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Ten things every neurologist needs to know about neuropsychological assessments and interventions in people with epilepsy.

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Abstract

This paper describes ten core features of a neuropsychological assessment with the aim of helping neurologists understand the unique contribution the evaluation can make within the wider context of diagnostic methods in epilepsy. The possibilities, limitations and cautions associated with the investigation are discussed under the headings below:

1. A neuropsychological assessment is a collaborative investigation.
2. Assessment prior to treatment allows for the accurate assessment of treatment effects.
3. The nature of an underlying lesion and its neurodevelopmental context play an important role in shaping the associated neuropsychological deficit.
4. Cognitive and behavioural impairments result from the essential comorbidities of epilepsy which can be considered as much a disorder of cognition and behaviour as of seizures.
5. Patient's subjective complaints can help us understand objective cognitive

impairments and their underlying neuroanatomy, resulting in improved patient care. At other times, patient complaints reflect other factors and require careful interpretation.

6. The results from a neuropsychological assessment can be used to maximise the educational and occupational potentials of people with epilepsy.
7. Not all patients are able to engage with a neuropsychological assessment.
8. There are limitations in assessments conducted in a second language with tests that have been standardized on different populations to that of the patient.
9. Adequate intervals between assessments maximise sensitivity to meaningful change.
10. Patients should be fully informed about the purpose of the assessment and have realistic expectations of the outcome prior to referral.

(239 words)

Introduction

This paper is written for neurologists to provide an introduction to the methods, possibilities and limitations of neuropsychological assessments and interventions for people with epilepsy. It is not a systematic review but rather the opinions and recommendations expressed within the manuscript are based on the authors combined experience of over 250 years of dealing with referrals from our neurology colleagues to see these patients. This paper describes ten core features of a neuropsychological assessment in epilepsy with the aim of helping neurologists understand the unique contribution the assessment can make within the wider context of diagnostic methods in epilepsy.

1. A neuropsychological assessment is a collaborative investigation

Clinical neuropsychological assessment requires skills and knowledge that go well beyond performing and reporting the results of neuropsychological tests. Neuropsychological tests are sensitive, indirect indicators of CNS dysfunction, but the meaning of any test result cannot be determined without careful consideration of symptoms, history and other clinical findings. For example, neuropsychological tests are sensitive to dysfunction in attentional systems, but attentional problems are highly nonspecific, occurring in a range of both neurological and non-neurological conditions. They can also arise as side effects of the treatments for these conditions. There are also a number of factors (e.g., anxiety, psychopathology, motivation) that influence neuropsychological test performance in a way

that is less true with other CNS evaluations[1] (see also point 4). These factors require careful evaluation when interpreting test results. Therefore, clinical neuropsychologists collaborate closely with neurologists and other medical professionals in integrating results of their evaluations with the clinical neuropsychological assessment to arrive at a comprehensive description of the patient's cognitive and functional capacities.

Take home message # 1: The more information the neurologist is able to give the neuropsychologist at the time of the referral, the better able the neuropsychologist will be to interpret the results of the assessment.

2. *A neuropsychological assessment can assess the impact of treatment on cognitive function in addition to the underlying condition.*

Although seizures and cognitive dysfunction are often symptomatic of a shared underlying pathology[2] it is often the case that medical and surgical treatments aimed at reducing seizures exacerbate other signs of cerebral dysfunction, such as cognitive and behavioural difficulties.

Determining the impact of antiepileptic drug (AED's) treatment on neuropsychological function is challenging, reflecting the significant methodological challenges of conducting studies in this field. Many AED's are associated with cognitive slowing, which can have a significant impact on performance in other cognitive domains. There is growing evidence that many of the newer antiepileptic drugs, used as monotherapy and given in therapeutic ranges are associated with less intrusive cognitive problems (3). However there are some exceptions to this broad rule of thumb. In addition to mood disturbance, Zonisamide has been associated with deficits in memory and executive function (4) whilst Topiramate can have a negative impact on memory, verbal and executive functions in a significant proportion of people who take it (5).

Surgical treatments are also associated with postoperative changes in neuropsychological function. Many of the people at highest risk of a postoperative decline following surgery can be identified preoperatively and can be counselled and prepared accordingly (6).

Neuropsychological assessments conducted prior to and following treatment can provide invaluable information in helping to disentangle the relative contributions of the various contributory factors. These assessments also ensure that people with epilepsy receive the best

possible advice about the factors important in the development and maintenance of their cognitive difficulties. This is particularly relevant for people with newly diagnosed epilepsy commencing antiepileptic drug (AED) treatment or for those individuals being considered as candidates on an epilepsy surgery programme.

Take Home Message 2: Treatments for seizures can exacerbate the neuropsychological comorbidities of epilepsy. A baseline assessment, *prior* to treatment allows for the more accurate assessment of treatment effects.

3. *The impact of underlying pathology on neuropsychological function*

Cognitive difficulties and seizures are frequently different symptoms of a common underlying pathology. This has been recognised in the new ILAE classification of epilepsy[2] and is emphasised in the findings of recent studies that have highlighted the probability that cognitive difficulties precede the onset of seizures in some people who go on to develop epilepsy (7). Although it is by no means the only contributory factor, the underlying pathology responsible for seizure generation in people with epilepsy often plays an important role in shaping the nature and extent of the cognitive difficulties associated with the condition. Whilst the lateralisation and location of the pathology is important, the impact on cognitive function will also be determined by the age and nature of the pathology. For example, the cognitive impact of a developmental lesion such as a dysembryoplastic neuroepithelial tumour (DNET) in the left temporal lobe will be different from that of a similar sized high grade glioma in the same location in an adult of the same age. In the former patient, cognitive functions will have organised around the lesion during development, in the latter, the lesion will have infiltrated tissue that developed normally. Thus it is the age of the underlying lesion, not just the age of onset of seizures that is important in shaping any associated cognitive difficulties. The lateralisation, location and age of the underlying pathology all interact to determine the associated profile of cognitive difficulties for each person with epilepsy. Following the onset of seizures, an individual's neuropsychological profile will be further shaped by the impact of seizures and treatments on their educational trajectory.

Take Home Message # 3: It is not just where a lesion is that determines the impact it has on neuropsychological function; the nature of the lesion itself and its neurodevelopmental context also plays an important role in shaping the associated deficit.

4. *The impact of comorbidities on neuropsychological function*

Comorbidities are recognised as a major source of disability in children and adults with epilepsy and may represent the most frequent and intrusive manifestation of the underlying disease. They can adversely affect the course of epilepsy and seizure outcome, and have significant negative effects on patient quality of life [2]. Approximately 50% of adults with active epilepsy have one or more comorbidities with conditions such as depression, anxiety, dementia, migraine, and heart disease up to eight times more prevalent in epilepsy than in the general population.(8),

Neuropsychological impairment may not always be contingent upon the presence of a lesion, but rather may be an intrinsic property of underlying network disease that also gives rise to seizures. This notion of a shared common mechanism underlying either cognitive and behavioural impairments, seizures, or both is known as ‘essential comorbidity’ This concept allows differentiation of essential comorbidities from cognitive and behavioural ‘secondary effects’ of seizures and their treatment This differentiation has significant implications for treatment. For instance, the issues underlying the choice of AED to treat seizures and cognitive dysfunction arising from shared intrinsic properties of network disease differ from those underlying the AED chosen to ameliorate secondary cognitive side effects. This is why determining whether cognitive difficulties are present at diagnosis via baseline neuropsychological assessment, prior to the commencement of AED treatment is so important.

Take Home Message # 4: Cognitive and behavioural impairments frequently result from the essential comorbidities of epilepsy which can be considered as much a disorder of cognition and behaviour as it is of seizures.

5. *The relationship between subjective cognitive complaints and neuropsychological measures of cognitive function*

Patients with epilepsy frequently express concern regarding everyday cognitive and memory problems and their progressive course. The fact that epilepsy patients link cognitive abnormalities to poor quality of life further reinforces clinical concern.

There are generally poor to modest associations between subjective memory complaints and tested memory function. Patient memory complaints have been found to be more related to factors such as mood and anxiety disorders and general psychological distress beyond depression. They also attribute difficulties in attention and language to memory failures. Thus, patient memory complaints offer little reassurance as a meaningful screen for formal assessment or for determining the outcomes of treatments, including epilepsy surgery.

Take Home Message # 5. Patient cognitive complaints may, at times, offer a road to understanding objective cognitive abnormalities and even their underlying neuroanatomy, resulting in improved patient care. At other times, patient complaints resist such insights and it is here that caution is warranted.

6. The role of the neuropsychological assessment in educational and occupational planning and support

Patients with epilepsy are at higher risk than their healthy peers and even patients with other chronic illnesses, of having educational and vocational problems. Reported rates vary but there is evidence that up to 42% of children with epilepsy (CWE) display academic underachievement and a higher percentage have low performance in at least one academic area (9). Epilepsy-related factors such as AED usage, type of seizures, aetiology and higher seizure frequency appeared to have an indirect effect in academic achievement through their negative impact on global cognitive functioning (10). There is a strong relation between IQ and exclusion from mainstream school systems. Moreover, up to 48% of CWE may meet psychometric criteria for learning disabilities (11).

A neuropsychological assessment can help in the early identification of children at greater risk for academic underachievement and cognitive deficits. Interventions for these children will include finding the most effective teaching method for each child. Neuropsychologists may also be asked to improve teacher, child and family knowledge and attitudes. Moreover, a neuropsychology report can be used to demonstrate a low achievement or underachievement, and in some countries, attest to the eligibility of the child for a special education service or an educational support program.

Up to 75% of people with epilepsy have employability problems (12). Neuropsychological assessments can help to accommodate work environment and demands, while managing work expectations by advising parties of what can be achieved by the patient. Equally important is

working with self-efficacy, self-directed behavior and active coping strategies.

Neuropsychological interventions emphasize active, problem-solving oriented, and goal-directed attitudes focused on vocational goals. Another rehabilitation technique that has been proven successful is training patients in requesting a more accommodating work environment thereby increasing their feeling of self-confidence and self-efficacy that will aid them in dealing with work-related problems.

Take Home Message #6. The results from a neuropsychological assessment can be used to maximise educational and occupational potential of people with epilepsy.

7. *Cautions: Not all patients are able to engage with the demands of a neuropsychological assessment*

To obtain optimal results, individuals undergoing neuropsychological testing need to be actively engaged in the testing process with adequate rapport between the neuropsychologist and the patient. This needs to be communicated to the patient and to all others involved in the assessment process. Suboptimal results will be obtained when testing is performed on individuals with severe deficits in attention or language comprehension secondary to neurological or other causes. The ability to focus on the testing will also be affected in individuals with high levels of anxiety, mood disturbance, or other emotional factors.

Neuropsychologists can use special tests to assess formally assess engagement, effort and the inflation or minimization of symptom reporting. However it is important to recognize that an assessment may not return valid results even if a patient 'passes' these tests.

Individuals making referrals for neuropsychological assessment of individuals with physical or sensory disability or other psychological or psychiatric impediments to full engagement must be aware of the lack of standardization that is often required for performing those evaluations and the inherent limitations on the validity of the results.

Take Home Message # 7. Is the patient able to engage with the demands of a formal cognitive assessment? If not, the conclusions that can be drawn from the assessment will be limited.

8. *Cautions: Language/cultural norms*

Language and culture exert significant influences on neuropsychological test performance in patients with epilepsy and all neurological conditions, both within and across countries and

geographic regions. These factors can have an influence on the degree to which an individual and his or her family members may be open to discussing cognitive disorders associated with epilepsy or their willingness to undergo a detailed neuropsychological assessment.

When performing the assessment, clinicians need to make efforts to employ neuropsychological tests that have been properly developed and/or translated using the language and dialect appropriate to the region of practice. The majority of the existing test materials, to date, have been developed and normed on English speaking samples residing in North America and Western Europe. Translation of written materials from these tests into other languages, including test stimuli and instructions, needs to be performed in a careful manner, using appropriate forward and backward translation techniques. It is also important to recognize that language usage varies widely across different countries and cultures.

If at all possible, attempts should be made to administer neuropsychological tests using examiners or technicians who are fluent in the patient's primary language and are aware of the social nuances associated with his or her culture. Examiners should refrain from using family members as interpreters, since relatives are often tempted to discuss and 'add' to the patient's answers and a 'joint IQ' can result! It is also the case that a neuropsychological assessment can be stressful with patients pushed to the limits of their capacity, this process can be made even more uncomfortable if a relative is actively engaged in this process. While performing neuropsychological evaluations under non-standardized conditions may be unavoidable in some instances, the clinician should be prepared to alert others to the effects on the validity of the test results obtained under those conditions and limitations to interpretations that can be drawn from the resulting data.

Patients' scores on neuropsychological tests need to be interpreted in relation to an appropriate normative group. Most tests provide norms that are stratified by age and sex. However, performances on many other tests are affected by literacy or years of education, which might vary in quality among geographic regions and countries.

Take Home Message # 8. There are significant of limitations in the conclusions that can be drawn from assessments conducted in a second language with tests that have been standardized on different populations to that of the patient.

9. *Cautions: Reassessment interval/practice effects*

All standardised neuropsychological tests have psychometric properties and test-retest reliability is one of the most important. This measures the reliability of a test score over time. As discussed above, there are many factors that influence test performance which mean that people do not always perform in an identical way every time they are tested. The score obtained on each occasion is representative of performance and indicates ability within a range of function. If someone retakes the test they may not get exactly the same score, but if nothing has changed in their underlying ability, the score they get should indicate ability within the same range, if the test is reliable.

Practice effects can have a significant impact on test performance, even in a reliable test. Unlike biological measures, cognitive performance increases when testing is repeated. Factors such as memory for specific test items, previous feedback, learned strategies, or test sophistication can strongly contaminate the test's results and can mask underlying deterioration if a reassessment is carried out too soon. In some cases, a stable score on a test administered on a second occasion soon after the first might even reflect deterioration rather than the absence of change. Some cognitive domains such as learning, memory, and executive functioning are known to be more susceptible to practice effects than others (i.e. processing speed, attention, and language). Healthy adults are also shown to have greater practice effects over multiple exposures than disease populations.

Neuropsychologists have developed a number of methods to counteract the impact of practice effects. These include methods based on the statistical properties of the tests and the development of parallel forms of tests, which avoid repeated exposure to the same material. However, they do not cancel practice effects or participants becoming familiar with the test procedure. It is recommended that an interval of at least 9 months, and preferably 12 months is given between assessments to maximise the sensitivity of subsequent assessments to change. Targeted re-evaluations with shorter intervals can however be helpful in some clinical scenarios, particularly in acute settings.

Take Home Message # 9. Ensure an adequate interval between referrals for a neuropsychological assessments to maximise the sensitivity of the assessment to change.

10. Realistic Expectations

Memory problems are among the most common complaints of people with epilepsy. Many patients will complain of memory problems to their neurologists, and such complaints constitute a legitimate reason to refer a patient for a neuropsychological assessment.

Memory deficits may be related to underlying brain dysfunction, to the effects of seizures or interictal discharges on memory consolidation, to medication side effects or to depression, and, as outlined earlier in this paper, the neuropsychological assessment can help to delineate if and how these factors may contribute to the patient's memory disorder. One encounters difficulties, however, when patients arrive for the neuropsychological assessment without a good understanding of its purpose. They often have the misunderstanding that the purpose of this referral is to provide them with a "cure" for their memory deficits, and they may ask for a medical treatment for the deficits. Given that such a cure does not yet exist, upon learning such, these patients may feel demoralized and let down. It is important, therefore, that when recommending a neuropsychological assessment, the neurologist is clear on communicating its purpose and likely benefits.

Although there is not a medical treatment for memory deficits, a benefit of the neuropsychological assessment is that the identification of the nature of the memory deficit can lead to interventions that may lessen the impact of the impairments on their everyday function. Cognitive rehabilitation teaches strategies that may be internally [such as use of mnemonics] or externally based [such as use of notes or electronic reminders]. Memory intervention programs have been shown to improve self-reports of memory, and, in some cases, to improve efficacy on certain tasks of recall and are effective in patients on AED monotherapy or polytherapy, in patients with and without depressive symptoms, and in patients who have undergone epilepsy surgery

Take home message # 10. When referring someone with epilepsy for a neuropsychological assessment ensure that they are fully informed about the purpose of the neuropsychology assessment and have realistic expectations of the outcome.

Conclusion

It is hoped that this discussion of the scope and limitations of neuropsychological assessment in epilepsy will help to optimise both referral patterns and subsequent outcomes in this group. We have primarily focused on neuropsychological assessment in this paper but increasingly

the value of the profession extends well beyond formal evaluation and the interested reader is referred to our recent publications which discuss in further detail the multiple roles neuropsychologists can play in the diagnosis and management of epilepsy(6,13).

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1. Drane DL, Williamson DJ, Stroup ES, Holmes MD, Jung M, Koerner E, et al. Cognitive impairment is not equal in patients with epileptic and psychogenic nonepileptic seizures. *Epilepsia*. 2006;47(11):1879–86.
2. Wilson SJ, Baxendale S. The new approach to classification: Rethinking cognition and behavior in epilepsy. *Epilepsy Behav*. 2014;41:307-310.
3. Aldenkamp AP, De Krom M, Reijs R. Newer antiepileptic drugs and cognitive issues. *Epilepsia* 2003;44 Suppl 4:21–9.
4. Park S-P, Hwang Y-H, Lee H-W, Suh C-K, Kwon S-H, Lee B-I. Long-term cognitive and mood effects of zonisamide monotherapy in epilepsy patients. *Epilepsy Behav* 2008;12(1):102–8.
5. Mula M. Topiramate and cognitive impairment: evidence and clinical implications. *Ther Adv drug Saf*. 2012;3(6):279–89.
6. Baxendale S, Wilson SJ, Baker GA, Barr W, Helmstaedter C, Hermann BP, et al. Indications and expectations for neuropsychological assessment in epilepsy surgery in children and adults. *Epileptic Disord* 2019;21(3):221–34.
7. Witt J-A, Helmstaedter C. Cognition in epilepsy. *Curr Opin Neurol* 2017;30(2):174–9.
8. Berg AT. Epilepsy, cognition, and behavior: The clinical picture. *Epilepsia* 2011;6;52:7–12.

9. Berg AT, Langfitt JT, Testa FM, Levy SR, DiMario F, Westerveld M, et al. Global cognitive function in children with epilepsy: A community-based study. *Epilepsia* 2008;49(4):608–14.
10. Fastenau PS, Jianzhao Shen, Dunn DW, Austin JK. Academic Underachievement Among Children With Epilepsy. *J Learn Disabil* 2008;41(3):195–207.
11. Hermann B, Jones J, Sheth R, Dow C, Koehn M, Seidenberg M. Children with new-onset epilepsy: neuropsychological status and brain structure. *Brain* 2006;7;129(10):2609–19.
12. McCagh J, Fisk JE, Baker GA. Epilepsy, psychosocial and cognitive functioning. *Epilepsy Res* 2009;86(1):1–14.
13. Wilson SJ, Baxendale S, Barr W, Hamed S, Langfitt J, Samson S, et al. Indications and expectations for neuropsychological assessment in routine epilepsy care: Report of the ILAE Neuropsychology Task Force, Diagnostic Methods Commission, 2013-2017. *Epilepsia*. 2015;56(5).

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