Neuropsychological evidence for subjective memory complaints in the neurologically well individual

M D Lucas, PhD
Sterkfontein Hospital, Krugersdorp, Gauteng

Background. Subjective memory and concentration difficulties are frequently expressed in modern society and, if sufficiently worrying, may elicit a medical consultation for elucidation. When a clear explanation cannot be given, a neuropsychological assessment may be a useful tool.

Method. The present naturalistic study recruited 20 patients who reported cognitive difficulties for which a medical explanation could not be found. Each subject underwent a clinical interview and neuropsychological assessment in order to identify the nature and severity of the problem, and to identify a possible cause of these complaints.

Results. Several possible explanations were documented but mood disturbance was considered the most likely reason for the identified cognitive difficulties.

Limitations. This was a naturalistic study with a specific sample, and consequently generalisability may be reduced.

Conclusion. Even in episodes of mild depression cognitive difficulties occur that may be presented to neurologists rather than psychiatrists. In such instances the patient is at risk of not receiving the appropriate treatment for his or her mood disorder.

Neuropsychology is the clinical science concerned with relationships between brain function and behaviour. Neuropsychological assessment comprises a detailed and comprehensive clinical interview accompanied by psychometric testing. It is a powerful tool in the clinical armamentarium, using both quantitative and qualitative methods to identify the nature and severity of a neuropsychological problem, make a diagnosis, and guide patient care and treatment.[1] It can be used for a wide variety of reasons, including the assessment and explanation of subjective cognitive difficulties for which a medical explanation cannot be found.

Typical examples of such difficulties are memory and concentration problems, which present as common complaints in modern society. Characteristically this takes the form of problems such as forgetting what was done 30 minutes previously, or forgetting appointments or what had been read in a book. Instructions are forgotten and doubts are raised about the locking of doors or the completion of specific chores. When such experiences become perturbing, a medical practitioner may be consulted for an explanation.

The present paper is a naturalistic study regarding the outcome of a small group of individuals who were worried about such memory and concentration difficulties. This particular group consulted a Johannesburg neurology practice. When no obvious explanation could be found after a full clinical and radiological examination, they were referred for a neuropsychological assessment, primarily to allay their worries.

Method

Subjects

Subjects were drawn from patients referred from a Johannesburg neurology practice for neuropsychological assessment. Over a 30-month period, from January 1999, the files of 20 patients were identified who met the criteria of reporting subjective memory and concentration difficulties for which no neurological explanation had been found. All were Caucasian and English-speaking.

Procedure

All patients referred for neuropsychological assessment first undergo a semi-structured clinical interview in which specific, but open-ended questions are asked of each patient. This elicits information on demographic data, the nature of the problem that provoked consultation with a neurologist, and medical and psychological / psychiatric history. Patients are specifically asked about previous head injuries, any periods of loss of consciousness, ongoing stressors, serious and / or chronic illnesses and current medication. In the present study, files were excluded for patients who had reported any of the above possible explanations for the cognitive

complaints. In addition, the Beck Depression Inventory (BDI)[2] is administered. A score of 10 or less is considered within a normal range of daily ups and downs. Scores of 11 - 16 are indicative of mild mood disturbances, and a score greater than 17 is a strong indication of depression.

After the clinical interview a psychometric evaluation is done. Neuropsychological test batteries are usually individualised to a patient's complaints.[1] However, as the starting point, a basic battery is generally administered which includes tests of attention, learning and memory function, visuomotor and visuospatial ability, conceptual reasoning and executive function. The tests used in the basic battery comprised the following: Information and orientation subtest of the Wechsler Memory Scale, Revised (WMS-R), mental control subtest from the WMS-R, digit span subtest from the WMS-R, Stroop Color / Word Test, Trail Making Test, logical memory subtest from the WMS-R, verbal paired associate subtest from the WMS-R, Rey Auditory Verbal Learning Test (RAVLT), Rey Complex Figure (RCF), visual reproduction subtest of the WMS-R, free drawing (bicycle), Modified Wisconsin Card Sorting Test (MWCST), Boston Naming Test, and Controlled Oral Word Association Test (COWAT).

The tests are all commonly used measures of cognitive function in the South African context. Lezak[1] and Spreen and Strauss[3] were the main sources of test function identification and these texts should be consulted for a more detailed explanation of each test. Administration and scoring measures were carried out in terms of the recommendations of the authors and developers of each test. Several of the tests have American origins; as the test scores of English-speaking South Africans have been found to compare favourably with American normative scores,[4] these norms were used in the present study.

Statistical analysis

In a neuropsychological evaluation each patient must be treated as an individual.[1] Consequently, individual analysis of test scores was undertaken. The presence of possible impairment was considered when a subject had two or more test scores at least one standard deviation (SD) below the mean.[5] Although this is a narrow definition, it seemed appropriate in the light of the above-average years of education in this group. Level of achievement on virtually every neuropsychological test is influenced by education level.[1]

Results

Demographic data

There were 12 women and 8 men in this study. The average years of education were 13.95 (SD 2.31, range 11 - 18 years). The mean age of this group was 49.8 years (SD 6.5, range 31 - 59 years).

Test scores

Of the 20 subjects in this study, half had two or more test scores that fell one SD or more below the mean. This would suggest that 50% of the sample had cognitive dysfunction which could be objectively identified. To have 50% of the sample with such scores is far greater than the expected base rate of 5 - 10% impairment expected in a generally well population.[6] The number of impaired scores per individual ranged from two to seven, with a mean of 4.1 scores.

The most frequently impaired function was in the domain of verbal memory, with deficits present in the test performance of 9 subjects. Memory is not a homogeneous function but involves a complex system of modality-specific learning, storage, and retrieval of previously experienced information.[1] The impairment found in the present study lay in the area of retrieval of new learned verbal information rather than encoding or storage. In addition, retrieval difficulties were accompanied by a high number of errors and repetitions made on the memory tests suggesting difficulties with response inhibition. There was also evidence of impaired divided attention (also referred to as mental flexibility)[7] in 6 subjects. To a lesser extent impaired visual learning and retrieval (2 subjects), visuoconstruction difficulties (2 subjects), and naming and word generation (3 subjects) were identified.

Semi-structured interview data

The information gained from the semi-structured interview was evaluated for possible explanations for cognitive impairment. Several possible reasons were identified, including chronic headaches and migraine, mild concussion, stressors, history of depression, current mood disturbances and current depression.

Half the subjects reported a history of chronic headaches and / or migraine, but presence of these symptoms did not correlate with cognitive impairment ($p > 0.05$). Eleven subjects perceived themselves to be under considerable stress. For example, 4 subjects had family problems, and difficulties in the workplace were cited by several others. However, presence of stressors did not correlate with cognitive impairment ($p > 0.05$). Four subjects reported

mild episodes of concussive confusion lasting less than 20 minutes and generally occurring in childhood, with no subjective consequences. This did not correlate with cognitive impairment ($p > 0.05$).

On the BDI, 6 subjects scored in the mood disturbance range and 7 described themselves as depressed. Of these 13 subjects, 9 reported previous episodes of depression. A significant positive correlation was found between scores on the BDI and number of test scores in the designated impaired range ($r = 0.4010$, $p < 0.05$).

Individual inspection of results of this small sample revealed that 10 of the 13 subjects with scores outside of the normal range (scores > 10) on the BDI had two or more test scores that fell at least one SD below the norm. Conversely, all subjects with defined cognitive impairment had a score on the BDI at least indicative of mood disturbances.

With regard to previous history of depression, a trend towards a significant correlation between history of depression and current cognitive impairment was found using the chi-square test ($p = 0.0736$).

Four subjects were actively taking psychotropic medication; another 4 subjects had been prescribed medication but had ceased taking it. All medications were of the selected serotonin re-uptake inhibitor (SSRI) type.

Discussion

The results of the present study showed that of those who consulted a neurologist for memory and concentration deficits, objective support for their complaints was found for half the subjects. Furthermore, all who were identified with cognitive dysfunction recorded disturbances of mood and depression. A positive correlation was found between severity of mood disorder and number of cognitive deficits.

Thus it was possible, with the use of a neuropsychological evaluation, to identify the extent and severity of cognitive dysfunction in this group of patients. Furthermore, a reasonable explanation could be given for the cognitive dysfunction using both quantitative and qualitative neuropsychological assessment techniques.

A variety of cognitive difficulties has been described in depression, particularly in the areas of learning, retention and retrieval of verbal and non-verbal facts, visuomotor and visuospatial functions and divided attention (mental flexibility and control).[7] The cognitive difficulties identified in the present study were generally congruent with the deficits typically found in depression. Cognitive deficits form part of the diagnostic criteria for depression and the *Diagnostic and Statistical Manual IV* (*DSM-IV*)[8] cites diminished ability to think or concentrate, or indecisiveness nearly every day as part of the diagnostic criteria. Although the results of the present study could therefore be considered predictable, several issues arise regarding these results in the light of very recent research.

Firstly, age of patients may have been an influencing factor in their increased awareness of memory difficulties. Dopamine metabolism in the frontal and cingulate areas declines in middle age and is associated with detrimental cognitive changes.[9] The nature of these changes is similar to that seen in depression.[7] In fact both frontal lobe dysfunction and dopamine metabolism have been implicated in major depression.[10-12] Dysfunction in these structures is associated with impaired executive skills (poor ability to plan and engage in purposive action, perseveration, ineffective performance, and inability to organise cognitive activities temporally), impairments of verbal and design fluency, complex attention deficits including mental flexibility and response inhibition, and memory deficits of retrieval rather than encoding type.[1,3] Several of these difficulties characterise the cognitive impairment in the present study, in which the age of the subjects ranged from 31 to 59 years, averaging around 50 years.

A second and even more worrying concern is the long-term consequences of depression on brain function. Historically, it has generally been thought that cognitive impairment in depression has a pathophysiological basis that is reversible with symptom resolution. However, more recent research has suggested that possible irreversible long-term implications in middle-aged subjects with chronic unipolar depression may also occur.[13] A variety of possible explanations have been postulated including developmental abnormalities, and raised levels of cortisol leading to hippocampal neuronal death, which in turn cause dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis.

Another study has shown that euthymic subjects with a history of depression showed reduced hippocampal volume on magnetic resonance imaging when compared with a control group.[14] Again the stress HPA hypothesis was postulated. In the present study 9 subjects both had a history of depression and scored above 10 on the BDI. Although there were no data available in the present research to comment on volume changes in cortical structures, possible permanent changes to brain functioning could have occurred. This is disturbing as cerebral reduction may have an impact on the rate and nature of further cognitive decline in this group.

In conclusion, the results of this study suggest that when a middle-aged client experiences memory and concentration difficulties, and no reasonable explanation can be found after a thorough medical investigation, a neuropsychological assessment contributes to clarification. The present study found that in half the cases, objective support could be found to uphold patients' complaints. Negative mood changes appeared to be the most likely explanation for the cognitive dysfunction found.

It would seem that many individuals in this group were aware of their mood disturbances as up to 8 subjects had either received or were taking relevant medication. Yet it is interesting that these individuals apparently did not make a connection between their depressed mood state and their cognitive complaints. Instead they took their subjective symptoms of memory and concentration loss to a neurologist. All professionals in the field of central nervous system disorders need to be aware of this dissonance when treating unexplained cognitive complaints. In the absence of overt neurological features, depression must be considered a likely cause. Appropriate intervention is vital, particularly as possible irreversible changes to the brain structures may occur.

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