

Neuropsychology – testing the brain

SALLIE BAXENDALE

Institute of Neurology, University College London, National Hospital for Neurology and Neurosurgery, Queen Square, London, and National Society for Epilepsy, Chalfont St Peter, Bucks

Defining and testing cognitive function

Cognitive function is the process by which an individual takes in information about the world, makes sense of it and acts upon it. Neuropsychological tests traditionally assess function in five cognitive domains, all of which can dissociate in the pathological brain. These are intelligence, language, memory, perception and executive functions. A large number of skills comprise each domain. For example, memory tests can assess the learning, recall or recognition of different types of material presented during the testing session, in addition to long-term autobiographical recall and prospective memory skills. The distinction between declarative memory, (encompassing episodic memory – the recollection of experiences and episodes, and semantic memory – knowledge of the world) and procedural memory (remembering how to do something, e.g. riding a bicycle) can also be made. Again, all of these abilities have been shown to dissociate in patients with focal lesions.

The majority neuropsychological tests tap multiple skills from more than one domain. For example, success on a complex figure recall task, ostensibly a visual memory test, also requires intact perception and adequate comprehension, concentration and praxis. It follows therefore that failure on this test may be the result of a breakdown in any one or a number of these processes. The aim of the neuropsychological assessment is not only to identify and quantify deficits in cognitive function, but more importantly to try to identify which processes are breaking down and responsible for the dysfunction. This is normally achieved by the careful interpretation of an individual's performance and scores on a wide range of tests.

When is neuropsychology useful in epilepsy?

Like many other investigations at the neurologist's disposal, neuropsychological test results rarely stand alone but are interpreted in relation to both the clinical question being asked (be it a diagnostic issue, the lateralisation or localisation of dysfunction, or the planning of an intervention) and the results from other investigations. The overall value of a neuropsychological assessment therefore very much depends on the validity of the questions being asked and the availability of other relevant data.

In patients with epilepsy, neuropsychological assessments are most frequently used to aid diagnosis, evaluate the cognitive side effects of antiepileptic medications and monitor the cognitive decline associated with some epileptic disorders. In conjunction with MRI and other presurgical investigations, neuropsychological scores are also used to assess the suitability of patients for epilepsy surgery and can be used to predict post-operative outcome, both in terms of cognitive change and seizure control.

In an ideal world, all newly diagnosed patients with epilepsy would undergo a brief neuropsychological screen prior to starting treatment. Whilst this may not provide significant additional diagnostic information at the time, it creates a valuable baseline against which future assessments can be measured. Serial neuropsychological assessments can be used to evaluate the cognitive side effects of new or existing antiepileptic drug (AED) regimens and to monitor the cognitive deterioration that may be associated with long-term poorly controlled epilepsy and episodes of status. They can also contribute to the diagnostic process. However, repeated assessments over a short period of time can lead to the development of practice effects which can mask deterioration in function. In most patients it is therefore recommended that there is at least a six-month interval between assessments to maximise the validity and utility of the results. Single assessments can be useful in the localisation of cognitive dysfunction associated with focal pathologies and also enable the setting of realistic education and employment goals. Single assessments may also reveal deficits that are amenable to rehabilitation.

Neuropsychological tools

General intellectual functioning

The majority of the tests used in the standard neuropsychological assessment remain pencil and paper, desktop tasks, though the use of computerised tasks is becoming more widespread. Almost all assessments will include the current gold-standard measure of general intellectual functioning in adults, the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III). The WAIS-III gives three measures of general intellectual functioning: a verbal IQ (VIQ), performance IQ (PIQ) and a full-scale IQ. The WAIS-III IQ distributions are constructed to have a mean of 100 and a standard deviation of 15 IQ points. An IQ of 100 therefore defines the performance of an average, healthy, adult at that age. Approximately two-thirds of the adult population obtain IQs between 115 and 85, one standard deviation above and below the mean, respectively. Any IQ between 80 and 119 is usually classified as falling within the average range. See Table I for the most frequently used IQ classifications.

Table I. General Intelligence Classifications (adapted from Wechsler, 1981)¹⁴.

IQ	Percentage of the population	Classification
130 and above	2.2%	Very superior
120–129	6.7%	Superior
110–119	16.1%	High average
90–109	50%	Average
80–89	16.1%	Low average
70–79	6.7%	Borderline
69 and below (50–69) (35–49) (20–34) (below 20)	2.2%	Extremely low (Mild) (Moderate) (Severe) (Profound)

Memory

Memory tests are most frequently divided into three groups: verbal, visual and behavioural memory tasks. The most frequently used verbal memory tests include story recall and list-learning tasks. In these tests the patient is typically read a short, local-news type story and asked to recall as much detail as they can immediately after they have heard it and again following a delay of between 30 minutes and an hour. List-learning tasks typically test an individual's ability to learn a list of 15–20 words over a number of trials and frequently include recall and or recognition conditions following distraction or a delay. Analogous tasks involving non-verbal material include complex figure-recall tasks and design-learning tasks. In the former an individual is required to copy a complex geometric figure and then reproduce as much as they can immediately afterwards and again following a delay of up to an hour. Behavioural memory tests are generally thought to be more ecologically valid in that they test 'everyday memory' skills, such as putting a name to a face and remembering appointments or to post a letter. Tests are also available to examine retrieval from long-term memory store, including autobiographical recall and memory for public events.

Most neuropsychological assessments will include a basic screen of expressive and receptive language skills, as well as perceptual abilities. They will also include some tests designed to be sensitive to frontal lobe disturbance. All of these areas can be examined in greater detail with specialist test batteries such as the Multilingual Aphasia Examination, (MAE) the Visual Object Spatial Perception battery (VOSP) and the Behavioural Assessment of the Dysexecutive Syndrome (BADs), in addition to a plethora of individual tests.

The neuropsychological assessment can be combined with other investigations, such as video telemetry or ambulatory EEG recordings, to investigate the cognitive correlates of unusual EEG discharges or sub-clinical events.

Pre- and post-operative neuropsychological evaluation in epilepsy

Neuropsychological assessment has an important role in evaluating candidates for temporal lobe surgery since the temporal lobes have long been implicated in memory functioning. Bilateral hippocampal excision is associated with profound anterograde amnesia. Unilateral resections are traditionally associated with material-specific memory dysfunction. The traditional view is that the dominant temporal lobe (usually the left) is important for verbal memory processing and the non-dominant temporal lobe (usually the right) for non-verbal or visual memory processing. However, within this model, the aetiology of the seizure disorder and the underlying pathology may play a critical role in shaping the nature and extent of pre- and post-operative neuropsychological deficits (see Table II). Different neuropsychological profiles are seen in patients with developmental lesions, such as those associated with cortical dysgenesis, compared to those with high-grade gliomas that develop in adulthood.

Post-operative deficits are dependent upon both the functional adequacy of the tissue removed and the functional reserve of the remaining structures. Some plasticity and the development of compensatory strategies post-operatively may also influence the nature and extent of post-operative neuropsychological deficits. Pre-operative neuropsychological scores, in conjunction with MRI and other clinical data, can be utilised to predict post-operative neuropsychological change using logistic regression techniques. Patients at high risk of a significant memory decline can be counselled pre-operatively and can be trained in compensatory strategies prior to the surgery when appropriate.

Table II. Influential factors in neuropsychological outcome following temporal lobe

resection.

Factors	Characteristics associated with post-operative deterioration in verbal memory
Pre-operative factors	
Age at Surgery	Older
Gender	Males
IQ	Lower IQ
Clinical features	Discordance with MTLE syndrome Absence of unilateral temporal slow waves
Age at onset	Older
Underlying pathology	Absence of HS or mild HS Presence of cortical dysplasia
Functional integrity of the proposed resected tissue	Good
Functional integrity of the contralateral structures	Poor
Surgical factors	
Laterality	Left or dominant hemisphere resection
Surgical procedure (Equivocal evidence)	? greater extent of lateral resection ? greater extent of mesial resection
Post-operative factors	
	No post-operative improvement in seizure Frequency

The intracarotid amobarbital procedure

The role of the intracarotid amobarbital procedure (IAP) or Wada test (after Juhn Wada who first introduced it in 1949) in the presurgical evaluation of epilepsy surgery candidates is in decline due to a number of factors. A worldwide shortage of sodium amytal in the early part of the decade led some to develop new procedures with other substitutes such as pentobarbital and methohexital with some success, although there is some evidence that methohexital may be associated with an increase in seizures during the procedure. There is increasing clinical confidence in functional imaging techniques to lateralise language functions in patients with proposed resections in possible eloquent areas. A survey in 2008 of centres across the world found that the majority of centres no longer conduct a Wada test on every surgical candidate and there is an evolving consensus that the clinical indications for a Wada test should be determined on a case-by-case basis to ensure an appropriate risk:benefit ratio for every patient.

Further reading

1. BAXENDALE S. The Wada test. *Curr Opin Neurol* 2009; 22(2): 185-189.
2. BAXENDALE S, THOMPSON PJ, DUNCAN JS. The role of the Wada test in the surgical treatment of temporal lobe epilepsy: and international survey. *Epilepsia* 2008; 49(4): 715-720, discussion 720-725.
3. BAXENDALE S. The role of functional MRI in the presurgical investigation of temporal lobe epilepsy patients: a clinical perspective and review. *J Clin Exp Neuropsychol* 2002; 24(5): 664-676.
4. BAXENDALE S. Amnesia in temporal lobectomy patients: historical perspective and review. *Seizure* 1998; 7(1): 15-24.
5. CHELUNE GJ. Hippocampal adequacy versus functional reserve: predicting memory functions following temporal lobectomy. *Arch Clin Neuropsychol* 1995; 10(5): 413-432.

6. HAMBERGER MJ, DRAKE EB. Cognitive functioning following epilepsy surgery. *Curr Neurol Neurosci Rep* 2006; 6(4): 319-326.
7. HELMSTAEDTER C. Neuropsychological aspects of epilepsy surgery. *Epilepsy Behav* 2004; 5 (Suppl 1): S45-S55.
8. LINEWEAVER TT, MORRIS HH, NAUGLE RI et al. Evaluating the contributions of state-of-the-art assessment techniques to predicting memory outcome after unilateral anterior temporal lobectomy. *Epilepsia* 2006; 47(11): 1895-1903.
9. PONDS RW, HENDRIKS M. Cognitive rehabilitation of memory problems in patients with epilepsy. *Seizure* 2006; 15(4): 267-273.
10. POWELL HW, DUNCAN JS. Functional magnetic resonance imaging for assessment of language and memory in clinical practice. *Curr Opin Neurol* 2005; 18(2): 161-166.
11. TELLEZ-ZENTENO JF, DHAR R, HERNANDEZ-RONQUILLO L, WIEBE S. Long-term outcomes in epilepsy surgery: antiepileptic drugs, mortality, cognitive and psychosocial aspects. *Brain* 2007; 130(2): 334-345.
12. VAN EMDE BW, JUHN A. Wada and the sodium amytal test in the first (and last?) 50 years. *J Hist Neurosci* 1999; 8(3): 286-292.
13. VINGERHOETS G. Cognitive effects of seizures. *Seizure* 2006; 15(4):221-226.
14. WECHSLER D. *Wechsler Adult Intelligence Scale*. San Antonio, Texas, The Psychological Corporation, 1981.