Neuropsychological testing remains the best method of characterizing and quantifying the nature and degree of cognitive dysfunction arising from epilepsy. The neuropsychological assessment is an integral part of a patient’s evaluation for temporal lobe surgery, and provides unique information not available through other regular investigations (e.g., electroencephalography, neuroimaging). In a recent review, neuropsychological assessment was routine at 85% of epilepsy surgery centres surveyed across North America, with the remaining ones using neuropsychological assessment on an occasional basis.1

A neuropsychological assessment comprises a comprehensive evaluation of cognitive functioning that includes intelligence, fronto executive skills, memory, attention, visuospatial abilities, language, and motor skills. In temporal lobe epilepsy, the primary cognitive deficit is in memory. Consequently, particular attention is focused upon this function.2 Most neuropsychological assessments also include determination of cerebral
dominance for language. This is typically achieved using the intracarotid amobarbital procedure (IAP), which will be discussed in some detail below. A different approach, however, has been adopted at the London Health Sciences Centre, where patients’ language lateralization is screened using a noninvasive task (the Fused Words dichotic listening test)\(^1\), followed at operation by stimulation for speech. Patients may also undergo personality testing and evaluation of psychosocial functioning in some institutions. Neuropsychological assessment is appropriate for most patients seen in an epilepsy surgery service, the only exception being the few patients whose intellectual level or lack of cooperation prohibits completion of the usual battery of tests.

**Benefits of Neuropsychological Assessment**

Neuropsychological assessment contributes to an epilepsy surgery program in five distinct ways.

1. It provides specific information about the patient’s cognitive functioning.
2. It provides information on the localization and lateralization of brain dysfunction.
3. It predicts the risk for postsurgical cognitive decline.
4. It is an important component in calculating predictions about the potential efficacy of surgery on seizure control for individual patients.
5. Its data on the impact of brain surgery upon cognitive functioning contribute important information on outcome.

Neuropsychological findings contribute important information towards localizing temporal lobe pathology and in detecting possible dysfunction contralateral to the primary seizure focus. Pathology of the dominant temporal lobe typically presents with deficits involving verbal memory and word retrieval skills.\(^5\)-\(^10\) Moreover, the predictive usefulness of verbal memory and confrontation naming tests for determining postsurgical decline is well established.\(^5\),\(^11\),\(^12\) In the nondominant temporal lobe, impairments on measures of visuospatial functioning and visual memory have been more difficult to document.\(^2\),\(^4\),\(^11\),\(^13\) but this may simply reflect the inadequacies of the traditional instruments used to assess these functions.\(^2\) Many of the traditional tests are quite old and psychometrically naive; they do not allow a detailed delineation of a patient’s deficits, and lateralization of dysfunction is difficult because the tests are “dually encodable” (can be coded both verbally and visually). Using an approach of matched verbal and visuospatial learning tests, we have shown that deficits in patients with right temporal lobe pathology can be elicited reliably,\(^14\),\(^15\) even in unoperated cases.\(^16\)

Neuropsychological assessment allows prediction of a patient’s postsurgical risk of cognitive change. Declines in memory functioning are of primary concern with temporal lobe operations, and these changes are seen most frequently after a dominant temporal lobectomy.\(^5\) Significant prognostic factors include level of presurgical performance, age of seizure onset, chronological age at the time of surgery, and the degree of medial temporal pathology.\(^5\),\(^7\),\(^13\) With dominant temporal lobectomy there is also the risk of postsurgical language deficits. This primarily takes the form of word retrieval or confrontation naming deficits,\(^13\) and while the deficits are persistent, they rarely occur to a degree that compromises patients’ daily functioning. Resection of the nondominant temporal lobe has been reported to exert a less marked effect upon memory,\(^5\),\(^7\),\(^8\),\(^11\) but it is difficult to assess the significance of these findings because the available studies were performed using traditional “nonverbal” memory tasks, most of which are easily verbalized.

There has been a resurgence of interest in the utility of neuropsychological testing to predict postsurgical seizure control. In keeping with the early report from Bengzon and colleagues,\(^17\) a recent study by Thadani and colleagues\(^18\) demonstrated that the likelihood of postsurgical relief from seizures was greatest when the results of the three primary modes of investigation (neuropsychology, EEG, neuroimaging) converged to identify a focal area of dysfunction.

**Localization of Dysfunction**

**Sensitivity versus specificity**

The ability to localize dysfunction based upon neuropsychological performance is dependent upon the sensitivity and specificity of the individual tests. We have already commented upon the need for, and existence of, better instruments than many of the traditional ones. Finer analyses of the cognitive dysfunctions associated with temporal lobe epilepsy are beginning to emerge. Thus, Saling and colleagues\(^19\) demonstrated a lateralization effect for the learning of verbal paired associates (sensitive to left hippocampal lesions) but not for the recall of short verbal passages; this finding was consistent with an earlier report from Rausch and Babb.\(^2\) Whereas Saling et al\(^19\) interpreted their results as suggesting that the learning of rote verbal material relies on a different neurocognitive system than does learning semantically complex material (and this may very well be true), we would argue that an important difference in task requirements also contributed to their findings. Their verbal passages task required recall after the material to be remembered had been presented just once. For a variety of reasons (e.g., lapse of attention, misunderstanding) patients with lesions in either the left or the right temporal lobe can show deficient recall after hearing the material only once, but when the material is presented more than once, patients without a memory impairment will improve while the impaired patients will not. Thus, when we study memory for verbal passages in a learning paradigm, a significant difference emerges between left and right temporal lobe patients.\(^20\) This dissection of impairments is an exciting new approach to work with temporal lobe epilepsy patients. It leads to better neurocognitive diagnosis and allows us to offer better advice to patients regarding details of their cognitive difficulties.

When interpreting results from a neuropsychological evaluation, one must bear in mind that few tests are “pure” measures of a single cognitive process, but are dependent upon multiple processes for normal performance. Disruption of different processes can result in impaired performance on the same test. A common example is impairment on memory tests arising from attentional deficits, as suggested above. Similarly, poor performance on a cancellation task may reflect an attention deficit or a perceptual one. Or, thinking in terms of brain regions rather than processes, deficits associated with temporal lobe pathology may also be seen in patients with dysfunction in other brain regions. For example, patients with dominant temporal lobe pathology show word finding deficits on tests of confrontation naming.\(^4\),\(^5\),\(^10\) However, reduced verbal fluency,
especially if disproportionate to the naming deficit, reflects left frontal lobe dysfunction. Conversely, right frontal lobe damage is suspected when dysfluency behaviour is observed in the nonverbal mode, elicited with figural (drawing) fluency tasks.5,21

It should be emphasized that the significance of any deficit must be interpreted in the context of the pattern of results on a battery of judiciously selected tests: no interpretation should be based upon performance on a single test alone.2,22 This “pattern analysis” allows convergent lines of evidence, rather than an over reliance upon single test measures, to support a conclusion of focal dysfunction.

In addition, we must take into account the fact that behaviour arises from systems of neural activity, not from the kind of discretely localized regions that are implied when we speak of, for example, the role of the temporal lobes in memory, as though temporal lobes function in a vacuum. This is demonstrated eloquently in results from cognitive activation studies using positron emission tomography (PET) and functional MRI. These studies allow us to begin to understand the complex networks of interacting brain regions involved in behaviour and cognition; an example is the delineation by PET of the frontal lobe contribution to learning and memory.23,24

Postoperative change

Postoperative changes in cognitive functioning are dependent partly upon the presurgical abilities of the patient. Thus, patients with very good memory preoperatively, or with normal hippocampal volumes according to measurements made of medial structures on MRI scans, are the ones most likely to show postoperative memory decrements,5,12,13 especially if the resection is made from the dominant temporal lobe. By the same token, patients with very deficient memory before surgery do not lose significantly after surgery, but do continue to show severe memory impairments.2

The Intracarotid Amobarbital Procedure (IAP)

Background and assumptions

In 1955 Juhn Wada introduced at the Montreal Neurological Institute a method of temporary hemianesthesia of the brain – the intracarotid amobarbital procedure (IAP) – that he had developed earlier in Japan.25 He and Theodore Rasmussen reasoned that his technique, injection of a barbiturate into each hemisphere in turn, would allow them to determine before surgery which hemisphere was dominant for speech. Milner, Branch and Rasmussen26 extended the use of the procedure to include testing memory, again for preoperative prediction of possible surgical sequelae. Because the IAP produces a state of temporary, reversible dysfunction in the injected hemisphere, Milner and her colleagues hypothesized that when injecting the side ipsilateral to proposed surgery, the procedure should mimic the potential effects of the surgical resection on memory.27

Behind their hypothesis were three assumptions:

1) Pharmacologic inactivation of a single temporal lobe should not create a global amnesia if the awake temporal lobe is healthy;
2) The critical regions to be resected during temporal lobectomy are functionally inactivated during the IAP; and
3) A transient amnestic state due to temporary bilateral medial temporal lobe dysfunction will result from amobarbital injection when the temporal lobe structures contralateral to injection are significantly dysfunctional. Such a result would then predict that resection of the epileptogenic temporal lobe could result in an amnestic syndrome.28

General challenges in the IAP

The IAP is a stressful, invasive procedure, and some low-functioning or highly emotional patients may be unable to cooperate sufficiently to undergo it. The amobarbital effect is short; thus, there is only a brief period during which to assess the patient. Transient aphasia, mental confusion, agitation, transient visual field defects, and (rarely) seizures or medication effects can also complicate the assessment. Cross-flow into the contralateral hemisphere occurs in about 30% of cases,29 but this is unrelated to slow waves contralateral to injection30 or to reduced metabolism contralateral to injection (measured as hypoperfusion via single photon emission tomography – SPECT),31 making the significance of angiographic cross-filling uncertain.

Who should undergo the IAP?

In many institutions all surgical candidates undergo the IAP. This is not the case at our centres. Only patients in whom there is reason to suspect atypical cerebral dominance, or in whom bilateral temporal lobe dysfunction is suspected, are selected to undergo the IAP.

Role in assessing language lateralization

Most centres, including the MNI, consider the IAP’s role in determining cerebral dominance for language to be critical in left-handed patients and those whose pattern on cognitive tests is discordant with the expected laterality of seizure focus. At the MNI and in some other centres, patients with atypical cerebral dominance according to the IAP undergo an additional PET cognitive activation study for language. These experimental studies are promising, but will not supplant the IAP in the near future because at present only one discrete aspect of language can be tested in a single PET study, leaving questions about other aspects of language unanswered.32

Another approach is to predict language lateralization using dichotic listening33 and tachistoscopic tests; this is the approach used in London, Ontario, where it is supplemented with intraoperative cortical stimulation at the time of surgery in the majority of cases. Thus, in London, the IAP is rarely administered solely to determine language lateralization, and is recommended primarily to assess memory. Most often, questions regarding memory function and its organization arise in patients with preoperative indications of bilateral temporal lobe dysfunction and/or evidence of atypical language lateralization.

Assessing risk to memory

Virtually every epilepsy surgery centre has its own IAP protocol. There are variations in dosage, injection procedure, stimuli, mode and/or timing of item presentation, scoring, and interpretation.28,34,35 Due to the variability in procedures for assessing memory during the IAP, it is difficult to generalize freely from one centre to another, although results from one centre can usually be interpreted by another if test parameters are known precisely.

The challenges listed above (e.g., mental confusion, transient
aphasia, medication effects) influence the reliability of the IAP. Nonetheless, McGlone and MacDonald demonstrated that among 18 repeat injections, 7/8 of the technically satisfactory tests yielded the same memory results. This finding provides some assurance that conclusions based on the IAP are reliable (repeatable) in most cases.

The validity of the IAP has been assessed by examining its relationship to other indicators of hippocampal dysfunction. Thus, Jones-Gotman demonstrated that IAP memory results are sensitive to seizure focus. As well, IAP memory results have been shown recently to be effective in lateralizing seizure onset, predicting postoperative seizure control, and predicting degree of memory decline following left temporal lobectomy. The validity of the procedure has also been supported by correlations between IAP memory performance and hippocampal pyramidal cell loss and MRI determined hippocampal volumes.

The ultimate test of the IAP’s predictive validity will never be attempted, as it would involve administering the IAP to a large number of patients with temporal lobe epilepsy and subsequently resecting medial temporal lobe structures radically regardless of the IAP results. Due to the rare, but catastrophic possibility of a global amnesia, few centres are willing to operate aggressively when there is IAP evidence that the contralateral temporal lobe cannot support memory. Affirming this reluctance, some cases have been reported in whom severe memory loss was observed after a unilateral temporal lobe resection was performed despite failure on IAP memory tests. Dade and Jones-Gotman studied a series of patients who had undergone IAP followed by temporal lobe surgery; they compared postsurgical memory in patients who had passed the IAP memory tests to those who had failed them, and among those who had failed, found severe postoperative memory loss in some but no significant change in others. In keeping with the latter cases, Girvin et al. described three cases who underwent unilateral temporal lobectomy despite bilateral failure on the IAP and who were not amnestic following surgery.

Thus it is clear that memory impairment in the IAP does not necessarily mean that a severe memory loss will occur after resection from a temporal lobe. One reason for this may be because more of the hemisphere is rendered inactive during an IAP than will be resected in surgery. In this view, functional tissue ipsilateral to, but lying outside of, the planned surgical site would be inactivated during the IAP but would subserve memory postoperatively. At present, we are unable to differentiate “false positive” IAP memory impairments from those that do indeed warn of a significant risk to memory, although taking into account the status of a patient’s hippocampi and his/her performance on other memory tests can help one decide whether or not a given failure makes sense. In the absence of compelling evidence suggesting that a failure is spurious, one should heed the warning of an IAP memory impairment.

The precise variables determining memory performance after amobarbital injection have yet to be defined, but we have made immense strides in the past five to ten years compared to the preceding 35. For now, the IAP retains its usefulness for evaluating memory in the isolated hemisphere, and for determining hemispheric speech dominance with the greatest certainty, as proposed by Wada so many years ago.

CONCLUSION

Surgery is increasingly recognized as a viable means of treating intractable epilepsy, and the number of centres offering surgery is growing. Such elective surgery is undertaken only after a thorough investigation, carried out by a team of professionals specialized in epilepsy, has demonstrated a resectable seizure focus. It is crucial to know what function is served by a brain region that may be surgically removed. This is the domain of neuropsychology, as part of its role in an epilepsy team. The more comprehensive a neuropsychological evaluation is, the more precisely the function/structure relationships can be defined. With the help of the field’s accrued experience and with input from neuroimaging, we neuropsychologists are improving the cognitive tests that define those relationships and are sharpening our skills at interpreting the patterns of results obtained with those tests. We are able to offer more precise input than ever before to the patient’s medical investigation, and to offer better advice about their strengths and weaknesses to patients and their families. With the strides that we have made in the past ten to fifteen years, we anticipate acceleration in the years to come. It is exciting to be a part of this field at the dawn of the next millennium.

REFERENCES

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