

## **Neuropsychology – testing the brain**

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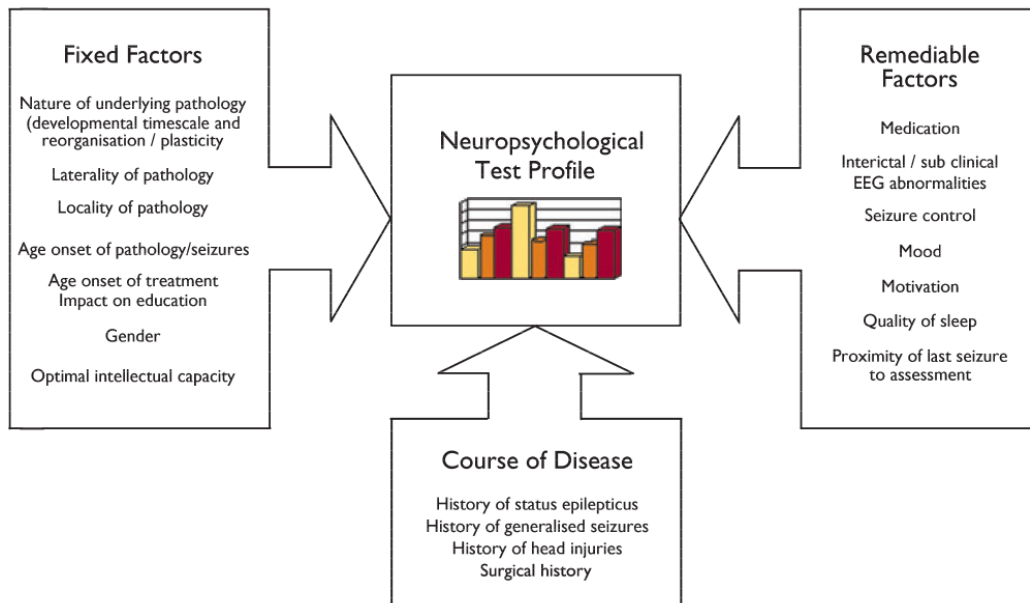
### **Defining and testing cognitive function**

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 different cognitive domains, all of which can dissociate in the pathological brain. These domains have a conceptual rather than an anatomical basis, although some anatomical correlates do exist. The domains include intelligence, language, memory, perception and executive functions. The way in which a function is tested can to a large extent determine whether a deficit will be found. For example, there is no single test of ‘verbal memory’. Memory tests can assess the learning, recall or recognition of different types of verbal material (narrative vs unstructured) 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 – and 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 of 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?**

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. There are numerous factors that can influence an individual’s performance on neuropsychological tests. Many of these factors are specific to epilepsy and can be fixed, transient or have a progressive influence (Figure 1).



**Figure 1.** Factors influencing performance on neuropsychological tests in epilepsy. (From Baxendale and Thompson 2010, see Further reading)

The overall value of a neuropsychological assessment very much depends on the validity of the questions being asked, the cooperation of the patient on the day and the availability of other relevant data to aid in the accurate interpretation of the test data once it has been collected.

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 2015, the ILAE Diagnostic Commission Neuropsychology Task Force published guidelines for the minimum standards in neuropsychological assessment for people with epilepsy.<sup>1</sup>

In an ideal world, all newly diagnosed patients with epilepsy would undergo a brief neuropsychological screen prior to the onset of treatment to create a valuable baseline against which future assessments can be measured. While local resources do not allow such a specialist assessment for most patients, it is possible to have some record of memory function at diagnosis if a self-report questionnaire is administered. 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 a deterioration in function. In most cases it is therefore recommended that there is at least a nine-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.<sup>2</sup> Almost all assessments will include the current gold-standard measure of general intellectual functioning in adults, the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV UK, 2010). The most recent incarnation of the Wechsler Intelligence Scale has dispensed with the traditional distinction between verbal (VIQ) and performance IQ (PIQ) and now provides four index scores, including the verbal comprehension index (VCI), the perceptual reasoning index (PRI), the perceptual organisation index (POI) and the working memory index (WMI). The full-scale IQ (FSIQ) has been retained and an additional general ability index (GAI) has also been added. The distributions of all the indices are constructed to have a mean of 100 and a standard deviation of 15 IQ points. An index score of 100 therefore defines the performance of an average, healthy, adult at that age. Approximately two-thirds of the adult population obtain scores 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 (Table 1).

**Table 1.** IQ Index Classifications used in the Wechsler Intelligence Scales

<i>IQ Index score ranges</i>	<i>Qualitative description</i>	<i>Percent of cases</i>
Below 69	Extremely low	2.2
70-79	Borderline	6.7
80-89	Low average	16.1
90-109	Average	50
110-119	High average	16.1
120-129	Superior	6.7
Above 130	Very superior	2.2

Measures of FSIQ may underestimate the intellectual abilities of a significant proportion of people with epilepsy (40%). Reductions in FSIQ are correlated with the number of AEDs taken and duration of epilepsy. Individual AEDs also differentially interfere with the expression of underlying intellectual ability in this group, via their selective actions on processing speed and working memory.<sup>3</sup>

### *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. There is a growing consensus that these complex figure-recall tasks may have limited validity in the assessment of epilepsy. 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 prospective memory functions (remembering that you have to do something at some point in the future). 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. It is important to recognise that this model of memory function suggests a specialisation of lateralised structures for verbal/visual material rather than an exclusive function. 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. 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.

### **The intracarotid amobarbital procedure (Wada Test)**

The long running debate on the future of the intracarotid amobarbital procedure (IAP) or Wada test (after Juhn Wada who first introduced it in 1949) and its role in the presurgical assessment of prospective epilepsy surgery candidates is gradually resolving. Traditionally the IAP was used to ensure that the memory capacity of the contralateral temporal lobe is adequate to maintain useful memory functions unilaterally prior to surgery and it is an effective test for language lateralisation. Recent studies have cast doubts on the reliability and validity of the IAP in predicting post-operative amnesia. The testing protocol, choice of behavioural stimuli, dosage and administration of the amytal and a host of factors related to the individual's reaction to the injection can interfere with the results, and many centres no longer conduct Wada tests as part of a presurgical evaluation.<sup>4,5</sup>

## Functional imaging

A number of fMRI paradigms have been developed to localise language function in adults and children and fMRI paradigms have also recently been used to examine memory function in prospective temporal lobectomy patients. Asymmetric fMRI activations during memory tasks are concordant with asymmetric memory performances observed during the IAP. These techniques have begun to supersede the complex and invasive IAP procedure in language lateralisation and are beginning to be combined with our traditional memory tests to further enhance the role of neuropsychology in providing lateralising and prognostic information for presurgical patients with temporal lobe epilepsy.<sup>6</sup> See Binder et al<sup>6</sup> and Beers et al<sup>7</sup> for useful summaries of this literature.

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