Neuropsychological deficits associated with uraemic encephalopathy

A report of 5 patients

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Summary

Although uraemic patients with end-stage renal disease (ESRD) often present with impaired cognitive functions, little information exists concerning the identification of some of the neuropsychological processes underlying overt behaviour that affect adjustment to ESRD. The results of a neuropsychological investigation of a sample of adult patients with ESRD, before being accepted for dialysis, is documented in order to determine their altered neuropsychological status, since this may have a bearing on patient management and compliance. The patients were assessed by a single-case study methodology and the Luria-Nebraska Neuropsychological Battery in which parts requiring verbal patient response were taped for later detailed analysis. Neuropsychological complications occurred in conjunction with high urea levels in all patients, indicating varying degrees of impaired performance in motor, tactile, receptive language, arithmetic, and intellectual functions. A common underlying pattern of performance decrement revolved around disturbed spatial synthesis and orientation in relation to visual perception, activity, logical-grammatical and arithmetical operations, and in intellectual tasks requiring identification of visual signs and spatial organisation. Further research is necessary to establish a possible correlation between physiological, biochemical and neuropsychological indices, and to compare neuropsychological differences between patients on different forms of treatment for ESRD.

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Neurological changes associated with uraemic and dialysis patients include dialysis encephalopathy related to aluminium toxicity,[1] cerebral disorders (uraemic encephalopathy, encephalopathy due to electrolyte disturbances and acidosis, disequilibrium syndrome, Wernicke's syndrome and drug-induced encephalopathy, cerebrovascular disorders, central nervous system infections, and response to anticonvulsants), peripheral neuropathies (uraemic polyneuropathy and mononeuropathy), and specific neurological aspects.[2] Consequently, clinical neuropsychological assessment of patients who present with both treated and untreated uraemia has developed as an important aspect of the psychological investigation of patients with end-stage renal disease (ESRD).[2,3] Neurobehavioural probes have demonstrated variations in nervous system functioning, which show clinical differences between normal subjects and treated and untreated patients with ESRD.[4] Studies[3,5] have also attempted to establish biochemical indices, such as correlations that have been reported between elevated serum creatinine levels and quantitative neuropsychological test findings, that might act as predictors of neurotoxic impairment in uraemic patients.

A number of studies[6-8] have demonstrated that uraemic patients as well as dialysands with ESRD present with impairment of many specific cognitive functions.[9,10] Potential neurotoxic complications in these patients seem to be particularly associated with: (*i*) deficit in intelligence (notably a deterioration in total IQ scores partly due to slowness in performance tests, performance IQ being a measure of the ability to accomplish relatively new tasks involving visuospatial components during conditions of time-pressure); (*ii*) deficit in attentional processes (especially concentration between dialysis intervals despite usual apparent adequate mental tracking abilities in patients on examination); (*iii*) deficit in memory and information processing capacities (especially in registration, learning and reproduction of recently acquired data rather than long-term retrieval); (*iv*) mild nonspecific deficit in language function in the form of word finding difficulty and written language, which may suffer control errors in, for example, anticipations and perseveration or lack of number structure (although clear-cut dyscalculia is infrequent) when writing dictated numbers; (*v*) mild deviations in gnosis and praxis (although these areas are usually intact) as in left-right mirroring and constructional disorders; and (*vi*) manifestations of the disequilibrium syndrome seen in increased prominence of irritability and restlessness towards the end of dialysis.[2,4,8,11,12]

Despite such indications of impaired neuropsychological functions resulting from ESRD, little information to date concerns the identification of possible basic neuropsychological processes underlying the overt behaviour described,[13] and few prospective studies compare cognition before, during and after dialysis.[2] In addition to certain other factors, such as specific personality variables, these cognitive deficits have important implications for patient compliance and management,[14] especially as encephalopathies of different aetiologies may result in the total neuropsychological symptom picture seen.[2] For an accurate evaluation of impaired cognitive efficiency, a complete neuropsychological assessment therefore becomes a prerequisite,[2] not only in dialysands but also in pre-dialysis uraemic patients. Although quantitative neuropsychological techniques have made it possible formally to investigate neurotoxic impairment and neurobehavioural outcomes in uraemic patients with ESRD and response to treatment,[4,8] further research is urgently needed. We still, for example, do not have sufficient knowledge of psychological problems associated with dialysis[15] and have therefore been unable to devise optimal psychological treatment methods to decrease patient stress in ESRD and its management.[16] Neuropsychological and neurobehavioural phenomena should be measured quantitatively in order to: facilitate objective estimation of the patients' successes in achieving the goal of maintenance dialysis treatment; assess the comparative adequacy of dialysis regimens regarding diminishing neuropsychological fall-out; and to provide objective end-point measures for further neuropsychological investigations of uraemic manifestations.[5,8,12]

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The present study, expanding on a preliminary communication,[8] was designed to assess objectively the effects of the uraemic state on neuropsychological functioning with a view to identifying basic neuropsychological processes underlying the overt impaired neurobehavioural dysfunctions that have implications for comprehensive patient management.

Patients and methods

The study was conducted in the Renal Unit and Department of Psychiatry, Addington Hospital, Durban. It is part of an ongoing series of psychological and neuropsychological investigations of patients with ESRD on various modalities of renal substitution treatment.[8,10,12,14,15,17] Because of the in-depth, time-consuming, single-case study methodology used, a total of 5 patients who were randomly selected for the study was considered adequate. The value of applying single-case methodology to the assessment of treatment benefits in medical psychology has been cogently argued.[18] The patients' ages ranged from 31 years to 62 years, and all had had a tertiary education. There were 4 men and 1 woman, this proportion being determined by patient availability. Their average predialysis history of ESRD did not differ significantly and, other than their uraemic state, their medical histories revealed no condition of note, such as Alzheimer's disease, cerebrovascular accidents, metabolic disturbances, head injuries, alcohol abuse, etc. that could account for any cognitive impairment. All 5 patients were accepted for dialysis on a chronic renal failure programme after careful screening by the Renal Unit team who also found them psychologically suitable. The patients were neuropsychologically assessed before their first dialysis.

Informed written consent for inclusion in the study was obtained from all patients. The patients were assessed individually using a mental status examination and the Luria-Nebraska Neuropsychological Battery (LNNB). This neuropsychological procedure was selected because: (*i*) it has been shown to be a valid, non-invasive neurodiagnostic technique; (*ii*) the subtests that have been selected sample the majority of abilities relevant to cerebral functioning; (*iii*) it is sensitive to a wide variety of neurological dysfunctions; (*iv*) the conversion of raw to standard scores facilitates comparison of the patients' scores on individual subtests with each other, provides a quantitative baseline for reassessment, and enables inter-patient performance comparisons; and (*v*) the qualitative approach advocated as an integral part of the LNNB assessment procedure allows for further exploration of performance with the aim of understanding its psychological basis in terms of cerebral function and in individuals who recover without structural damage to the brain. It is this qualitative analysis that may identify specific areas, reflecting residual damage, in the absence of elevations of the scale scores.

All assessments were done according to the instructions given in the LNNB manual.[19] A few minor substitutions were included to replace some of the items found to be ineffective with English-speaking South African adults. In addition, all parts of the test that required the patient to talk were taped in order to make possible a later detailed individual analysis of the responses.

TABLE I. NEUROPSYCHOLOGICAL DEFICITS IN URAEMIA ($N = 5$)

Area of functioning	No. of patients
Motor functioning	
Simple motor movements requiring spatial organisation (displaying a tendency to mirror-image)	3
Complex motor tasks involving sequential behaviour (dynamic organisation)	2
Construction dyspraxia	4
Oral praxis	1
Accousticomotor (rhythm)	
(no significant impairment displayed by any patients)	—
Tactile	
Mild disturbances in tactile spatial discrimination (2-point threshold) and tactile sensation	3
Stereognosis: predominant difficulty in meeting the requirements (indicative of residual parietal lobe dysfunction)	3
Visual	
Although basic visual skills were intact, impairment in visual recognition, visual orientation with regard to spatial relationships, and spatial synthesis underlying constructive activity and intellectual operations in space were evident	5
Receptive speech	
Impairment in performance requiring complex logical grammatical structures	5
Expressive speech	
Complex grammatical explanations	2
Reading	
No notable impairment	—
Writing	
No notable impairment	—
Arithmetic	
Mild impairment with regard to spatially orientated operations (difficulty in maintaining the integral whole in the course of arithmetic operations)	3
Memory	
Basically intact, but some diffuse impairment in short-term and immediate memory modalities were nonspecific (visual, rhythmic, tactile)	4
Impairment in immediate sensory trace recall	1
Intellectual functions	
Difficulty in understanding and explaining thematic pictures and texts	4
Difficulty in discerning emotional tone	2
Impaired concept formation	5
Discursive intellectual activity impaired	3

Results

For ease of reference, results are presented within broad areas of functioning in Table I.

Apart from the previously reported difficulties these patients have in the areas of intelligence, memory and attentional processes,[11] we found evidence of additional cerebral concomitants of uraemia. Our findings indicated impaired performance, to varying degrees, in the areas of motor, tactile, receptive language, arithmetic and intellectual functions as indicated in Table I. Furthermore, from Table I it can be seen that only items sensitive to visual spatial synthesis are characteristically impaired across the group of patients. Other tasks sensitive to response time, without the element of visual spatial synthesis, do not indicate any impairment across the group of patients. Thus the underlying pattern of performance decrement common to all 5 patients was not found to be due to other

factors, such as slowed response time, but instead primarily revolved around disturbances of different types of spatial syntheses, that is, disturbed spatial syntheses and orientation in relation to visual perception, activity, speech processes (in logical-grammatical operations and arithmetical operations), and in intellectual functions that require the identification of visual signs and their spatial organisation.

Discussion

The clinical picture in uraemic patients allows for a distinction between two main areas of neurological changes, those concerned with motor disturbances (such as tremulousness, asterixis and myoclonus) and those concerned with complex mental functions and level of consciousness.[2] Given the results discussed here, it is tentatively suggested that, in the patients studied, deficits appeared on tasks involving functions associated with the posterior cortex, mainly with parietal, parieto-occipital and/or inferoparietal lobe activity. Although this has to be verified by further research, it is consistent with our previous findings.[8] It is postulated that the present study, unlike some others, suggests a core pathological process (namely a primary disturbance of visual-spatial synthesis) underlying the various cognitive deficits that have been noted previously in uraemic encephalopathy.

Prominent changes in the higher cognitive functions have, however, also been associated with the ageing process and other aetiologies, such as hepatic and diabetic encephalopathies. In order to describe these findings as characteristic of the uraemic syndrome, additional research involving larger samples and younger uraemic patients is required to distinguish these effects from those of conditions associated with other aetiologies, specifically the ageing process. In addition, we concur that further research should be done in an attempt to establish a correlation between physiological, biochemical and neuropsychological indices.[11,20] There is also a need to compare possible differences in the aetiology of ESRD and the neuropsychological status of patients on different treatment modalities for ESRD. There has, for example, been some evidence to show a relationship between organic mental disorder and analgesic nephropathy, which affects pre-dialysis neuropsychological status,[21] that a reduction in cognitive inefficiency occurs after successful dialysis, and that higher general intellectual levels with less marked pre-dialysis cognitive dysfunction appear to facilitate more rapid treatment adjustment and adherence behaviour,[2,14] although the long-term predictive value of these factors is uncertain. The present preliminary findings in our study add another step in this direction and in our attempt to understand the psychological adjustment of patients to a chronic disease and its management.

Although lesions associated with uraemic encephalopathy can be reversed in some patients after efficient dialysis, and the nature of the uraemic toxins is still a matter of dispute,[2] the present findings have several practical implications. These include: (*i*) a possible reason why pre-dialysis patients often claim not to have had the consequences of the renal programme explained to them in detail, apart from inordinately employing psychological defence mechanisms such as denial;[14,15] (*ii*) awareness by the renal unit staff that these cerebral dysfunctions are present, which could facilitate enhanced patient management (for example, by not giving detailed instructions/explanations while the patients are uraemic); (*iii*) the potential for better management of the non-compliant patient who is often seen as either a difficult patient or as one who has given up hope; and (*iv*) the need for careful assessment of such a patient (in order to determine how much of the non-compliant behaviour is functional or psychoneurological in origin), which could have important ramifications for the formulation of a treatment strategy. Finally, these findings illustrate the value of a comprehensive psychonephrology service[14,15] in which the adequacy of dialysis can be monitored by repeated neuropsychological assessments (since cognition-dependent indices vary directly with the degree of uraemia), including the use of choice reaction time and continuous performance tests, which are known to be sensitive indices.[2,3]

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