also important to note the strong correlation between injuries less than six months old. This can be attributed to the plasticity of the brain and also to the rehabilitation process of patients (Kay & Lezak, 1990). After a period it is therefore more difficult to diagnose minor problems in respect of functioning in patients with cerebral injuries.

It is also clear that the Bender Gestalt Test overshadowed the other tests used in this study. The Bender Gestalt Test does not require that the testee possess a lot of skills – only the basic scholastic abilities of holding a pencil, using an eraser and copying deigns. In the application of the Bender, language also does not seem to be very important. It is therefore less culturally biased than the other tests used. It is also a brief test and patients with poor concentration are not unfairly discriminated against. This finding is comparable to that of previous studies of the Bender's reliability and validity (Broadhurst & Phillips, 1969). Though the Folstein's Mini Mental State

Examination is one of the most widely used tests, it did not seem to have any clear benefit, except in evaluating a patient's memory.

CONCLUSION

The findings of this study regarding the agreement between the diagnoses of cerebral lesions made by means of psychological tests and the diagnoses made by MRI in different subgroups should be interpreted with care. Because of the small sample size and skewness of the sample, the results may not be an accurate representation of the reliability and validity of psychoneurological assessment. The use of tests that may not be culture-fair could also have influenced the results.

Patient variables with a significant influence on the results seem to be educational level, co-morbidity and culture. It is therefore crucial to develop tests that are culture-fair or to stick to those tests that seem to be less influenced by culture and education, e.g. the Bender Gestalt Test.

The type of lesion seems to have an effect on the agreement between the psychometrical evaluation and the MRI diagnosis, but this can be ascribed to the different localisation of the lesions and the more widespread effect of trauma (primary and secondary injuries). The plasticity of the brain must also be kept in mind and a patient should not be "sentenced" to the current diagnosis, but rather re-evaluated at intervals to determine the effectiveness of rehabilitation programmes.

The use of only one interpreter who had to interpret the results blindly (which is in contrast with the "real-life" situation), together with the small and skewed sample could have influenced the results negatively. Better trained professionals could have made better diagnoses. However, the fact remains that many professionals who are not well-trained conduct and interpret these tests in practice. This can lead to unreliable and invalid diagnoses.

The results of this investigation suggest that the injudicious use of psychometrical instruments not standardised for different cultural groups, especially by untrained individuals, could result in an unacceptably high diagnostic rate of neuropsychological impairment in otherwise healthy patients. Though the accuracy of neuropsychological assessment seems disappointingly low, it could contribute crucial information regarding the functional impairment of the patient as well as the probability of the presence of structural cerebral lesions and therefore may be useful in deciding whether to request a neuro-imaging study.

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