Epileptic Disord 2019; 21 (3): 221-34

Indications and expectations for neuropsychological assessment in epilepsy surgery in children and adults

Report of the ILAE Neuropsychology Task Force Diagnostic Methods Commission: 2017-2021

Neuropsychological assessment in epilepsy surgery

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Received April 11, 2019; Accepted May 20, 2019

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doi:10.1684/epd.2019.1065

ABSTRACT – In our first paper in this series (*Epilepsia* 2015; 56(5): 674-681), we published recommendations for the indications and expectations for

neuropsychological assessment in routine epilepsy care. This partner paper provides a comprehensive overview of the more specialist role of neuropsychological assessment in the pre and postoperative evaluation of epilepsy surgery patients. The paper is in two parts. The first part presents the framework for the mandatory role of neuropsychologists in the presurgical evaluation of epilepsy surgery candidates. A preoperative neuropsychological assessment should be comprised of standardised measures of cognitive function in addition to wider measures of behavioural and psychosocial function.

The results from the presurgical assessment are used to: (1) establish a baseline against which change can be measured following surgery; (2) provide a collaborative contribution to seizure characterization, lateralization and localization; (3) provide evidence-based predictions of cognitive risk associated with the proposed surgery; and (4) provide the evidence base for comprehensive preoperative counselling, including exploration of patient expectations of surgical treatment.

The second part examines the critical role of the neuropsychologist in the evaluation of postoperative outcomes. Neuropsychological changes following surgery are dynamic and a comprehensive, long-term assessment of these changes following surgery should form an integral part of the postoperative follow-up. The special considerations with respect to pre and postoperative assessment when working with paediatric populations and those with an intellectual disability are also discussed.

The paper provides a summary checklist for neuropsychological involvement throughout the epilepsy surgery process, based on the recommendations discussed.

Key words: neuropsychology, epilepsy surgery, adult, paediatric, assessment, outcome, guidelines, ILAE

In our first paper in this series, the members of the ILAE Diagnostic Commission Neuropsychology Task Force published recommendations for the indications and expectations for neuropsychological assessment in routine epilepsy care (Wilson *et al.*, 2015). This partner paper examines the more specialist role of neuropsychological assessment in the preoperative evaluation and postoperative follow-up of epilepsy surgery patients. The recommendations in this paper do not supersede the indications and expectations set out in our previous publication, but rather, the two papers are complementary, with the first setting out basic standards for all neuropsychological assessments, and this paper describing the indications for and expectations of a neuropsychological assessment in people undergoing epilepsy surgery. As before, we have not set out to provide an exhaustive review of the epilepsy surgery literature, but rather, this paper provides a comprehensive overview of the role of the neuropsychological assessment in epilepsy surgery programmes today.

Methods

The paper is in two parts. The first part presents the framework for the mandatory role of neuropsychologists in the presurgical evaluation of epilepsy surgery candidates. The second part sets out the critical role of the neuropsychologist in the evaluation of postoperative outcomes. The special considerations with respect to these roles when working with paediatric populations and those with an intellectual disability are then discussed. We have also provided best practice recommendations for neuropsychologists working with patients in these settings. Our recommendations build on previous task force consensus guidelines (Jones-Gotman *et al.*, 2010), guidelines derived from an independent international meeting of neuropsychological experts (Helmstaedter *et al.*, 2011), the current literature, and the outcome of detailed discussions between the specialist epilepsy neuropsychologists currently serving on the ILAE Neuropsychology Task Force (2017-2021). A checklist is provided which summarizes our recommendations for best practice in each of the domains discussed (*table 1*).

PRE-SURGICAL EVALUATION

The role of the neuropsychological assessment in the pre-surgical evaluation of epilepsy surgery candidates has evolved over time (Baxendale and Thompson, 2010). The understanding of the multifactorial

Table 1. Checklist of the indications and expectations for neuropsychological assessment in epilepsy surgery in children and adults.

Function	Considerations
Pre surgical assessment	Must be up-to-date. Function in all cognitive domains should be assessed. Should include objective & subjective measures of cognitive function. Should include formal measures of psychosocial function and health-related quality of life. Must also include parental/caregiver evaluations of behaviour and ability in paediatric populations. Teacher/educator evaluations may also be helpful in some cases in paediatric populations.
1. Baseline for outcome comparison	The timing of the formal assessment with respect to the proximity to the last seizure and medication effects will impact on the stability of the baseline measurements and must be considered in the interpretation of results.
2. Contribution to seizure characterisation, lateralisation & localisation	Results must be interpreted in a developmental context. The organic and non-organic, static and dynamic influences on function must be examined in the interpretation of results from the preoperative assessment.
3. Identification of cognitive risks associated with the procedure	The preoperative baseline data should be used to predict the likely cognitive outcomes and identify the primary cognitive risks associated with the procedure. Predictive models and nomograms may aid these predictions in adults undergoing standardised operations. Amnesic risk must be identified in temporal lobe surgery candidates.
4. Feedback and preoperative counselling	Should include explanation of the results of the pre-surgical assessment and education about the aetiology of cognitive and functional deficits identified. Must include detailed discussion of any predicted cognitive changes following surgery. Must include discussion of the patients' (and their families') expectations of surgery. May include prehabilitation for anticipated cognitive losses or psychosocial difficulties.
Post-surgical assessment	Should evaluate all aspects of cognitive and behavioural function assessed prior to surgery. Change must be identified using reliable methods. The nature of the surgery and postoperative seizure outcome must be considered in the interpretation of the postoperative results. The timing of the postoperative assessment will have a significant impact on the results and must be considered in the interpretation of the results. The longer the follow-up, the more accurate the picture of postoperative outcome that emerges. It may take at least 5 years after the surgery for quantifiable changes in HRQoL to become evident in adults and for cognitive changes to emerge in children. Psychotherapeutic input may be required in some cases to help surgical candidates maximise their postoperative potential.

'*Must*' denotes a mandatory minimum requirement '*Should*' denotes good clinical practice '*May*' denotes helpful in some cases

aetiology of cognitive difficulties conferred by an expert neuropsychological assessment is now used to fulfil four primary roles prior to epilepsy surgery. These are as follows:
– (1) to provide a baseline assessment for outcome comparison;
– (2) to provide a collaborative contribution to seizure lateralization, localization, and characterization;
– (3) to provide evidence-based predictions of cognitive risk, including but not limited to amnesic risk and psychosocial outcome;
– (4) to provide feedback and neuropsychological education to the patient and family.
Each of these roles is discussed below. There are special considerations with respect to these roles associated with paediatric populations and those with an intellectual disability.

Baseline assessment for outcome comparison

A comprehensive neuropsychological assessment provides a baseline against which changes in postoperative function can be identified and expectations of postoperative change can be managed. The pre-surgical assessment should therefore include assessment of function in the core domains of cognition using standardized tests, taking into account all of the considerations set out in our previous guidelines (Wilson *et al.*, 2015). In the surgical setting, in addition to formal neuropsychological test scores, behavioural measures of cognitive function are useful, together with subjective ratings of the patients' difficulties in each cognitive domain. The latter are particularly important given the generally poor correlation between performance on formal neuropsychological tests and memory complaints (Lineweaver *et al.*, 2004). It is important to ascertain baseline levels of social cognition and behavioural executive functions, particularly prior to frontal lobe resections. The pre-surgical neuropsychological assessment should also include formal measures of mood and health-related quality of life. The measures used to establish these baselines should be standardized on appropriate populations to provide a reliable and accurate measure of the impact of the patients' epilepsy on the core domains of day-to-day function.
In most adult surgical candidates, it is also valuable to obtain similar ratings from a close family member. Family members not only provide an additional perspective on the impact of epilepsy on the patients' life, they can also provide valuable information on the impact of the condition on wider family dynamics. In children, parental and educator evaluations of behaviour and ability also make a valuable contribution to the creation of a detailed picture of baseline function, and an external evaluation of function is an integral part of the neuropsychological assessment in this group (*see section "Consideration of special populations"*).
The scheduling of the preoperative neuropsychological assessment should be carefully planned. Tests conducted within close proximity to a seizure (particularly a generalized seizure) or following sleep deprivation (as a provocative technique or due to seizure activity) may obscure potentially useful lateralizing signs and lead to an underestimate of true interictal ability. Sometimes this cannot be avoided, but if an assessment is conducted within close proximity to a seizure, the possible impact of the ictal state on the scores obtained both prior to and following the seizure should be recognized.
It is also important to be cognizant of medication effects with respect to the timing of the assessment. This may influence scheduling of the assessment in relation to the patient's individual medication schedule during the day. It may also be possible to postpone the assessment for some patients, following the withdrawal of medications which are known to have a significant impact on cognitive function.
It is important to ensure that the surgical decision-making process is based upon up-to-date information. Ideally, in adult populations, surgical decisions should not be based on the results of neuropsychological assessments that are more than 18 months old. Reassessments will be required following events which are likely to have had a significant impact on cognitive function, such as a period of status epilepticus. Given the dynamic nature of cognitive function in some of these patients, the assessment will need to be repeated to ensure stable function in these circumstances. The interval between the neuropsychological assessment and surgical decision-making process should be shorter in paediatric populations with an interval of no more than one year, and ideally much less in younger children.

Contribution to seizure characterization and lateralization/localization

Neuropsychological tests can be used to identify and quantify ictal and postictal deficits, which in turn can provide useful lateralization and localization data. Although language deficits such as aphasia are the most commonly documented difficulties in the peri-ictal phase (Privitera *et al.*, 1991), memory abilities have also been tested peri-ictally and test asymmetries can indicate laterality in TLE patients (Vulliemoz *et al.*, 2012).
Many lateralizing and localizing neuropsychological characteristics do not emerge until mid to late

adolescence and may not be present in younger paediatric populations (*see section "Consideration of special populations"*). Results from a neuropsychological assessment therefore need to be set into a neurodevelopmental context since lesions and seizures can impact brain and cognitive development in the maturing brain (via developmental hindrance) and in the ageing brain (via accelerated decline).

Our understanding of the aetiology of the cognitive and behavioural problems in epilepsy is based on a complex multifactorial model in which the epilepsy syndrome, the underlying brain disorder, the characteristics of the epilepsy, and aspects of brain development must all be considered together with the treatments for the condition (Lin *et al*., 2012). These factors and their interactions determine the patients' cognitive state prior to surgery and their prognosis afterwards. These factors can be loosely grouped into two categories. In the first, there are structural, congenital, or acquired lesions including surgical defects which are chronic and mostly stable, but can also be dynamic and progressive as in tumours, limbic encephalitis, or degenerative CNS diseases. The related damage and impairment are mostly irreversible and sometimes progressive. In adult TLE patients, preoperative performance on memory tests is correlated with a number of indices of hippocampal integrity including hippocampal volumes (Trenerry *et al*., 1993), cell counts (Sass *et al*., 1990), and temporal mesial functional activation (Sidhu *et al*., 2013).

The second group contains dynamic factors such as seizures, interictal epileptic discharges, sleep disorders, somatic comorbidities, and pharmacological treatments, which can lead to impairments which are potentially reversible (Dinkelacker *et al*., 2016).

The presence and severity of cognitive drug side effects depend on the substance, on the dose and total drug load if more than one drug is administered, and on titration speed (*see* Helmstaedter and Witt [2014]). In addition to the impact of each individual medication, the drug load, *i.e*. the number of drugs in combination with the defined daily dose, also has a major impact on cognition (Witt *et al*., 2015). This is an important consideration as most surgical candidates come to the programme taking many antiepileptic medications, often at high doses.

Psychiatric comorbidity can also have a significant impact on cognitive function prior to and following surgery. The psychiatric co-morbidity can occur independently or arise from the same organic substrate as the seizures and cognitive impairment (Kanner *et al*., 2012). Risk factors for psychiatric illness include a previous patient or family history, a structural brain abnormality, seizure frequency, medication effects, cognitive impairment, personality traits, and social and family functioning (Wrench *et al*., 2011a). This may account for the increased rate of psychiatric comorbidities identified in patients referred for surgery, as they tend to have more severe or frequent seizures, be on a higher medication load, and have a focal brain abnormality. It is beyond the scope of this paper to provide a full review of the psychiatric literature in this group, but neuropsychologists should be aware of the very significant impact these comorbidities can have on neuropsychological function in both pre and postoperative evaluations and should work closely with their psychiatric colleagues to assess and manage this impact.

The baseline neuropsychological scores should therefore be interpreted in the light of the results from all other pre-surgical evaluations in order to evaluate their lateralizing or localizing significance in terms of underlying pathology. Many different factors can combine to create the same profile of strengths and weaknesses within a neuropsychological profile. For example, at the simplest level, patients may present with significant word finding difficulties because they have a glioma in the posterior dominant temporal lobe, or because they are taking a high dose of topiramate (Thompson *et al*., 2000). It is only when the neuropsychological test scores are interpreted through the lens of the full clinical history of the patient and the results of other investigations that the lateralizing and localizing significance of the neuropsychological profile becomes clear.

It is beyond the scope of this paper to explain in further detail how to interpret a neuropsychological profile with respect to the significance of each of these factors. This knowledge is part of the specialist training of a clinical neuropsychologist.

Identification of cognitive risk and prediction of cognitive outcome following surgery

Epilepsy surgery is an elective treatment and cognitive decline is the most common morbidity associated with the procedure. In order to give informed consent for the treatment, all patients (or their carers) must be given as accurate information as possible regarding the risks and benefits of their proposed surgery. A neuropsychological assessment is therefore mandatory and should form an integral component of the presurgical evaluation and assessment of postoperative outcome for all epilepsy surgery patients.

The determination of language laterality is important in both planning surgical resections and predicting cognitive outcomes. Whilst baseline neuropsychological tests can provide useful information in this respect, standalone pencil and paper tasks are not definitive. The Wada test was considered the gold

standard in language lateralization but the procedure has now largely been superseded in modern surgery programmes by functional MRI language lateralization paradigms, which are both sensitive to lateralization and have greater localizing power (Janecek *et al.*, 2013a).

In temporal lobe resections, postoperative changes in cognitive function are most usefully conceptualized as a function of both the adequacy of the structures removed during the surgery and the reserve of the contralateral structures (Chelune, 1995). Baseline neuropsychological test scores can be used to predict outcome in many domains following surgery, including seizure control (Yu *et al.*, 2009), cognitive change (Baxendale *et al.*, 2006), and psychiatric difficulties (Cleary *et al.*, 2013). Prognostic data may include single indices of function in a specific domain (*e.g.* a verbal memory test score) or neuropsychological test scores can be combined with other measures of functional and structural integrity to provide proxy measures of hippocampal adequacy and functional reserve, which are used in multivariate predictive models (Baxendale *et al.*, 2006). These models or nomograms can be used to identify those most likely to experience an improvement in cognitive function postoperatively, in addition to those who are most likely to decline (Baxendale *et al.*, 2008a). Large numbers of neuropsychological scores can be statistically reduced to provide indices of function in broad domains, which in turn can also be used in statistical models to predict outcome (St-Laurent *et al.*, 2014). The outcome prediction literature not only identifies the prognostic features associated with both good and bad outcomes, but it also provides statistical models which explain how these factors interact. In patients who undergo standardized resections, these statistical models can be used to provide personalized predictions of outcome (Baxendale *et al.*, 2006). In some cases, where the risks of postoperative cognitive change are high, the proposed surgery may be deferred or modified in response to the results of the preoperative neuropsychological assessment, with more individualized surgical approaches offered to minimize the cognitive risks in some patients (Witt and Helmstaedter, 2017).

These statistical models cannot yet be used to predict outcomes in patients who are undergoing non-standardized resections. In these populations, predictions of postoperative outcome are based on the application of clinical knowledge and experience with respect to the cognitive and behavioural functions of the structures that will be removed. In paediatric populations, the assessment of postoperative change is more complex and is conceptualized as the impact on the child's subsequent developmental trajectory of cognitive and behavioural functions (*see section "Consideration of special populations"*).

Amnesic risk

The Wada test has been traditionally used to screen for amnesic risk in presurgical patients. It is also called the intracarotid amobarbital procedure (IAP) in the literature, although a number of alterative drugs can now be used to anaesthetize the hemisphere including propofol and etomidate. In adult populations, there has been a trend to move away from a reliance on the Wada test to screen for amnesic risk over the past decade (Baxendale *et al.*, 2008b; Baud *et al.*, 2018). This has been primarily driven by the advances in functional and structural brain imaging (Baxendale *et al.*, 2008c; Sidhu *et al.*, 2013).

Functional MRI (fMRI) protocols for language and memory function are gradually making the transition from research to clinical tools in the pre-surgical evaluation of epilepsy surgery candidates (Szaflarski *et al.*, 2017). A number of centres now exclusively rely on fMRI protocols for the clinical lateralization of language function and fMRI has a number of advantages over the Wada test in this regard. fMRI memory protocols primarily remain in the research domain although many show promise in the prediction of post-operative changes in memory function (Dupont *et al.*, 2010; Szaflarski *et al.*, 2017; Cabrera *et al.*, 2018).

Whilst functional neuroimaging is proving to be at least equal to and possibly better than the Wada test in lateralizing language function (Janecek *et al.*, 2013b), both structural and functional imaging play important complementary roles in screening for amnesic risk in adults.

There has been very little research on using the Wada test to predict memory outcomes after surgery in children (Lee *et al.*, 2005), and a recent survey of clinicians involved in the preoperative neuropsychological assessment of children also indicated a decline in the use of the Wada test due to the increased use of other mapping procedures (Berl *et al.*, 2017).

Neuropsychological feedback and education (patient and family)

Feedback of the results of the neuropsychological assessment to the patient is an integral part of the presurgical evaluation. The aim of the presurgical feedback session(s) is to explain the results of the assessment and help the surgical candidate and their family understand the aetiology of any cognitive or behavioural difficulties identified.

The feedback session should also include a full explanation and discussion of any changes in cognition that are expected following surgery, with an exploration of how these might impact on everyday function. It is vital

that the patient understands the cognitive risks associated with their procedure if they are to give informed consent.

Discussion of the possible psychiatric and psychosocial outcomes with the patient and their family should also form part of routine pre-operative care, since it is often these outcomes that impact the patient and family more than seizures. Recent research has highlighted that some individuals with epilepsy show traits of the broader autism phenotype, suggesting a neurological underpinning to social difficulties for some patients (Richard *et al*., 2017). This is important as individuals undergoing surgery often hope that it will expand their social horizons and offer them the chance to find a partner and have a family of their own (Coleman *et al*., 2018). Many of the problems identified in the presurgical assessment will not be changed by surgery regardless of the outcome in terms of seizure control, and it is important to use the feedback session to explore the surgical candidates' expectations of surgery, and those of their family. It is sometimes necessary to spend some time ensuring that surgical candidates and their family members have realistic expectations of what successful surgery can and cannot achieve (Wilson *et al*., 1999).

The surgical decision-making process is complex. Prospective candidates need to weigh up the chances of being seizure-free or having a significant reduction in seizures and the importance of all of their goals and expectations that go well beyond seizure reduction against the potential risks of the surgery. They also need to consider the risks associated with continued, uncontrolled seizures if they do not pursue surgery (*e.g*. accidents/injury, SUDEP, epilepsy progression, cognitive decline) (*see* Laxer *et al*. [2014]). The potential risks of not proceeding to surgery also factor into presurgical decision-making, and a discussion of these issues should be included in preoperative counselling. Neuropsychologists play a key role in identifying the cognitive risks associated with all of the possible treatment scenarios in the surgical decision-making process.

If the presurgical neuropsychological assessment indicates that the patient is at high risk of a postoperative deterioration in cognitive function, cognitive rehabilitation can be implemented prior to surgery to prepare the patient for the anticipated losses; this has been termed "pre-habilitation". The pre-habilitation approach has the advantage of utilizing functions before they are lost to establish the compensatory cognitive routines and strategies that the patient will need after the surgery. The same approach should be applied to treating any anticipated postoperative mood, vocational or psychosocial adjustment difficulties (Wrench *et al*., 2011b).

POSTOPERATIVE ASSESSMENT

Since cognitive decline is one of the most significant sequelae of epilepsy surgery, a postoperative neuropsychological assessment is essential in assessing outcome in this population. A postoperative neuropsychological assessment should be a mandatory component of epilepsy surgery. The same principles that inform the comprehensive nature of the preoperative neuropsychological assessment should guide the assessment of postoperative outcome. The postoperative assessment should evaluate all aspects of cognitive and behavioural function, as assessed prior to surgery. In addition to all of the factors that influence an individual's neuropsychological profile in a presurgical assessment, the nature, timing and extent of the surgery, and other facets of postoperative outcome, particularly seizure control, must be considered in the interpretation of the results from a postoperative neuropsychological assessment.

A detailed picture of postoperative changes in seizure control should form an integral part of the postoperative neuropsychological assessment. The relationship between postoperative seizure control and cognitive change is complex. There is some evidence that cognition improves with seizure control following successful epilepsy surgery, at least in some patients, whilst other studies have found no association or report greater cognitive declines in those with ongoing seizures following surgery (Baxendale, 2015). To some extent, this heterogeneity probably represents the nature and focus of any postoperative seizures and whether they arise from ipsilateral or contralateral regions.

The timing of the postoperative assessment needs careful consideration; this group is not exempt from the general concerns of practice effects contaminating serial assessments in neuropsychological practice. The use of tests with parallel forms can overcome some, but not all of the difficulties associated with multiple assessments conducted over a short period of time. In both individual cases and group studies of postoperative cognitive outcome in this population, deterioration and improvement should be identified with reliable methods which take into account the psychometric properties of the cognitive tests employed. These methods include reliable change indices and standardized regression-based norms (Hermann *et al*., 1996; Martin *et al*., 1998).

In addition to consideration of the interval between assessments, the interval between the postoperative assessment and the surgery itself (such as oedema and Wallerian degeneration) will also have an impact on the results obtained. Postoperative cognitive function following surgery is a dynamic entity. Acute effects of the

surgery are likely to be evident in a neuropsychological profile up to six months after the operation. After this phase, a gradual improvement in function may occur which tends to plateau by one year, although group studies mask the considerable individual variations in the postoperative trajectories of cognitive function that can take place well beyond the one-year anniversary of surgery (Engman *et al*., 2006). By one year, function may not have returned to preoperative levels in some cognitive domains in up to one third of adult surgical candidates. Full recovery may take a long time period, particularly when patients are older (Helmstaedter *et al*., 2003), and an early assessment may underestimate an individual's ultimate postoperative level of function. After surgery, children show faster recovery from surgically caused impairments than adults (Gleissner *et al*., 2005), whilst older adults are more at risk of significant postoperative decline in cognitive function (Helmstaedter *et al*., 2002; Thompson *et al*., 2015; Tai *et al*., 2016). These trajectories need to be considered when planning the postoperative evaluation of cognitive outcomes in these groups. As a minimum, we recommend a postoperative assessment between six and 12 months following surgery.

In addition to the exacerbation and continuance of presurgical psychiatric difficulties, neuropsychologists should be especially alert to the development of *de novo* psychiatric presentations following surgery and the impact they can have on post-operative neuropsychological function and psychosocial outcomes (Wrench *et al*., 2011a). Postsurgical depression and/or anxiety are the most frequent psychiatric disorders identified in adults following resective surgery, although anxiety may be reduced for some in whom the amygdala is resected (Dellacherie *et al*., 2011). Symptoms have a tendency to occur within the first 3-6 months and remit by 12-24 months, with persistent symptoms found in up to 15% of patients at the 12-month follow-up period (Wrench *et al*., 2011b).

Evaluating psychosocial outcomes

It has long been recognized that seizure freedom or improved seizure control following the surgical treatment of epilepsy does not automatically translate to better psychological and social functioning. Consideration of an individual's psychosocial status following surgery therefore has the potential to not only improve the patient's quality of life and well-being but also to reduce the rates of psychiatric readmission to hospital post-surgery. A comprehensive assessment should include consideration of depression, anxiety, illness beliefs and coping strategies, quality of life, and daily psychosocial functioning as well as screening for any other psychiatric disorders or behavioural comorbidities (Wilson *et al*., 2015).

Overall, research points to an improvement in Health-Related Quality of Life (HRQOL) following surgical treatment compared to ongoing medical treatment (Wiebe *et al*., 2001). While post-surgical seizure freedom has consistently been associated with HRQOL outcomes, other factors are also pertinent including pre-surgical psychological functioning, post-surgical antiepileptic (AED) adverse events, employment status, ability to drive, and psychological functioning (Baker, 2001; Seiam *et al*., 2011).

Although there have been a number of studies that have documented the outcome of epilepsy surgery, research has lacked uniformity in the choice of outcome measures or the length of follow-up (Malmgren and Edelvik, 2017). Moreover, the majority of research has focused on the initial 12-24 months post-surgery, which may underestimate the benefits of seizure freedom in the long-term due to early post-operative adjustment difficulties (Wilson *et al*., 2007; Jones and Hanson, 2015; Coleman *et al*., 2018). Research into quality of life in people with epilepsy who do not undergo surgery suggests that improvement occurs in HRQOL and social functioning in individuals who attain seizure freedom, leading some to suggest that surgical status itself has little effect on quality of life and psychosocial outcomes. Here, we recommend that in order to establish the impact of epilepsy surgery, patients and families should be followed for at least five years.

The minimum clinically important difference (MCID) is an informative metric when looking at HRQOL as it reflects the smallest change in an outcome a patient would identify as important. It allows for identification of those patients who have improved, worsened or remained unchanged following treatment (Seiam *et al*., 2011). While it has been routinely used to assess change in neuropsychological functioning, its value for assessing change in HRQOL has only recently been recognised. Positive meaningful changes in MCID have been associated with surgical treatment compared to ongoing medical management and with post-surgical seizure freedom compared to continued seizures (Taft *et al*., 2014).

In order to determine the MCID, a clinician must make an assessment of HRQOL. There is currently no gold standard for measuring HRQOL, however, a number of epilepsy-specific instruments are available, such as the Epilepsy Surgery Inventory-55 (ESI-55), or the expanded and more generic measure, Quality of Life in Epilepsy Inventory-89 (QOLIE-89 or its short form: QOLIE-31) (Hermann *et al*., 2017). While there is some variation in the usefulness of these measures to differentiate between the magnitude of change, overall, they are psychometrically robust with a MCID available for the QOLIE-89 that allows categorisation of patients

into various levels of change in HRQOL status (Wiebe *et al*., 2002).

Behavioural, mood and adjustment difficulties following surgery

For both paediatric and adult patients who attain seizure relief following surgery, a complex process of adjustment for the patient and family can occur as they transition from chronically ill to "suddenly well". This adjustment process, known as the "burden of normality", has been well described in the literature and impacts behavioural, psychological, social, and affective domains of functioning (Wilson *et al*., 2001; Wilson *et al*., 2007; Micallef *et al*., 2010). The interactions between domains are also important to consider as they may represent targets for therapeutic intervention. For instance, poor postoperative family dynamics have been shown to predict postoperative depression, with early post-operative family psychoeducation and therapy providing a potential means of preventing this (Wrench *et al*., 2004).

To date, there has been a relative lack of work examining the patiente and family experience of epilepsy surgery, particularly over the long term (Malmgren *et al*., 2015). Unsurprisingly, seizure outcome has been found to make the largest independent contribution to a patient's satisfaction with surgery, however, preoperative expectations and post-operative mood have also been identified as making additional and unique contributions (Wilson *et al*., 1999). For example, unrealistic expectations, such as expecting surgery to make you more clever or skilful at work, have been found to negatively impact post-surgical HRQOL, whereas patients with more achievable expectations are more likely to consider surgery a success (Baxendale and Thompson, 1996; Wilson *et al*., 1999).

For both adults and parents of children who undergo epilepsy surgery, dissatisfaction is consistently related to psychiatric, behavioural or neurological complications of the surgery (Keene *et al*., 1998; Sajobi *et al*., 2014; Ozanne *et al*., 2016). This provides clear red flags for clinicians to consider when working with patients having surgery. Patient satisfaction is an extremely important measure to include in routine follow-up as it predicts treatment success, compliance, and appropriate use of services (McCracken *et al*., 1997; Albrecht and Hoogstraten, 1998).

Neuropsychological intervention following epilepsy surgery

Neuropsychological interventions following surgery are informed by the findings of the postoperative assessment of outcome and are designed to help the patient adjust to their postoperative status, whether they are seizure-free or not. Rehabilitation can reduce the impact of memory decline following both dominant and non-dominant temporal lobe surgery (Helmstaedter *et al*., 2008; Mazur-Mosiewicz *et al*., 2015).

Formal cognitive rehabilitation programmes, which may have been implemented prior to surgery should continue and should be tailored to address the specific deficits identified in the postoperative neuropsychological follow-up. However, the role of the neuropsychologist in interventions following epilepsy surgery extends beyond the cognitive realm.

In adults, this may include working with patients and their families to help them adjust to the burden of normality conferred by postoperative seizure control, or managing post-operative mood symptoms, typically anxiety and depression (Wilson *et al*., 2007; Wrench *et al*., 2011b). The burden of normality can have profound effects on a patient's family unit and social functioning as people adjust to the patient's increased level of independence. This can include attempts by the patient to make up for "lost time" by engaging in a range of activities, often over-doing it. Patients may also try to assert increased control within an established relationship, upsetting existing marital or family dynamics in which the patient has occupied the "sick role". For some families, this adjustment is resolved, however, for others it can result in the dissolution of relationships or falling out with families (Coleman *et al*., 2018). This highlights the importance of including family members in the post-operative rehabilitative process, with counselling of family or couples sometimes required to navigate this difficult period (Wilson *et al*., 2001, 2007).

Vocational therapy may play a critical role in helping adults maximize their employment potential following successful epilepsy surgery. Overall, the literature points to improved vocational outcomes for adults following epilepsy surgery (Dupont *et al*., 2006; Andersson-Roswall *et al*., 2013), with vocational therapy of particular value to those who have a limited history of employment prior to surgery (Thorbecke *et al*., 2014).

Those who are not seizure-free following surgery, or who have developed significant cognitive sequelae, also undergo an adjustment process that differs from the burden of normality, but nonetheless is characterized by common psychological themes (Shirbin *et al*., 2009; Fernando *et al*., 2014). These include a sense of ambivalence towards surgical success and an acceptance of the return of seizures and the need for continued AEDs, as well as their impact on personal autonomy and independence. Patients engage in cognitive reframing and benefit finding in the

context of seizure recurrence (Shirbin *et al*., 2009), which may be enhanced by supportive counselling or cognitive/behavioural therapy to help patients or family members come to terms with a disappointing outcome. Ideally, this therapeutic input should be an extension of the comprehensive preoperative counselling process and should be managed in close clinical collaboration with other treating members of the multi-disciplinary team, particularly psychiatric colleagues.

Consideration of special populations

Children

The assessment of paediatric surgical candidates should also address a range of cognitive and behavioural functions, as described above. However, the neuropsychological assessment of children both prior to and following surgery is complicated by the fact that the epilepsy and the surgical resection influence the developing rather than the mature brain and hence developing cognitive and behavioural systems (Smith and Berl, 2016). With young children, particularly those with significant developmental delay, the assessment may have to be focused on the development of language, motor, and adaptive function (Smith and Berl, 2016). As patterns of cerebral lateralization of function may emerge only after a period of development (*e.g*. language [Kadis *et al*., 2011]), early onset of seizures in either hemisphere may negatively impact the development of those functions, or result in atypical representation. Furthermore, it has been demonstrated that cognitive phenotypes are similar across some childhood epilepsy syndromes (Hermann *et al*., 2016), and that there can also be an overlap of cognitive impairment between symptomatic epilepsies arising from the temporal or frontal lobe (Smith, 2016). Thus, the neuropsychological profile in paediatric cases, particularly in younger children, may not yield lateralizing or localizing signs. In teenagers with temporal lobe foci, the patterns are more similar to those described in adults, and thus similar approaches for interpretation and analysis of risk are appropriate (Law *et al*., 2017).

It can be challenging to identify test measures that are normed across a wide age range from early childhood to late adolescence, which further complicates the comparison of results at different ages and longitudinal assessment of surgical outcomes. Nevertheless, evaluation of long-term outcomes is critical in understanding the impact of epilepsy and surgery as it has been shown that there are changes in the neuropsychological profile over time (Gleissner *et al*., 2005; Puka and Smith, 2016). Measures of academic skills should be incorporated into the assessment. As well as serving their roles in the surgical evaluation process, the test results also provide valuable information on the need for academic or other remedial interventions for children. Such interventions may need to be revised over time to account for changes in the child's neuropsychological profile resulting from development, surgery or change in seizure frequency, or due to the increasing challenges placed on the child with progression to higher academic grades. Such expected changes represent another argument for following children over a relatively long period of time after surgery.

When considering epilepsy surgery in children, the impact on behaviour and ongoing development must be especially considered. Broadly speaking, the psychiatric outcomes for children and adolescents appear similar to those of adults; some may experience an improvement in mental health, some may see no change, while others may experience deterioration in psychiatric symptoms or develop *de novo* symptoms. Unfortunately, there is a dearth of long-term prospective studies on children to elucidate the lasting impact on behaviour and well-being. Overall, however, earlier age at surgery has been associated with improved outcomes, while longer duration of epilepsy has been negatively correlated with developmental and behavioural outcomes (Rayner *et al*., 2019).

It is particularly important to consider both patient and parental perceptions of surgical success in this group. Similar to adults, paediatric outcome studies have shown that parental satisfaction is related to seizure outcome (Iwasaki *et al*., 2013). Even when patients do not report satisfaction with the outcome of surgery, they may still be able to recognize that it was the right decision to make, allowing opportunities for reframing and benefit finding in therapeutic follow-up.

People with intellectual disability/learning disability

Intellectual disability (ID) should not be considered a contraindication to neurosurgery for epilepsy and access to epilepsy surgery for this group has significantly improved in the 21st century (Davies *et al*., 2009). Neuropsychological evaluation of people with epilepsy with ID is challenging since they often score at the "floor" of many standardized tests. Establishing the baseline level is not easy, particularly in the presence of language deficits. Quantitative and qualitative assessments of intellectual level, attention, memory, language, and spatial and executive functions should be nonetheless carried out with standard cognitive measures, rigorously selected and adapted to avoid floor effect (*for domains, refer to Wilson et al. [2015]*).

Given the high prevalence of behavioural problems in people with ID, specific attention should be given to assess adaptive and psychosocial skills in activities of daily living (*i.e.* communication, social responsibility, autonomy at home, work, leisure) with appropriate questionnaires. Although some psychometric tools are valuable, it remains difficult for clinicians to gain evidence of impairment in these patients because of a lack of validation in this patient population. The cognitive and behavioural profiles that usually provide information for seizure characterization, lateralization and localization are not easy to interpret. A further challenge is detecting post-surgical changes in patients already impaired because of the lack of sensitivity of measures. Finally, communication barriers can complicate the acquisition of informed consent, necessitating the involvement of a surrogate or legal guardian. Additional time should be taken to help patients to express their expectations and goals of treatment and manage any postoperative adjustment issues working alongside family members or caregivers.

Conclusion

A neuropsychological assessment is a mandatory part of the preoperative evaluation of epilepsy surgery patients. The assessment should comprise standardized measures of cognitive function in addition to wider measures of behavioural and psychosocial function. The results from the presurgical assessment are used to establish a baseline against which change can be measured following surgery. The presurgical assessment also contributes to seizure lateralization, localization and characterization, and provides evidence-based predictions of cognitive risk associated with the proposed surgery. It forms the psychological basis for comprehensive preoperative counselling, including exploration of patient and family expectations of surgical treatment.

The assessment of neuropsychological and psychosocial outcomes following surgery should be an integral part of the postoperative follow-up. Neuropsychological changes following surgery are dynamic and careful consideration should be given to the potential impact of the interval from surgery on the results of any postoperative neuropsychological assessment. The neuropsychologist plays a key role in the pre-habilitation and postoperative rehabilitation and support of the patient and family members, working closely with other members of the multidisciplinary team. In summary, *table 1* provides a checklist to outline the indications, expectations, and recommendations of neuropsychological assessment in epilepsy surgery in children and adults. □

Acknowledgements and disclosures.
All of the authors are currently serving on the ILAE Neuropsychology Task Force 2017-2021. C. Helmstaedter reports grants from the EU, honoraria from UCB, Eisai Inc., GW pharma, Precisis for counselling and advisory board activities, travel support by Desitin, a honorary for editorial work for the journal Seizure (Elsevier), honoraria from insurance companies and court for testimonies, license fees from UCB in the past, and license fees from Eisai Inc. None of the other authors have any conflict of interest to declare.

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