4 Neuropsychological Evaluation of the Epilepsy Surgical Candidate

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Neurosurgical intervention is the primary treatment option for patients with partial epilepsies that are refractory to treatment with antiepileptic drugs (AEDs). The probability that a patient with epilepsy will be successfully treated with an AED greatly diminishes after two drug trial failures (Kwan & Brodie, 2000), and such patients are typically considered for surgical intervention (Kwan et al., 2010). Neuropsychological assessment is an integral component of the surgical management of patients with epilepsy, representing a useful clinical method for identifying optimal surgical candidates and maximizing outcome parameters while serving as a primary research tool. The practice of neuropsychology in the setting of the epilepsy monitoring unit has greatly enriched our understanding of neurocognitive processes and their underlying neural substrates, as this environment provides a unique opportunity to study brain functions in a highly controlled fashion before and after surgical resection. Likewise, the clinical impact of neuropsychology has been profound, as it represents a means to confirm seizure onset, to predict the possible effect of surgical intervention, and to track changes over time. Neuropsychologists are also ideally equipped to explain the potential risks and benefits of surgery to patients, to identify and address comorbid psychiatric issues, and to direct the course of cognitive rehabilitation when necessary following surgery. The goals of the current chapter include elucidating the purpose of neuropsychology in epilepsy surgery, exploring potential difficulties involved in obtaining a valid assessment of the epilepsy patient (e.g., dealing with the possible effects of acute seizure activity or the confounding effect of AEDs), and providing concrete recommendations regarding the selection of tests to achieve both clinical and research goals. A summary of the findings that have been amassed over the years regarding the presurgical confirmation of the seizure focus and postsurgical identification of neurocognitive deficits resulting from surgery is provided. In this context, research regarding the usefulness of neuropsychological results to predict surgical outcome is covered as well, and a clinical vignette is included to highlight several of the central topics.

Role of Neuropsychology in the Evaluation of the Epilepsy Surgical Patient

Neuropsychological assessment can make multiple contributions to the assessment of the epilepsy surgical patient including:

1. *Confirming the lateralization and localization of seizure focus for surgical planning.* While the gold standard of determining

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seizure focus remains the electrophysiological data obtained through video-EEG monitoring, neuropsychological testing provides a useful adjunct for confirming seizure focus. Studies have demonstrated that surgical outcome is better in terms of neurocognitive functioning and seizure freedom when independent sources of data (e.g., neuroimaging, electrophysiology, neuropsychological testing) point to the same probable seizure focus (Holmes, Miles, Dodrill, Ojemann, & Wilensky, 2003; Lineweaver et al., 2006).

2. *Establishing the presurgical neurocognitive and emotional/psychological baseline for the potential surgical candidate*. This allows us to recognize presurgical emotional/psychological factors that may require treatment to improve postsurgical success. Establishing a baseline also makes it possible to recognize change following surgery, allowing for appropriate neurological rehabilitation interventions, education/vocational adjustments, or assistance from social services.
3. *Predicting surgical outcome*. Establishing a presurgical neuropsychological baseline allows us to estimate the risk of potential decline in neurocognitive, functional, emotional, or psychosocial status following surgery. Baseline neuropsychological status is one of several predictors of neurocognitive outcome and the likelihood of achieving seizure freedom. Some have attempted to create formulas for predicting outcome that are based in part on neurocognitive performance.
4. *Providing outcome markers that can be useful in the context of research and program development/evaluation*. The overall goal of epilepsy surgery is to alleviate seizure occurrence while minimizing any secondary neurocognitive, emotional/psychosocial, or physical sequelae of this procedure. Neuropsychological assessment plays a pivotal role in quantifying baseline performance, predicting and evaluating change, and elucidating underlying brain-behavior relationships.

Review of Research Outlining Commonly Observed Pre- and Postsurgical Deficits in Epilepsy Surgical Patients

It is essential that the clinical neuropsychologist has a working knowledge of the commonly observed presurgical deficits in epilepsy patients in order to conduct an optimal evaluation. In this section, commonly observed presurgical deficits are described for each of the major epilepsy surgical populations, including temporal lobe epilepsy, frontal lobe epilepsy, and the posterior cortical epilepsies. Knowledge of the most common postsurgical deficits is also essential in order to select tests that will be useful for monitoring change over time. A summary of findings for each syndrome appears in a table at the end of each section.

Findings in Temporal Lobe Epilepsy (TLE)

Approximately 50 % of patients with epilepsy are believed to experience partial seizures (Williamson, 1987). Among patients diagnosed with complex partial seizures, 70–90 % of patients have seizures arising from the temporal lobe (TL). Patients with mesial temporal sclerosis (MTS), which is neuronal loss and gliotic scarring of the hippocampal formation/mesial TL structures, are typically medication refractory. Individuals with TLE are often ideal candidates for surgical treatment to achieve seizure control (Wiebe, Blume, Girvin, & Eliasziw, 2001).

For many years, the prototypical pattern of deficit in presurgical TLE patients has been described as a material-specific pattern of memory dysfunction (Milner, 1958). More specifically, auditory/verbal memory deficits are often observed in patients with dominant TL seizure onset, while visual memory deficits have been more associated with nondominant TL seizure onset (Blakemore & Falconer, 1967; Jones-

Gotman, 1986; Loring, Lee, Martin, & Meador, 1988; McDonald, Bauer, Grande, Gilmore, & Roper, 2001; Milner, 1968a; Pillon et al., 1999). Neuroimaging studies have bolstered this finding, demonstrating that auditory/verbal and nonverbal stimuli can preferentially activate the left or right MTL, respectively (Golby et al., 2001; Powell et al., 2005). In contrast, other behavioral studies have not found this material-specific pattern (Barr et al., 1997; Pigott & Milner, 1993), and some neuroimaging studies have suggested an interaction between the mesial TLs modulated by specific task demands (Kennepohl, Sziklas, Garver, Wagner, & Jones-Gotman, 2007). Visual memory deficits associated with nondominant hemisphere dysfunction have been particularly difficult to establish. Overall, a material-specific pattern of memory dysfunction can be observed in presurgical TLE patients, which can be useful for confirming seizure focus in the individual patient. However, a variety of confounding factors can obscure this pattern and can lead to divergent findings at both the individual and group level. Emerging research also suggests the material-specific pattern of memory dysfunction model may be affected by other task parameters and disease-related variables. For example, material-specific findings may be easier to detect when examining both learning and recall patterns rather than only examining one-trial learning (Jones-Gotman, Zatorre, Olivier, et al., 1997). Further, material-specific findings may be altered by side of seizure onset (Vannest, Szaflarski, Privitera, Schefft, & Holland, 2008; Weber, Fliessbach, Lange, Kugler, & Elger, 2007), and both TLs may eventually be impacted by a chronic duration of unilateral TLE (Cheung, Chan, Chan, Lam, & Lam, 2006).

Jones-Gotman and colleagues at the Montreal Neurological Institute have suggested that dominant and nondominant presurgical TLE patients may differ in terms of their ability to learn and retain information (Jones-Gotman et al., 1997; Majdan, Sziklas, & Jones-Gotman, 1996). Their data indicated that left TLE patients had minimal difficulty with initial learning for words but demonstrated significant impairment on recall following a delay, while right TLE patients demonstrated impaired learning of abstract designs but recalled what they were able to learn. This pattern represents a possible way that a task paradigm might interact with material-specific findings.

Hermann and colleagues provide evidence that both TLs may eventually be affected in a number of patients by seizures of unilateral TL onset. In one study, they used a cluster analysis to demonstrate that common presurgical neuropsychological profiles may exist for patients with TLE (Hermann, Seidenberg, Lee, Chan, & Rutecki, 2007). Approximately half of their sample did not differ from healthy controls with regard to IQ, perception, primary attention, or immediate memory yet showed mild deficits (no more than 1 SD below the mean of the control sample) on tasks tapping delayed memory, confrontational naming ability, executive control processes (e.g., generative fluency), and cognitive/psychomotor processing speed. These deficits sound reminiscent of the prototypical findings reported over the years, with the exception that these patients showed disruption of both verbal and visual memory functioning. A second group, which comprised another 24 % of the TLE sample, was described as primarily experiencing memory impairment, with immediate and delayed memory scores that were more than 2 SDs below the mean of the control sample. They also displayed mild deficits in all remaining cognitive domains. Finally, the third cluster, including another 29 % of participants, was described as a memory-, executive-, and speed-impaired group and performed more than 2 SDs below controls on all administered measures. The third cluster exhibited the greatest impairment, took the most AEDs, and had the longest duration of epilepsy and greatest MRI volumetric abnormalities. This group also exhibited the worst cognitive course of the three samples. Limitations in this study included a small sample size and an exclusive focus on patients with childhood or adolescent onset of epilepsy. Work of this nature is promising and needs to be replicated across epilepsy centers and with other tests, in order to rule out the impact of latent variables as described below and to determine how such patterns may differ from patients with adult seizure onset.

There is also growing evidence that different types of learning tasks are mediated by different subregions of the TL. In general, associational learning (e.g., word pairs) has been thought to be related to the hippocampus, but it appears that other aspects of the mesial TL region may actually prove to be more critical (e.g., perirhinal or entorhinal cortices) (Weintrob, Saling, Berkovic, & Reutens, 2007; Weniger, Boucsein, & Irle, 2004). In either case, associational learning tends to be one of the more sensitive tasks to mesial TL dysfunction (Saling, 2009; Squire, 1993). Recall of easier, semantically related word pairs is often mildly impaired in patients with dominant TL dysfunction, while recall of more difficult, unrelated word pairs is often severely compromised. Contextual learning, such as reflected by the commonly used paragraph and story recall tasks, has proven less sensitive to mesial temporal lobe pathology (Rausch & Babb, 1993; Saling et al., 1993). These tasks, along with other measures that lend themselves to being organized semantically (e.g., category-related word list learning), may be more dependent on lateral TL structures. For example, Helmstaedter and colleagues (Helmstaedter, Elger, Hufnagel, Zentner, & Schramm, 1996; Helmstaedter, Grunwald, Lehnertz, Gleissner, & Elger, 1997) demonstrate that selective amygdalohippocampectomies contribute to declines in associational learning (particularly for unrelated information), while standard TL resections (which includes lateral TL as well) also affect list learning and semantically related word pairs. They suggest that lateral TL cortex is related to data acquisition and working memory, while the medial TL is involved in consolidation processes. Saling and colleagues have suggested that the medial TL structures (particularly perirhinal cortex) play a critical role in establishing a relationship between items that are yet to be linked in either personal episodic or semantic memory or which may conflict with preexisting knowledge (Saling, 2009).

TLE patients, particularly those with dominant seizure onset, are also more likely to experience deficits in naming ability (e.g., confrontational naming, naming to description) than healthy controls or patients with extratemporal seizure onset (Mayeux, Brandt, Rosen, & Benson, 1980). Several studies have found that left TLE groups perform worse than right TLE groups on visual confrontational naming tasks (Hermann & Wyler, 1988; Hermann, Wyler, & Somes, 1991; Langfit & Rausch, 1996), although the right TLE groups often perform worse than healthy controls (Langfit & Rausch, 1996). A few studies have found both left and right TLE patients to be equally impaired preoperatively (Hermann, Wyler, Steenman, & Richey, 1988). Patients may be impaired on these tasks for reasons other than seizure focus. For example, those with lower IQ show restricted naming scores which are more likely due to their general level of impairment and subsequent limitations on learning. One recent study provided a regression equation that takes into account such moderator variables in an effort to use a naming task (i.e., Boston Naming Test) to aid in preoperative seizure localization (Busch, Frazier, Haggerty, & Kubu, 2005). This study provides promising results but requires further confirmation and possible refinement. Hamberger and colleagues have introduced a naming-to-description task which appears promising for predicting preoperative lateralization as well (i.e., Columbia Auditory Naming Test) (Hamberger & Seidel, 2003; Hamberger & Tamny, 1999). Finally, patients undergoing dominant TL resection often show significant declines on naming tasks (Davies et al., 1998; Hermann, Davies, Foley, & Bell, 1999), while those undergoing nondominant TL resection do not (Saykin, Stafiniak, Robinson, et al., 1995). This pattern again highlights the seemingly critical involvement of the dominant TL in naming ability.

Evidence exists that the naming deficits of TLE patients may be more extensive than previously recognized. A few studies demonstrate that left (dominant) TLE patients are impaired at naming famous faces (Drane, Ojemann, Aylward, et al., 2008; Glosser, Salvucci, & Chiaravalloti, 2003; Seidenberg, Griffith, Sabsevitz, et al., 2002), and at least two of these studies suggest that these deficits may be worse following ATL resection. Drane et al. (Drane et al., 2008; Drane, Ojemann, Tranel, Ojemann, & Miller, 2004) recently extended these findings to include other visually complex item categories (e.g., famous landmarks, animals) even when performance is completely normal on standard naming measures (e.g., BNT). They have argued that commonly used naming measures lack sensitivity to the specific item categories that appear the most affected by anterior TLE surgery, as such measures employ a restricted range of object type (i.e., mostly man-made objects). Once again, these findings are bolstered by functional imaging paradigms highlighting a critical role for the anterior TLs in naming certain object categories (Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996; Griffith, Richardson, Pyzalski, et al., 2006).

It is also relatively common for presurgical TLE patients to exhibit deficits on verbal fluency tests (i.e., generating items from categories, letter fluency) (Troster et al., 1995). However, deficits in semantic fluency are often present preoperatively in patients with either dominant or nondominant TL seizure onset (Bartha, Benke, Bauer, & Trinka, 2005; Joanette & Goulet, 1986; Martin, Loring, Meador, & Lee, 1990) and can be observed in patients with either dominant or nondominant frontal lobe (FL) seizure onset as well (Drane et al. 2006). As these findings could be affected by the use of AEDs, many of which affect generative fluency and speech production rates (Fritz et al., 2005), it should be noted that other types of lesions in these regions have also been shown to impact semantic fluency in patients without epilepsy (Joanette & Goulet, 1986; Stuss et al., 1998). The complex nature of semantic fluency tasks likely requires the involvement of several neural systems for successful completion. Therefore, the presence of baseline semantic fluency deficits may not be of lateralizing or localizing value when viewed in isolation but may be helpful in this regard if the component parts of this task are examined. For example, one recent study suggests that preoperative patients with FL onset can often be distinguished from those with TL onset using a semantic fluency paradigm that contrasts cued and uncued performance (Drane et al., 2006). This builds upon the idea that semantic fluency requires both an executive component mediated by FL regions (i.e., organization/retrieval problems making it difficult to search one's own semantic memory stores and/or deficits involving initiation of action or self-monitoring) (Sylvester & Shimamura, 2002) and a semantic memory component that is thought to be mediated by the TLs (Martin & Fedio, 1983).

While studies examining postoperative semantic fluency appear to be limited in nature, there is evidence that performance in this domain (e.g., generating types of animals) declines following dominant TL resection (Loring, Meador, & Lee, 1994) and perhaps following nondominant TL resection as well (Martin et al., 1990), although the latter study had only a 1-week postoperative follow-up period. One additional study supports the idea that both left and right TL resections may both affect semantic fluency performance but found that the relative impact of surgery may vary greatly between hemispheres depending upon the category of object (Jokeit, Heger, Ebner, & Markowitsch, 1998).

Performance on letter fluency tasks can be impaired preoperatively due to both FL and TL impairment (Helmstaedter, Kemper, & Elger, 1996; Martin, Sawrie, Edwards, et al., 2000), although performance on these measures typically does not decline following TL surgery. Deficits observed on this task in TL patients may occur due to the disruption of widespread neural networks secondary to epileptiform activity, and some evidence exists that improvement on these measures can be seen if the TL patient becomes completely seizure-free following surgery (Martin et al., 2000). Therefore, as letter fluency performance appears not to decline following TL surgery, this provides further evidence that the anterior TL does not play a major role in performance of this task.

Despite the deficits mentioned in naming ability and generative fluency, presurgical TLE patients do not demonstrate a classic aphasia (unless it is due to a separate neurological injury or disease, such as a prior stroke). Most TLE patients will not exhibit problems with comprehension, speech fluency, or repetition of words or phrases, nor will they present with positive signs of aphasia in spontaneous speech (e.g., paraphasic errors). Similarly, standard anterior TL resection does not typically lead to declines in these areas (Saykin et al., 1995).

With the exception of interest in visual memory functioning, less work has been focused on the nondominant TL in the context of epilepsy. Most have assumed that the nondominant TL is less critical than the dominant one, and there is likely some truth to this idea. Declines in auditory/verbal memory and naming ability, findings predominantly associated with the dominant TL epilepsy and resective surgery, can be particularly devastating, while many patients seem to be less hampered by visual memory declines. Nevertheless, there is evidence that we may not fully appreciate the functions of the nondominant TL, and the field's tendency to think of visual memory as a unitary construct may be misleading (e.g., creating a visual memory index with several disparate tasks that may eventually prove to rely on different neural substrates). Evidence outside of epilepsy indicates that visual memory may involve several dissociable components (Bird & Burgess, 2008). For example, human "place" cells in the hippocampus are believed to respond to one's position, functioning to activate (recall) broader spatial maps in order to allow for successful localization of position in relation to the environment and objects within it (Byrne, Becker, & Burgess, 2007). In addition, functional neuroimaging studies demonstrate that route learning/way finding, which is rarely assessed clinically, appears to activate both mesial TLs (Treyer, Buck, & Schnider, 2005), and several experimental studies (some examining TLE patients) suggest that performance on these tasks can be compromised by right anterior TL damage (Spiers, Burgess, Maguire, et al., 2001). Finally, object-location tasks also tend to be impaired following right mesial TL dysfunction (Crane & Milner, 2005; Pigott & Milner, 1993), although performance here can be affected by varying task parameters. For example, while right TL patients tend to perform worse on tasks that are three-dimensional, a few studies suggest that left TL patients are more impaired on object-location tasks that are two-dimensional (Kessels, Hendriks, Schouten, Van Asselen, & Postma, 2004).

Recent studies also indicate that nondominant TLE patients often exhibit object recognition deficits. For example, at least four studies demonstrate that postoperative right ATL patients exhibit recognition deficits for famous faces when compared to controls (Drane et al., 2008; Glosser et al., 2003; Seidenberg et al., 2002). There is also evidence that recognition deficits for animals and famous landmarks may occur in patients following nondominant resection as well and that even a sense of "familiarity" may be impaired in these individuals (Drane et al., 2004, 2008). Patients with these deficits have greater difficulty recognizing familiar individuals, which may compromise social functioning.

One perhaps unexpected neurocognitive finding in presurgical TLE patients is evidence that such patients often exhibit deficits in executive functioning tasks thought to be mediated by FL regions (see above paragraph on letter fluency deficits in TLE). This pattern of dysfunction has been attributed to widespread disruption of neural networks by recurrent seizure activity. The "nociferous cortex hypothesis" of Wilder Penfield is sometimes invoked to explain this phenomenon (Penfield & Jasper, 1954). Evidence includes impaired performances observed on neurocognitive measures such as complex problem-solving tasks (e.g., Wisconsin Card Sorting Test) and generative fluency measures (Hermann & Seidenberg, 1995; Kim, Lee, Yoo, Kang, & Lee, 2007; Martin et al., 2000). Similar findings have also recently been reported in children (Rzezak, Fuentes, Guimaraes, et al., 2007). Preliminary work has shown that patients with successful seizure control following TL resection may show significant improvement on these tasks (Hermann, Wyler, & Richey, 1988; Martin et al., 2000), suggesting that these distributed networks are functioning better in the absence of electrophysiological disruption. Similarly, functional neuroimaging studies have demonstrated that TLE patients often show hypometabolism of the FLs that correlates with aspects of executive function performance (Jokeit et al., 1997; Takaya, Hanakawa, Hashikawa, et al., 2006). One additional fMRI study provides evidence that patterns of FL cerebral activation can show "normalization" following successful TL resection (Maccotta, Buckner, Gilliam, & Ojemann, 2007).

Depression is the most common psychiatric comorbidity in epilepsy (Fuller-Thomson & Brennenstuhl, 2009), and preoperative depression has been associated with worse seizure outcome following TL resective surgery (Anhoury, Brown, Krishnamoorthy, & Trimble, 2000). Other psychiatric comorbidities of TLE, most of which have been less well studied than depression, include anxiety disorders, substance abuse, psychosis, and personality disorders (Table 4.1).

Findings in Frontal Lobe Epilepsy (FLE)

Research examining the neurocognitive functioning of presurgical frontal lobe epilepsy (FLE) patients has been less commonly completed. In part, the lack of research in this area is likely due to greater difficulty obtaining adequate sample sizes for such studies, as FLE patients are believed to reflect only 10–20 % of all surgical referrals (Jokeit & Schacher, 2004). It is usually necessary to collaborate across epilepsy centers or to spend many years obtaining large enough sample sizes to achieve adequate statistical power to answer basic questions. Research is also hampered in this area by limitations in our understanding of FL functions and the adequate development of tests and methods to assess them, as well as the same latent variables that plague epilepsy research in general. In addition, there is a great deal of heterogeneity in terms of pathology and seizure localization within FL regions, which contributes to differing neurocognitive profiles. Complex partial seizures in FLE commonly arise from the frontal poles and from the orbital, medial, and dorsolateral FL regions (Williamson, Spencer, Spencer, Novelly, & Mattson, 1985).

While the conclusions drawn in this section should be viewed as more tentative in nature due to the limited number of completed studies, some clear trends appear to be emerging. For example, there is growing evidence that presurgical patients with FLE often exhibit problems with response inhibition (McDonald et al., 2005; Upton & Thompson, 1996), although this problem has not been universally observed (Helmstaedter, Kemper, et al., 1996). One study that compared a sizeable number of FLE and TLE patients found that FLE patients performed significantly worse than the TLE group on a measure of response inhibition (Stroop Color-Word Interference Test) (Upton & Thompson, 1996). In contrast, Helmstaedter, Kemper, et al. (1996) found that their FLE sample performed worse than TLE patients on all Stroop conditions, which suggests their primary limitation may have involved reading or processing speed. McDonald et al. (2005) added a matched control sample to the previous paradigm of comparing FLE and TLE patients, demonstrating that the FLE group was impaired on the Stroop task from the Delis-Kaplan Executive Functioning System (DKEFS) when compared to the control subjects while the TLE group was not. The left FLE group was more impaired than the right FLE group or either TLE group on this portion of the task. There is at least one study suggesting that response inhibition performance may decline with unilateral FLE resections (Helmstaedter, Kemper, et al., 1996).

Performance on motor tasks is often decreased in FLE patients as compared to controls or other samples of epilepsy patients, and there is some evidence that decline occurs on these tasks with some FLE resections. For example, Helmstaedter, Kemper, et al. (1996) demonstrated that a small sample of FLE patients ($n=23$) performed worse than a set of TLE patients on measures of psychomotor speed and motor coordination. Upton and Thompson (1996) compared the performance of presurgical FLE patients to that of TLE patients on a variety of motor tasks, finding that the FLE group performed worse than the TLE group on tasks of motor sequencing and bimanual hand movements (left FLE worse than right FLE). Studies in children with FLE seizure onset have

Table 4.1 Core pre- and postsurgical deficits in temporal lobe epilepsy patients

Type of presurgical deficit	Laterality findings	Change with surgery
Language functions		
Naming (auditory/visual)	Both left and right TLE—frequently exhibit deficits (left > right)	Left TLE—decline Right TLE—no decline
Semantic fluency	Both left and right TLE—frequently exhibit deficits (may vary by type of category)	Left TLE—decline Right TLE—data is sparse/appears decline possible
Letter fluency	Both left and right TLE—often exhibit deficits	Left and right TLE—no decline/may improve with seizure freedom
Action (verb) fluency	Possibly same pattern as letter fluency/data is sparse	Possibly same/data is sparse
Other language functions	Left TLE—usually normal unless patient has dysphasia secondary to an additional neurological cause (e.g., stroke) Right TLE—intact core language functions	Left TLE—no decline unless encroaching on classic language areas Right TLE—no decline
Memory and learning		
Material-specific memory deficits may be observed	Left TLE—often exhibits auditory/verbal memory deficits Right TLE—sometimes (but less consistently) exhibits visual memory deficits	Left TLE—auditory/verbal memory often declines Right TLE—visual memory often declines (depends more on specific tasks than previously recognized)
Task-specific dissociations in performance	Left TLE—impairment on difficult associational and rote learning paradigms more associated with mesial TL dysfunction. Impairment on semantically related tasks more associated with lateral TL dysfunction (e.g., story recall, easy word pairs) Right TLE—often exhibits deficits involving object-location recall (particularly when assessed in three dimensions) and route learning	Declines in functioning can occur that are consistent with the specified preoperative patterns More research is needed to pin down specific structure-function relationships
General memory dysfunction is observed in some TLE patients	Both left and right TLE—sometimes exhibit general or global memory dysfunction at baseline	Decline still seems to reflect the task and material-specific patterns that occur with surgery
Learning and retention patterns may differ by side of seizure onset	Left TLE—often exhibits good initial retention of words, but poor retention over time Right TLE—often exhibits problems with initial learning of visual material but retain most of what is encoded/learned over time	No data has been published examining the differential learning patterns postoperatively
Visuo-perceptual/visual-spatial processing and object recognition		
Visuo-perceptual deficits tend to be infrequent	Right TLE—occasionally has visuo-perceptual deficits	Both left TLE and right TLE—may experience a visual-field cut following surgery Left TLE—no decline on perceptual tasks Right TLE—mild decline on some tasks on occasion
Visual-spatial deficits tend to be infrequent	Right TLE patients—may rarely have visual-spatial deficits (e.g., problems judging spatial features)	Left TLE—no decline Right TLE—very rare decline on some tasks
Category-related object recognition deficits	Left TLE—occasionally sees mild recognition deficits for man-made objects with posterior TL involvement Right TLE—frequently exhibit recognition deficits for famous persons/faces, landmarks, and animals with anterior TL dysfunction	Left TLE—possible decline on recognition of man-made objects with encroachment on left posterior regions Right TLE—frequent decline on recognition of famous persons/faces, landmarks, and animals

(continued)

Table 4.1 (continued)

Type of presurgical deficit	Laterality findings	Change with surgery
General intellectual functioning		
IQ scores	Typically normal in TLE Left TLE will sometimes show greater problems with verbal tasks, and right TLE will sometimes show greater problems with perceptual tasks	May see "material-specific" declines in line with presurgical status
		May see improvements in processing and attention regardless of hemisphere of seizure focus if patient experiences a reduced seizure burden and a reduction in AEDs
Executive control processes		
Complex problem solving, response inhibition, generative fluency, complex attention	Both left and right TLE—often exhibit deficits in one of more of these areas that is assumed to result from the disruption of temporofrontal networks secondary to epileptiform activity	Both left and right TLE—frequently show improved performance in these domains if experiencing seizure freedom

For the purposes of this table, we are assuming normal language lateralization to the left cerebral hemisphere (i.e., left = dominant)
TLE temporal lobe epilepsy, *TL* temporal lobe, *AEDs* antiepileptic drugs

reported greater problems with motor coordination (Hernandez, Sauerwein, Jambaque, et al., 2002) as compared to normal controls or children with other seizure onset.

Performance on complex problem-solving tasks also appears to be impaired in some FLE patients, and this finding has been observed both pre- and postoperatively (Upton & Thompson, 1996). Milner published a classic case study involving patient "K.M.," who demonstrated severe deficits on the WCST following bilateral resection of the anterior FLs for the control of seizures despite maintaining normal IQ. As noted in the section on TLE, however, complex problem-solving deficits can also be seen in patients with TLE, likely due to the spread of seizure activity to FL regions.

Verbal fluency, as noted in the TLE section, is often impaired in presurgical FLE regardless of laterality of seizure onset and includes both semantic and letter fluency. There is also some data indicating that action (verb) fluency is also decreased in FLE patients. Preliminary evidence exists that performance on these tasks can sometimes yield localizing data when explored in ways that examine component skills required for successful completion (Drane et al., 2006).

Design fluency has also been shown to be decreased in FLE patients relative to other epilepsy patients or healthy controls, with some studies suggesting lateralization to the nondominant hemisphere (Jones-Gotman & Milner, 1977) and others not (McDonald, Delis, Norman, Tecoma, & Iragui, 2005). One study reported worse performance for patients with left FLE (McDonald, Delis, Norman, Tecoma, et al., 2005) as compared to right FLE while another demonstrated that FLE patients performed worse than TLE patients regardless of seizure onset laterality (Suchy, Sands, & Chelune, 2003). A fourth study found that patients with FLE produced a similar number of designs as did patients with TLE but made more design errors (Helmstaedter, Kemper, et al., 1996). Discrepancies across studies may in part reflect differences in the design fluency tasks themselves, as these measures differ in regard to the structure they provide, the presence or absence of concomitant task demands (e.g., shifting attention), and the aspect of performance emphasized (e.g., design generation, self-monitoring, shifting).

Some evidence suggests that FLE patients may perform worse than TLE patients on measures of attention, working memory, and psychomotor speed. For example, Helmstaedter, Kemper, et al. (1996) demonstrated that a small sample of FLE patients performed worse than a set of TLE patients on measures of attention and psychomotor speed. In the FLE group, differences were not related to side of seizure focus or presence of a structural lesion. Upton and Thompson (1996) found that a small group of FLE patients made more errors on a complex visual scanning and tracking measure than did a comparable TLE group.

There are many additional studies with FLE patients demonstrating deficits on a variety of tasks presumed to be sensitive to FL dysfunction, but most of these are isolated findings that have yet to be replicated. Areas of reported dysfunction have included deficient cost estimation (Upton & Thompson, 1996), an elevated rate of questions required to identify objects on the Twenty Questions Test from the DKEFS (Upton & Thompson, 1999), problems with determining temporal order (McAndrews & Milner, 1991), and aspects of social cognition (e.g., humor appreciation, recognition of facial emotion, perception of eye gaze expression) (Farrant, Morris, Russell, et al., 2005). Kemper, Helmstaedter, & Elger (1993) reported that FLE patients performed much worse than TLE patients on a planning task, suggesting that this difference correctly predicted the seizure focus of 80 % of all cases.

Memory performance has not been studied extensively in patients with FL seizure onset, and available results are somewhat mixed. Most studies have either compared performance between FLE and TLE patients with one another or with healthy controls. While some of these studies have failed to demonstrate differences between FLE and controls on memory measures (Delaney, Rosen, Mattson, & Novelly, 1980), others have reported worse functioning for FLE, at least on some types of tasks. FLE patients tend to perform worse on more complex learning paradigms (e.g., list-learning tasks), with their limitations attributed to problems with encoding and/or retrieval.

There have also been some interesting studies suggesting that certain aspects of learning and memory are perhaps more impaired in FLE than in other epilepsy groups. For example, Pigott and Milner (1993) demonstrated that preoperative FLE patients exhibit problems with release from proactive interference (i.e., earlier memories interfere with of learning new information). Milner attributed this deficit to problems with encoding and retrieval mechanisms. McDonald and colleagues (2001) more recently demonstrated this pattern in postoperative FLE patients and provided further evidence that encoding/retrieval deficits may underlie this pattern. In their study, postsurgical TLE patients did not display release from proactive interference, and there was no difference between the TLE and FLE groups in terms of consolidation of stimuli (i.e., they showed similar rates of retention over trials). Milner has also shown that FLE patients have difficulty structuring and segregating events in memory (Milner, 1968b), and her FLE patient samples have also exhibited problems with organization of materials to be learned and have had trouble recalling the temporal order of information (Milner, Petrides, & Smith, 1985). These findings applied to a wide range of stimuli and may be material specific in nature (Milner, Corsi, & Leonard, 1991).

There have been few systematic studies of psychiatric functioning in patients with FLE, although a number of case reports describe wide-ranging interictal behavioral abnormalities. For example, Boone et al. (1988) described a young adolescent girl with FL seizures who experienced reversible behavioral changes including sexual disinhibition, loss of concern for personal hygiene, physical and verbal aggression, and pressured and tangential speech accompanying interictal anterior FL discharges. Patients with anterior cingulate seizure foci have also been reported to develop interictal psychosis, aggression, sociopathic behavior, sexual deviancy, irritability, obsessive-compulsive disorder, and poor impulse control (Devinsky, Morrell, & Vogt, 1995). Additionally, Helmstaedter (2001) has also reported that FLE patients have an elevated rate of behavioral problems compared to other epilepsy patients and controls but noted that these tended to be mild as compared to the findings obtained in other neurological patients with structural FL lesions. Based on the limited studies available, psychiatric conditions such as depression and anxiety appear to be more common in TLE (Gilliam et al., 2004).

In summary, it appears that patients with FLE present with a variety of deficits involving motor functioning, executive control processes, attention, speed of processing, and aspects of memory performance, as well as some possible behavioral abnormalities. These functions have been minimally explored in FLE patients with few studies using a presurgical/postsurgical decline and most seeming to be underpowered. There have been virtually no attempts to explore functions by FL subregion in any epilepsy study, yet this methodology has proven useful in other areas. Similarly, numerous cognitive functions attributed to the FLs have yet to be explored in FLE patients. Some areas of dysfunction observed in patients with FLE have also been observed in patients with TLE, presumably due to seizure spread across large interconnected neural networks. There also appear to be some distinct patterns between patients with FLE and TLE that may yet be useful for confirming the region of seizure onset (Table 4.2).

Findings in Posterior Cortical Epilepsy (PCE)

Seizures arising from the parietal lobe, the occipital lobe, the occipital border of the temporal lobe, or a combination of these regions are sometimes referred to as posterior cortical epilepsies, as it is difficult to find clear anatomic or pathophysiological differences in these regions (Dalmagro, Bianchin, Velasco, et al., 2005). The occurrence of posterior cortical epilepsies tends to be much rarer, and such conditions have been less well studied (Binder, Lehe, Kral, et al., 2008). Therefore, for the purposes of this chapter, we have decided to consider all of the work related to neurocognitive profiles related to parietal or occipital lobe seizure onset together. Dalmagro and colleagues (2005) reported that just over 5 % of their total referrals for long-term video-EEG monitoring experienced PCE, and of these, approximately half were actually surgical candidates. Overall, this group makes up well under 10 % of the total surgical referrals seen by a standard epilepsy surgical program, making this type of seizure onset even less common than FLE.

Cognitive studies of PCE patients are lacking in general, and there have been no systematic prospective studies of neurocognitive functioning in these patients that include both pre- and post-operative analysis. Studies appearing in the literature tend to involve retrospective analysis of clinical data. For example, one recent study examined retrospective pre- and postsurgical clinical data collected on 28 PCE patients between 1991 and 2000 (Luerding, Boesebeck, & Ebner, 2004). These investigators indicated that mild declines occurred in performance IQ from the WAIS-R regardless of resected hemisphere and also reported declines in some measures of visual-spatial processing. Postsurgical gains were made on some tasks thought to be mediated by the FLs, and there was no decline in WAIS-R verbal IQ. Of note, however, not only was the sample size very small, but this resulted in a pool of subjects with potentially very different lesions (e.g., left temporo-occipital verssu right inferior parietal). Also, only a limited number of subtests from the WAIS-R were available for examination. Overall, while this type of study of neurocognitive function of patients with PCE is sorely needed, such studies cannot definitively answer these questions due to a lack of sufficient power and inadequate coverage of potential domains to be examined. Other retrospective studies of PCE, particularly those involving parietal lobe dysfunction, have reported changes in visual functioning, visual-spatial processing, and visuo-perceptual abilities (Siegel & Williamson, 2000). Sensory changes are sometimes observed when surgical resection extends into the postcentral gyrus, and one study has reported disturbances of body image in a few patients with right inferior parietal corticectomies (Salanova, Andermann, Rasmussen, Olivier, & Quesney, 1995). One very small, retrospective study examining the neurocognitive status of children with occipital lobe (OL) seizure onset suggested that such patients experience an elevated rate of scholastic difficulty, psychiatric disorders (i.e., primarily depression), and cognitive dysfunction involving problems with face processing and making spatial judgments (Chilosi, Brovedani, Moscatelli, Bonanni, & Guerrini, 2006).

A recent study completed in Germany with a small series of OL epilepsy surgical patients

Table 4.2 Core pre- and postsurgical deficits in frontal lobe epilepsy patients

Type of presurgical deficit	Laterality findings	Change with surgery
General intellectual functioning	Typically normal in FLE	Typically no significant change
Language	Typically normal apart from verbal fluency deficits (unless neurologic/functional disruption of classic speech regions, e.g., Broca's area)	Typically no significant change with the exception of verbal fluency performance (see below)
Motor functioning	Left and right FLE—often exhibit motor deficits contralateral to side of seizure focus (e.g., gross motor speed, fine motor speed, and dexterity)	Both left and right FLE—may show a decline in the motor performance of their contralateral limbs (particularly when surgery encroaches on precentral gyrus region)
Response inhibition	Both left and right FLE—often exhibit deficits	Both left and right FLE—may decline depending upon location of FL resection
Complex problem solving	Both left and right FLE—often exhibit deficits	Both left and right FLE—may decline depending upon location of FL resection
Verbal fluency	Both left and right FLE—often exhibit baseline deficits on all types of verbal fluency tasks	Both left and right FLE—may decline on all verbal fluency tasks, although semantic fluency may improve in some cases
Design fluency	Both left and right FLE—often exhibit deficits	Both left and right FLE—may decline
Memory functioning	Both left and right FLE—often exhibit poor learning/encoding and decreased free recall with good recognition memory Both left and right FLE—often exhibit problems with release from proactive interference	Surgery may improve or worsen baseline problems based on location of surgery and postsurgical seizure freedom
Attention	Both left and right FLE—often exhibit deficits in primary and complex attention	Data is lacking. Any change is likely dependent upon seizure status and AED regimen at follow-up assessment
Social cognition	Some patients, regardless of laterality, have shown problems with recognizing humor and faux pas errors, recognition of facial emotion, and perception of eye gaze expression	Data is lacking. Theoretically, it appears that some functions could decline depending upon surgical variables, while seizure freedom and decreased AEDs may contribute to mild gains
Visuo-perceptual, visual-spatial, and constructional praxis	Typically normal on most visuo-perceptual and visual-spatial tasks Often exhibit decreased performance on constructional tasks due to poor organization and planning	Data is lacking. However, no reports of significant declines in these areas exist in the research literature

For the purposes of this table, we are assuming normal language lateralization to the left cerebral hemisphere (i.e., left = dominant)

FLE frontal lobe epilepsy, *AEDs* antiepileptic drugs

prospectively examined visual-field integrity, demonstrating that a significant proportion of these patients experienced visual-field defects postoperatively (i.e., 42 % of OL patients experienced new or increased visual-field defects) (Binder et al., 2008). This study and others have shown that preoperative patients with seizure onset involving the mesial OL are more likely to exhibit baseline visual-field defects (e.g., reports suggest approximately 40–50 %) than those with

Table 4.3 Core pre- and postsurgical deficits in posterior cortical epilepsy patients

Type of presurgical deficit	Laterality findings	Change with surgery
General intellectual functioning	Typically normal in PCE at baseline	Limited research suggests possibly mild declines in PIQ for PCE patients regardless of side of surgery/laterality and mild improvements in VIQ
Language	Depends on seizure focus: Left PLE—may exhibit classic language deficits (e.g., naming, repetition, comprehension) Right PLE and both left and right OLE—unlikely to exhibit language deficits	Typically no significant change with the exception of possible language declines with some left parietal lesions
Visuo-perception, acuity, and visual fields	Both left and right OLE—often exhibit problems with visuo-perception (including face processing/recognition) Left and right OLE—often exhibit baseline visual-field cuts (much more common for medial OL seizure onset) Left and right OLE—might expect baseline deficits in color processing and object localization, as well as positive visual phenomena (yet epilepsy specific research is absent)	Left and right OLE—often exhibit new or increased visual-field cuts Left and right PCE—in general, may exhibit mild or greater visuo-perceptual decrements depending on aspects of surgery (i.e., location and extent)
Visual-spatial processing	Both left and right OLE and right PLE—often exhibit problems with visual-spatial judgments	Both left and right PCE—declines in some aspects of visual-spatial processing (limited research)
Memory	Presumed to be normal	Presumed to remain at baseline apart from possible gains related to improvements in seizure status and reduced AED regimen
Sensory functioning	Both left and right PLE—may exhibit baseline problems with sensory discrimination	Sensory functioning is often worse in patients if surgery encroaches upon postcentral gyrus Disturbance of body image has been reported in patients with inferior parietal resections
Motor	Presumed to be normal	Presumed to be normal

For the purposes of this table, we are assuming normal language lateralization to the left cerebral hemisphere (i.e., left = dominant)
PCE posterior cortical epilepsy, *PLE* parietal lobe epilepsy, *OLE* occipital lobe epilepsy, *AEDs* antiepileptic drugs

lateral OL onset (e.g., ranging from 0 to 18 %) (Binder et al., 2008; Blume, Wiebe, & Tapsell, 2005). While focusing on perceptual rather than cognitive testing per se, this type of pre-/postoperative design is exactly what is needed in this area. At present, we lack definitive profiles for preoperative functioning in the posterior cortical epilepsies and have no prospective postsurgical outcome studies available for this patient group. One would assume, based on available lesion studies in other neurological disorders and functional imaging paradigms, that dysfunction in the OL could cause problems with face recognition, object localization, color processing, or object recognition (Kiper, Zesiger, Maeder, Deonna, & Innocenti, 2002) and that lesions in the parietal region could cause deficits involving visual-spatial processing, object recognition, sensory discrimination, arithmetic skills, and aspects of language functioning (Table 4.3).

Potential Confounds in the Neuropsychological Assessment of the Epilepsy Surgical Patient

In assessing epilepsy surgical patients, a variety of factors can obscure an individual's true neurocognitive profile, including disease- and treatment-related variables, as well as limitations associated with current assessment paradigms and our knowledge of brain-behavior relationships. The clinical neuropsychologist must be aware of these issues in order to take them into consideration when interpreting assessment results. Specific factors with the potential to create "noise" in our assessments include the effect of AEDs on brain functioning, problems with the specific tests being employed, comorbid medical and psychiatric conditions, acute ictal/interictal epileptiform activity, and the acute and long-term impact of seizure activity on brain regions distant from the seizure focus. There is no absolute approach to dealing with these issues, and this leads to a number of decisions regarding when and where to conduct the neuropsychological assessment and the selection of appropriate tests.

Effects of AEDs

Many AEDs can have an appreciable impact upon brain functioning, as they function to dampen the neuronal irritability that constitutes a seizure, yet they also more broadly dampen neuronal excitability in general (Drane & Meador, 2002). This can lead to the emergence of cognitive deficits that are unrelated to the epileptic focus. For example, a TLE patient treated with topiramate may present with limitations in primary attention, verbal fluency, and processing speed that have nothing to do with their underlying seizure focus (Kockelmann, Elger, & Helmstaedter, 2003; Ojemann et al., 2001). Presurgical evaluation in such a patient may fail to confirm the lateralization or localization of the seizure focus and will provide a significant underestimation of the patient's abilities. Knowledge of the effects of AEDs is therefore critical to interpreting neurocognitive results in this patient population, and there may be instances where it is worthwhile to take a patient off of their usual AEDs prior to evaluation.

Problems with Instrument Design

Problems with features of test design and selection can also muddle the interpretation of neurocognitive data. For example, test selection potentially becomes a barrier to discovering accurate brain-behavior relations when we employ measures that require the interaction of multiple cognitive skills controlled by different brain regions without a clear awareness of these relationships. For example, the Family Pictures subtest of the 3rd edition of the Wechsler Memory Scale (Wechsler, 1997) contributes to the Visual Memory Index from this battery, yet there is strong evidence that it loads on a verbal factor (Dulay et al., 2002). This is likely due to the necessity to accurately name the pictured individuals in order to get credit for any aspect of recall on this task. In turn, however, we often see a decline on Family Pictures, as well as the Visual Memory Index to which it contributes, in patients who undergo a dominant (typically left) hemisphere resection (Chapin, Busch, Naugle, & Najm, 2009). If someone were to explore the possibility of material-specific memory deficits in TLE using the Verbal and Visual Memory Indices of the WMS-3, they could easily draw wrong conclusions if they were unaware of this pattern of findings.

Nociferous Cortex Hypothesis

The nociferous cortex or "neural noise" hypothesis suggests that seizure activity can disrupt more expansive neural networks that extend beyond the irritative zone of the seizure (Penfield & Jasper, 1954). As covered earlier, executive control processes thought to be primarily mediated by FL regions (e.g., letter fluency, complex problem solving) can be disrupted in patients with TL seizure onset (Hermann & Seidenberg, 1995). These apparent deficits frequently resolve with the successful control of the TL seizure activity (Martin et al., 2000), and these alterations in the functioning of the FL cortex can be captured with functional neuroimaging (Jokeit et al., 1997; Maccotta et al., 2007). It is also thought that FL seizures will disrupt limbic and TL regions, although less research is available to confirm such patterns. Overall, the potential for distal effects of epileptiform activity can obviously obscure the central seizure focus.

Effect of Comorbid Conditions

Medical and psychiatric conditions that are often comorbid with epilepsy can also introduce greater noise into a patient's neurocognitive profile. For example, patients with epilepsy experience a higher rate of depression and a slightly elevated rate of psychosis as compared to the general public (Blumer, Montouris, & Hermann, 1995; Manchanda, 2002). Epilepsy patients struggling with mood issues or perhaps even actively psychotic may be less able to actively engage in testing. Similarly, epilepsy sometimes reflects a secondary condition resulting from a more primary medical condition (e.g., brain tumor, stroke, HSV encephalitis) or injury (e.g., traumatic brain injury). The primary disease or injury contributes uniquely to the patient's pattern of dysfunction and can mask any potential lateralizing/localizing neurocognitive findings. For example, patients with focal TL seizure onset resulting from posttraumatic epilepsy may exhibit significant executive function impairment that is related to potentially widespread cerebral dysfunction resulting from the head trauma.

Effect of Ictal and Interictal Discharges

There is growing awareness that acute ictal or interictal epileptiform discharges can alter neurocognitive profiles. While the impact of such epileptiform activity can sometimes accentuate a profile pattern in the case of focal seizure onset, it can also obscure this pattern when there is secondary generalization or non-focal patterns of interictal discharges (Aarts, Binnie, Smit, & Wilkins, 1984; Aldenkamp & Arends, 2004; Binnie, 2003; Kasteleijn-Nolst Trenite & Vermeiren, 2005).

Practice Effects

Neuropsychological assessment in epilepsy requires repeated testing over time, which necessitates consideration of possible practice effects. Some studies have been completed that examine test-retest changes in either epilepsy patients or in healthy controls and that provide *reliable change indices* to allow one to determine if a given change is related to the treatment intervention as opposed to a simple practice effect (Martin, Sawrie, Gilliam, et al., 2002). This can be particularly important when one recognizes that a lack of an expected practice effect may reflect a limitation in a postsurgical patient.

Atypical Language Lateralization

Given that epilepsy is often associated with comorbid neurological disorders/injury, it is not surprising that one observes an elevated rate of atypical language lateralization in this population (i.e., right or bilateral language). Many of these cases appear to represent language reorganization that has occurred in individuals experiencing early-life injuries, although a few studies suggest there is likely a subset of patients with rare but naturally occurring atypical language lateralization (Drane, Ojemann, Ojemann, et al., 2009; Knecht, Jansen, Frank, et al., 2003). The possibility of atypical language lateralization must be borne in mind when analyzing neurocognitive data and making outcome predictions.

In summary, it is recommended that the clinical neuropsychologist makes every effort to be aware of potential latent variables and to control for their presence when possible. In this manner, one may be able to better localize or lateralize a seizure event in a patient that otherwise showed no focal findings. One may also gain better insight into the patient's genuine performance baseline in the absence of seizure activity. Occasionally, it may also be possible to use these variables to one's advantage such as using ictal or postictal assessment techniques to enhance focal findings.

Decisions About Neuropsychological Assessment in Epilepsy Surgical Patients

Inpatient Versus Outpatient Assessment

There are various pros and cons to either testing presurgical epilepsy patients on the inpatient unit versus in the outpatient clinic, and both practices continued to be employed with regularity by epilepsy surgical programs throughout the world.

Conducting evaluations in the epilepsy monitoring unit (EMU) allows one to be aware of the presence of ictal and interictal epileptiform discharges, as the patient is undergoing continuous video-EEG monitoring. This is probably its largest advantage, as increasing data demonstrates that subclinical and interictal epileptiform activity can have a transient disruptive impact upon neurocognitive functioning (Aldenkamp & Arends, 2004; Kasteleijn-Nolst Trenite & Vermeiren, 2005). It is likely that transient changes in performance sometimes lead to an underestimation of the patient's baseline functioning (see current clinical vignette), which can obscure change over time (e.g., leading one to miss declines in performance subsequent to surgical intervention or other treatment) and contribute to false predictions regarding outcome. For example, if someone appears to have severely impaired verbal memory due to transient epileptiform activity, we might erroneously predict that their risk of decline is small due to their poor baseline. This sort of error potentially gives the patient, the neurosurgeon, and the rest of the treatment team misinformation for making their decisions regarding the risk associated with surgery. On the other hand, having concurrent electrophysiological data allows the neuropsychologist to explore changes in performance in relation to ictal and interictal discharges. Inpatient testing also gives the examiner a greater span of time to conduct tests.

The downside of inpatient assessment involves potentially dealing with acute changes in medications, as the patient's standard AED regimen may be altered or discontinued in order to provoke seizures. Similarly, some EMUs will also employ sleep deprivation as a means to induce seizures more rapidly. Depending upon the practice of the inpatient unit, these issues can often be more effectively managed by agreeing upon a standard start time for neurocognitive testing. In our practice, we initiate the baseline testing at the first full day of monitoring, prior to the patient being sleep deprived and often prior to any changes in AED regimen. This also provides us with electrophysiological data from the day of admit to insure that acute seizure activity has not immediately preceded our assessment.

Ideally, the epilepsy neuropsychology service will have dedicated rooms on the inpatient monitoring unit that preserve the uninterrupted, private environment while allowing the patient to continue with their video-EEG monitoring. If such rooms are not available, bedside testing can also work adequately, if proper steps are taken to educate staff about not interrupting. While dealing with additional staff creates additional work for the examiner, having them available to assist with the patient if a seizure occurs is quite advantageous, particularly with patients that experience seizures on a frequent basis.

The advantages and disadvantages of conducting presurgical evaluations in the outpatient setting are essentially the opposite of those just cited for inpatient assessment. The major disadvantage is that one has no objective knowledge of the immediate electrophysiological functioning of the patient that they are assessing. Epileptiform activity may be occurring during the examination, with direct impact upon the assessment, and neither the examiner nor the patient will be aware of its occurrence. Similarly, the patient may have experienced a seizure within the last 24 h yet lack any recollection of this occurrence. In contrast, the patient is less likely to be sleep deprived, and they are most likely continuing with their standard treatment regimen.

Our group, as well as others, has suggested that the eventual standard for outpatient neuropsychological assessment of epilepsy should include obtaining simultaneous EEG recordings (Patrikelis, Angelakis, & Gatzonis, 2009).

Financial considerations may also play a role in deciding upon assessment venue, as some payors may incentivize one type of assessment over another. Nevertheless, we have often been successful in getting policies adjusted by providing data to explain our preferences in assessment location depending upon the factors involved. This is an area where standardized policies could conceivably be established by interested practice organizations.

Reliable Change Indices Versus Alternate Test Forms

The serial assessment of epilepsy patients undergoing surgery necessitates correction for practice effects. Since the early 1990s, some neuropsychologists have started using advanced methods of measuring change, including the Reliable Change Indices (RCIs) and standard regression-based (SRB) change score norms (Hermann et al., 1996; Sawrie, Chelune, Naugles, & Luders, 1996). Both are methods that attempt to statistically control for test-retest effects and measurement error, allowing the clinician to better evaluate whether change in performance is actually related to a specific treatment intervention. RCI and SRB scores based on the performance of unoperated patients with epilepsy and on healthy control subjects are available for a number of neurocognitive measures (Dikmen, Heaton, Grant, & Temkin, 1999; Heaton et al., 2001; Temkin, Heaton, Grant, & Dikmen, 1999). Examining the performance of the same type of patient allows for the greatest control of other disease-related variables.

Another approach is to use alternative forms of commonly used tests when available. The major problem involved in using alternative test forms relates to the difficulty we have insuring that each alternative version of a test is actually equivalent to the original.

Choice of Neuropsychological Tests

In general, when putting together a battery to assess epilepsy surgical patients, one wants to cover all of the standard neurocognitive domains. However, the relative emphasis to place on a given domain and the choice of specific tests should be guided by the overarching purposes of the neuropsychological evaluation in the epilepsy surgical setting. More specifically, tests should be chosen that are potentially useful for:

(a) *Confirming the epileptic focus*: Knowledge of deficits commonly observed in various epilepsy syndromes preoperatively will aid in the selection of tests that are useful for lateralizing/localizing purposes.

(b) *Demonstrating postoperative change in function*: One should include measures that examine functions known to commonly decline with a particular type of surgery (e.g., verbal memory decline following dominant TL resection), allowing one to assess outcome. Of note, postsurgical change can also be positive, as in the case of someone showing improvement in processing speed and attention secondary to becoming seizure-free and discontinuing their AED regimen.

(c) *Insuring valid interpretation*: Measures chosen in this area assess the impact of latent variables commonly occurring in the epilepsy surgical setting. For example, by using performance validity measures, one determines whether the evaluation has been invalidated by factors such as poor motivation or task engagement on the part of the patient or the possible effect of other disease-related variables (e.g., subclinical or interictal epileptiform discharges).

(d) *Allowing research to be performed*: Measures should be used allowing one to research basic questions about brain-behavior functions and surgical outcome for specific cognitive skills, psychosocial and vocational functioning, emotional/psychiatric processing, seizure freedom, and quality of life.

Table 4.4 lists specific neurocognitive functions proven important to assess for several common types of epilepsy and specific tests that have

Table 4.4 Core neurocognitive functions to be assessed in epilepsy surgical patients and suggested tests

Neurocognitive domains	Within domain areas to emphasize during assessment	Possible tests to consider
Language	– Naming (e.g., visual, auditory/ naming to description, category related) – Verbal fluency (semantic, letter, and action) – Screen reading and other core language tasks	– Boston Naming Test, Columbia Auditory Naming Test, Category- Related Naming Tests – Category fluency tasks (e.g., animals, supermarket items), DKEFS Verbal Fluency, Controlled Oral Word Association Test, action fluency – Recognition Reading Subtest of the Wide Range Achievement Test, American Version of the National Adult Reading Test (AMNART), Wechsler Test of Adult Reading, Token Test, sentence repetition
Attention	– Primary attention (auditory and visual) – Complex attention (auditory and visual) – Sustained attention (auditory and visual)	– Digit Span Forward (WAIS), Picture Completion (WAIS) – Digit Span Backwards and Letter-Number Sequencing (WAIS), Trail Making Tests, spatial span – Continuous Performance Test (not used as commonly by most epilepsy centers)
Visual processing	– Visuo-perception – Visual-spatial – Object recognition	– Visual Object and Space Perception (VOSP) Battery, Facial Recognition Test – Judgment of Line Orientation – Famous Faces Test, Category-Related Object Recognition Tests
Constructional praxis	– Graphomotor copying tasks – Assembly tasks	– Copying simple shapes (e.g., Greek cross, Necker cube), Rey Complex Figure Test (Copy) – Block Design (WAIS)

Memory and learning	– Auditory/verbal Learning, memory retention, and recognition
	  – List-learning Tasks
	  – Contextual memory
	  – Associative learning
	– Visual learning, memory retention, and recognition
	– Simple geometric designs
	  – Face recall
	  – Complex visual designs
	– Remote recall
		– Rey Auditory/Verbal Learning Test, California Verbal Learning Test, Verbal Selective Reminding Test
		– Logical Memory Subtest (Wechsler Scales), Reitan Story Memory
		– Verbal Paired Associates (VPA) Subtest (Wechsler Scales; WMS-III VPA appears less helpful than other versions, as it eliminated the easier word pairs)
		– Visual Reproduction (Wechsler Memory Scales: older versions appear to be more useful for lateralization than the 3rd edition)
		– Face Recall/Hospital Facial Recognition Task
		– Rey Complex Figure Test, MCG Complex Figures
		– Information Subtest (WAIS)

Executive control processes	– Complex problem solving – Response inhibition – Complex attention/mental flexibility – Abstract reasoning – Generative fluency tasks (verbal and visual) – Metacognition	– Wisconsin Card Sorting Test, Brixton Spatial Anticipation Task, Iowa Gambling Task – Color-Word Interference (Stroop) Test, Hayling Test, Go/No-Go Tasks – Trail Making Test, Mental Control (WMS) – Similarities Subtest/Matrix Reasoning Subtest (WAIS) – DKEFS Verbal Fluency, DKEFS Design Fluency, 5-Point Design Fluency – Cognitive Estimation Tasks
General intellectual functioning	– Verbal and performance IQ	– Wechsler Adult Intelligence Scale (various editions) – Wechsler ASI

(continued)

Table 4.4 (continued)

Neurocognitive domains	Within domain areas to emphasize during assessment	Possible tests to consider
Academic achievement	– Reading recognition – Reading comprehension – Mathematical skills – Spelling ability	– Wide Range Achievement Test (WRAT)—reading recognition – Gray Oral Reading Test (GORT) – WRAT—arithmetic – WRAT—spelling
Performance validity testing	– Determine task engagement. This can be disrupted due to issues including poor motivation as well as the impact of acute seizures and epileptiform activity	– Word Memory Test – Medical Symptom Validity Test – Victoria Symptom Validity Test – "Embedded" Measures of Task Engagement[a]

WAIS Wechsler Adult Intelligence Scale, *WMS-III* Wechsler Memory Scale (3rd edition), *MCG* Medical College of Georgia

[a]Embedded measures of task engagement refer to attempts to use improbable performances on standard clinical tests in order to recognize possible test invalidity

Table 4.5 Sensory, motor, mood and personality, and quality-of-life variables to be assessed in epilepsy surgical patients and suggested tests

Neurocognitive domains	Within domain areas to emphasize during assessment	Possible tests to consider
Sensory	– Visual, auditory, and tactile acuities	– Snellen eye chart – Extinction to double simultaneous stimulation – Tactile Form Recognition – Reitan-Klove Sensory Examination
Motor	– Handedness – Gross motor speed – Fine motor speed and dexterity – Grip strength – Psychomotor speed	– Edinburgh Handedness Scale – Finger Tapping Test – Grooved Pegboard Test – Hand dynamometer – WAIS subtests (e.g., symbol search, digit symbol)
Mood and personality	– Mood and emotional status – Psychopathology – Personality features – Somatizational/conversion profile	– Minnesota Multiphasic Personality Inventory (2nd edition or restructured form) – Personality Assessment Inventory (PAI) – Brief Self-Report Inventories (e.g., Beck Depression and Anxiety Scales) – Mini Psychiatric Inventory (MINI)
Quality of life	– Adjustment to seizures and treatment (e.g., AEDs, surgical intervention) – Satisfaction with social support and vocational and interpersonal functioning	Quality of Life in Epilepsy (QOLIE) Washington Psychosocial Seizure Inventory (WPSI)

WAIS Wechsler Adult Intelligence Scale, *AEDs* antiepileptic drugs

been used to assess these functions in the context of epilepsy. Table 4.5 presents similar data for motor and sensory functioning, mood, personality, and quality-of-life assessment. Obviously, tests selected for use need to be psychometrically sound (e.g., valid, reliable) and preferably have RCI or SRB scores or alternative forms for repeat assessment. In addition, the following section provides a brief overview of how the findings in each of these neurocognitive domains may be used and integrated in the neuropsychological assessment.

Language

It is essential to assess aspects of naming and verbal fluency given the presurgical baseline deficits in these areas and due to the postsurgical decline in these skills observed following dominant TL resection (see the presurgical/postsurgical deficits section above and corresponding tables for specifics). Studies suggest sampling a wider array of categories with these tasks and indicate that altering basic task demands can lead to different yet equally important findings (e.g., use of auditory naming-to-description tasks versus standard visual confrontational naming) (Drane et al., 2008; Hamberger & Seidel, 2003). An assessment of reading ability is useful to establish a patient's ability to perform tasks requiring reading, to estimate premorbid function, and to monitor postsurgical changes in this function. Screening other language functions (e.g., auditory comprehension, repetition) is also recommended with epilepsy surgical patients. However, a complete language assessment is typically not required, unless the proposed surgical resection is thought to encroach upon classic language regions (e.g., Wernicke's and Broca's areas), which most do not, or when the epilepsy surgical candidate is experiencing baseline aphasia (e.g., usually the aphasia and seizures are resulting from a common neurological cause in these cases, such as stroke or tumor).

Attention

An assessment of primary attention processing (i.e., with minimal demands placed upon mental manipulation of information) is recommended for a variety of reasons, including the assessment of the effect of AEDs and other medications (which can disrupt this domain) and insuring a patient has the ability to focus on more complex tasks (which can be disturbed in patients not fully recovered from a seizure). More complex aspects of attention should also be assessed that require mental flexibility and alternation/switching between tasks and that place greater demands on working memory capacity. Assessing both auditory and visual aspects of attention is useful, as discrepancies between domains can sometimes be of lateralizing value (Duncan, Mirsky, Lovelace, & Theodore, 2009). Examining sustained attention and response inhibition using a continuous performance paradigm may also be worthwhile but does not appear to be routinely implemented in most clinical evaluations of epilepsy.

Visual Processing and Object Recognition

A thorough assessment should include a screen of visual acuity and gross confrontational evaluation of visual fields to insure that the patient can adequately process visual information (sometimes this information is available from the neurology exam). Additionally, we routinely assess both visuo-perception and visual-spatial processing. We use the former term to denote the ability to perceive visual images (including object recognition) and the latter to refer to the processing of spatial relationships between objects and potentially the viewer. Theoretically, the visual processing stream is divided into an inferior component which mediates visuo-perception/object recognition processing (ventral stream "what" pathway) and a superior stream that is involved in visual-spatial processing (dorsal stream "where" pathway) (Ungerleider & Mishkin, 1982). The ventral stream runs from the occipital lobe to the temporal lobe, while the dorsal stream runs from the occipital lobe to the parietal lobe, and both can be disrupted in a variety of ways by seizures and surgical resection. For example, occipital lobe disturbances can cause a primary loss of vision or disturbance in color processing, parietal lobe disturbances are often associated with deficits in spatial and constructional processing, and inferior TL dysfunction can be associated with object recognition deficits. The Visual Object and Space Perception (VOSP) Battery (Warrington & James, 1991) has four subtests that load on a perceptual factor and four that load on a spatial factor, making it a solid, efficient method of evaluating many of these functions (Rapport, Millis, & Bonello, 1998). Despite a lack of clinical tests, an assessment of object recognition is recommended for epilepsy surgical patients given recent evidence of category-related object recognition deficits in patients with right anterior TL dysfunction (e.g., famous faces, landmarks, animals)

(Drane et al., 2008, 2009; Glosser et al., 2003; Seidenberg et al., 2002). FL dysfunction can also potentially contribute to problems with frontal eye fields and visual tracking (Thurtell, Mohamed, Luders, & Leigh, 2009), as well as the organization/planning that is required for many constructional tasks.

Memory and Learning

Assessment of memory and learning is a core part of the evaluation of epilepsy surgical patients, as the majority of them have seizures arising from TL or FL regions. Patterns of memory dysfunction, as outlined above, can be very helpful for confirming seizure localization to one of these regions and for lateralizing side of seizure onset. In addition, these functions are potentially at risk in such patients and therefore need to be carefully examined.

A minimal assessment of memory in epilepsy should include a variety of test formats (e.g., free recall versus recognition), measures with different learning demands (e.g., associational learning, rote recall, contextual and gist learning), and stimuli tapping different sensory modalities (e.g., auditory/verbal, visual). Including a recognition task format can help to distinguish encoding from retrieval deficits, which can contribute to localization of brain dysfunction (e.g., FL versus TL impairment). Using both auditory/verbal and visual stimuli, one can explore possible material-specific patterns, which can aid in lateralizing the involved cerebral hemisphere. Using tasks that place different demands on forms of learning is recommended due to mounting evidence that performance dissociations frequently occur between learning approaches, which presumably reflects the underlying involvement of different brain regions (Saling, 2009). Ultimately, such data will likely contribute to more specific identification of dysfunctional regions within a hemisphere. While the specific structure-function relationships in this regard remain murky (i.e., which mesial TL structures are associated with which forms of learning?), research is starting to provide preliminary models. In addition, testing different forms of learning can uncover residual functions in a patient upon which one can capitalize in future memory training and target in efforts to improve surgical outcome.

In general, associational learning (e.g., word pairs) has proven to be one of the more sensitive tasks to mesial TL pathology (particularly unrelated word pairs) (Akanuma, Alarcon, Lum, et al., 2003; Hermann et al., 1994; Squire, 1993). Nevertheless, semantically related word pairs may be impacted by lateral TL resection and should be included as well. Having both easy (semantically related) and hard items also provides a better performance floor, which some believe improves our ability to lateralize dysfunction across the cerebral hemispheres. In this regard, the original versions of the Verbal Paired Associates task from the Wechsler Memory Scale have fared better in terms of seizure lateralization than did the version from the 3rd edition of this test, which dropped the easy items. Animal and experimental literature suggests that other forms of associational learning may be beneficial for the assessment of epilepsy as well (e.g., binding sensory/perceptual data with verbal labels).

List-learning tasks have also been shown to be sensitive to left mesial TL dysfunction (Grammaldo, Giampa, Quarato, et al., 2006; Loring, Strauss, Hermann, et al., 2008). As with associational tasks, using lists of words that are more difficult to link semantically places greater demands on mesial TL structures. This is borne out in studies examining the usefulness of various list-learning paradigms, with those allowing for easier categorization (e.g., California Auditory/Verbal Learning Test) appearing less able to lateralize dysfunction (Loring et al., 2008).

Contextual learning, such as reflected by the commonly used paragraph and story recall tasks that are available, has proven less sensitive to mesial temporal lobe pathology (Rausch & Babb, 1993; Saling et al., 1993). However, these measures are affected by lateral TL pathology, and some patients will experience decline on these tasks with a standard TL resection. Inclusion of contextual memory tasks also helps establish whether the patient has any functional memory capacity remaining. Someone performing well on these tasks seems to retain the capacity to work at many jobs despite declines in other aspects of more complex learning, as they appear to retain the gist of what transpires despite having a difficult time recalling specific details. Such persons can still decline with surgery (particularly resections including lateral cortex), even if associational and rote learning are already severely impaired. Performance on contextual learning tasks has also been associated with drug effects (Salinsky et al., 2005), which can be useful for teasing out the effect of AEDs.

Finally, there are a number of learning paradigms that have yet to be commonly employed in the clinical epilepsy realm that should be explored. These include route learning/wayfinding tasks, visual memory tasks that place greater demands on allocentric memory (i.e., memory that is not based on one's own position in relation to the stimulus of interest), semantic learning, autobiographical memory and learning to criteria paradigms, and complex associational tasks that combine different styles of learning.

Executive Control Processes

Executive control processes refer to complex cognitive activities typically attributed to the FL regions of the brain (e.g., abstract reasoning, self-monitoring, problem solving, response inhibition, mental flexibility, complex attention). These skills coordinate the activity of more general cognitive and perceptual functions mediated by other brain regions (e.g., effectively coordinating motor and perceptual skills while altering performance in response to changing task demands). As mentioned, dysfunction associated with the FLs is often observed in both FL and TL epilepsy patients, with the latter patients presumably experiencing disruption of broader interconnections between brain regions secondary to epileptiform activity (Hermann & Seidenberg, 1995; Penfield & Jasper, 1954). FL dysfunction observed in TL patients will often resolve with successful seizure control (Martin et al., 2000). Given that FL and TL seizure onset represent the bulk of partial epilepsies, the assessment of executive functions frequently plays a role in confirming seizure focus, estimating risk of decline with FL surgery and helping to make predictions about possible areas of post-surgical improvement in TL patients. A thorough evaluation of executive control functions should assess the three major divisions of the FLs (e.g., dorsolateral, orbitofrontal, and mesial frontal). Assessment of executive functions often requires development and use of new tasks, as this is one cognitive area where novelty is particularly important (e.g., problem-solving tasks often become easier once a successful solution has been derived on a given occasion).

General Intellectual Functioning

An assessment of general intellectual functioning, which provides a broad overview of one's overall level of ability, is useful for estimating performance in specific neurocognitive domains and making determinations regarding functional capacity (e.g., ability to live independently, manage finances and medications, capacity to succeed in a vocational or academic environment). General cognitive ability also enters into determining the patient's capacity to make decisions regarding surgery. Performance patterns on IQ testing have not proven to be reliable indicators of lateralized seizure onset. However, they are sometimes helpful for this purpose, particularly when purer indices of verbal and perceptual ability are compared after controlling for problems with attention, processing speed, and motor dysfunction. Finally, general intellectual functioning remains normal in the majority of patients with epilepsy, although lower scores will be observed in a large number of patients, particularly those experiencing an early onset of refractory epilepsy, a long disease duration, comorbid neurological pathology, and a history of multiple episodes of generalized tonic-clonic seizures and status epilepticus (Glosser, Cole, French, Saykin, & Sperling, 1997).

Academic Achievement

An assessment of academic ability can be beneficial for making decisions regarding school functioning, which is particularly important for children and adolescents and adult patients engaged in educational pursuits. A brief screening of academic skills typically assesses word recognition, reading comprehension, spelling, and arithmetic. Presurgical performances in these areas are occasionally helpful in localizing extratemporal seizures. Postsurgical changes in these functions are not very common in FL and TL resections, which again represent the vast majority of surgical patients.

Sensory Functioning

As noted previously, a gross screening of perceptual functioning is essential to establish that patients can adequately perceive test stimuli. This should include checking visual acuity (e.g., Snellen eye chart), testing visual fields to confrontation, and examining basic tactile and auditory sensory functioning. Testing these functions can be incorporated into an evaluation of hemi-inattention to visual, auditory, and tactile stimulation (e.g., exploring unilateral as well as bilateral simultaneous stimulation of the sensory modality being tested). Evaluation of apraxia, finger agnosia, astereognosis, right/left orientation, and achromatopsia and a more in-depth examination of tactile form recognition can provide lateralizing/localizing data in some patients. Some research has been completed examining olfactory functioning in TLE patients as well, suggesting that such patients are often deficient at odor naming, discrimination, and recall (usually right TLE worse than left TLE and other epilepsies) (Carroll, Richardson, & Thompson, 1993; Eskenazi, Cain, Novelly, & Mattson, 1983) and that they may experience further decline with surgery. A thorough sensory examination is certainly warranted in cases where posterior cortical epilepsy is suspected and can be useful in all epilepsy surgical patients even if they have recently undergone a neurological exam.

Motor Functioning

Evaluation of grip strength and manual dexterity of both upper extremities is recommended. The Finger Tapping Test provides a measure of gross motor speed while a task like the grooved pegboard evaluates fine motor dexterity and speed. These functions are sometimes diminished in patients with FL dysfunction (Helmstaedter, Kemper, et al., 1996) and may decrease in patients undergoing resections that encroach upon the precentral gyrus of the FL (motor strip) (Helmstaedter et al., 1998). A careful assessment of handedness is also needed, as this can inform predictions regarding language lateralization. Research suggests that "footedness" may add additional predictive value as well (Drane, 2006). A quick way to assess both in lieu of a standardized rating scale can be to ask about which hand the patient uses to write and which foot they would prefer to use to kick a ball through a goalpost in American football.

Mood, Personality, and Psychiatric Inventories

Measures are needed to examine current mood and emotional issues, to examine lifetime prevalence of psychiatric disorders, and to rule out psychogenic nonepileptic spells (PNES). Measures of mood are useful for monitoring levels of distress, tracking change over time, and picking up on critical issues in need of intervention (e.g., active suicidal ideation). Epilepsy patients exhibit higher rates of psychiatric disturbance than does the general population, with commonly occurring comorbid conditions including depression, anxiety disorders, and substance abuse (Manchanda, 2002). In the surgical context, it is important to recognize and effectively deal with any psychiatric issues prior to undergoing surgery and to recognize the development of any postsurgical problems in this regard. Of note, however, measures of mood do not typically allow for making psychiatric diagnoses and do not provide any information with regard to lifetime prevalence rates. Kanner and colleagues have demonstrated that knowledge of psychiatric syndrome and personal and familial psychiatric history can be of benefit in predicting adverse responses to AEDs (Kanner, 2009; Kanner, Wuu, Faught, et al., 2003) and in determining the optimal treatment regimen for patients with such comorbid conditions (Kanner & Barry, 2003). Therefore, structured psychiatric inventories are helpful for both clinical and research purposes if time permits for their use.

PNES occurs in a subset of epilepsy patients, although base rates of comorbid occurrence of this condition tend to be overestimated in most studies. Research using the most rigorous diagnostic criteria suggests that approximately 5–10 % of patients with epilepsy will also experience PNES events (Martin, Burneo, Prasad, et al., 2003). There are also a handful of studies suggesting that some patients undergoing surgery will develop these events and that these events were not apparent prior to their surgery. We have found that there may be risk factors for developing PNES following surgery.

Quality of Life

Measures have been developed to examine patient satisfaction with various aspects of life functioning, and these measures have frequently been adopted as end points in outcome studies. Quality-of-life measures attempt to evaluate the noxious impact of seizures and their treatment (e.g., side effects of AEDs) on self-ratings of cognitive functioning, mood, and satisfaction with social support, vocational/academic performance, and other aspects of daily functioning. One criticism with quality-of-life measures has been that they sometimes share too much overlap with measures of mood and psychopathology.

Clinical Interview and Medical Record Review

There are key pieces of supporting information that need to be gathered through clinical interview and record review that set the context for the neuropsychological data and make it possible to predict outcome related to surgery. Such information includes age of seizure onset, duration of epilepsy, occurrence of febrile seizures, number of AEDs being taken, and developmental history. One also needs to know about general medical and psychiatric history, a history of head trauma, and a detailed history of the patient's seizures (e.g., types of spells, frequency of each seizure type, occurrence of secondary generalization, episodes of status epilepticus). Knowledge of AED regimen is also required to take their impact on cognitive into account. There will often be available neuroimaging data (e.g., MRI, SPECT, PET) and EEG findings available for review, as well as information regarding language laterality (e.g., fMRI data, Wada results). Video-EEG results will frequently provide information regarding seizure focus and can be informative regarding interictal discharges (discharges occurring between seizures). Results of the MRI of the brain will often identify structural abnormalities if present. In particular, the presence of mesial temporal sclerosis has proven useful in predicting neuropsychological outcome.

Throughout the entire interview and assessment, one should take note of signs of seizure occurrence, including brief pauses in performance or alterations in response style. When subtle changes appear to be observed, it can be useful to ask the patient if they have experienced a loss of time or if they recall what they were thinking about, and orientation can be rechecked as well.

Common Test Batteries

Given the difficulty involved in amassing adequate data to answer many research questions, there has been a recent push by the National Institutes of Health to create "common data elements" for many neurological diseases including epilepsy. A committee was tasked with creating a core set of neurocognitive tests for use in epilepsy during 2009 and these suggestions were published during 2011 (Loring et al., 2011). As with other common data element projects, the resulting battery is intended to serve as a minimum collection of tests, taking no more than 1 h to administer. This provides epilepsy researchers with a common core of data available for future studies pooling information across centers. It also provides epilepsy researchers who do not traditionally include cognitive elements with some very basic guidelines for collecting such data when appropriate.

Since the 1980s, a loose collaboration of neuropsychology labs from several major epilepsy centers in the USA has existed as the Bozeman consortium. This group has used this model of sharing data to publish a number of papers that the member sites could not have completed on their own (Hermann, Perrine, Chelune, et al., 1999; Lee, Westerveld, Blackburn, Park, & Loring, 2005; Wilde et al., 2003). Their data-sharing initiative should serve as a model for future collaborations, which can be particularly useful for studying events with low-frequency base rates, such as the occurrence of FL and posterior cortical epilepsies. Such collaborations also lead to new projects as interactions contribute to cross-fertilization of ideas.

Predicting Outcome in Epilepsy Surgery

Neuropsychological assessment can be useful in the prediction of neurocognitive outcome, postsurgical emotional and psychiatric status, and even seizure freedom. There are some general rules of thumb that have developed related to outcome prediction (see Table 4.6), and there are also a limited number of available prediction formulas. However, most of the available formulas relate to specific tests only and often have been produced exclusively for TLE patients.

Functional Reserve and Functional Adequacy Hypotheses in TLE Surgery

The *functional reserve hypothesis* was based primarily on studies documenting severe amnestic disorders of patients with bilateral mesial TL dysfunction resulting from disease or resection (Scoville & Milner, 1957). Research with the Wada procedure contributed additional support to this model, as it has become clear that patient's performing poorly on memory tasks during testing of the contralateral (i.e., remaining) TL structures are at increased risk for significant postsurgical memory decline (Chelune, 1995). While the structural integrity of the contralateral hippocampal structures appear to be important for avoiding global amnesia, having a functionally adequate hippocampus has not prevented material-specific memory loss with unilateral TL resection (such changes are common).

The *functional adequacy* model has support from growing evidence that the adequacy of the ipsilateral hippocampus (i.e., structure on side to be resected) better predicts material-specific postsurgical memory declines. This model predicts that TLE patients with intact memory function are likely to experience more pronounced decline in memory performance than those for whom memory is already impaired. This is a common finding from years of memory research in TLE surgery, and the functional adequacy model also accounts for the observation that patients with high presurgical memory function-

Table 4.6 Factors predictive of outcome in temporal lobe epilepsy patients undergoing surgery

Factors associated with a favorable neurocognitive outcome	Factors associated with a poor neurocognitive outcome
Presence of mesial temporal sclerosis on MRI	Normal brain imaging
Younger age of patient at time of surgery	Older age of patient at time of surgery
Early age of seizure onset (<15 years at onset)	Adult onset of seizures
Surgery performed on nondominant cerebral hemisphere	Surgery performed on language dominant cerebral hemisphere
Wada memory performance intact for cerebral hemisphere contralateral to seizure focus	Wada memory performance impaired for cerebral hemisphere contralateral to seizure focus
Impaired neurocognitive ability	Intact neurocognitive ability (more to lose)

ing are at greater risk for significant decline in this area than those with low average or impaired presurgical memory performance.

Pertinent Information to Relay to the Referring Physician or Epilepsy Monitoring Unit Team

In preparing a written report of the neuropsychological assessment of an epilepsy patient, it is typically important to comment on whether the findings suggest lateralized or localized dysfunction and to relate these findings to the other available test results (e.g., MRI, video-EEG results). One should also convey a thorough baseline of performance in terms of both neurocognitive ability and emotional status and attempt to assess the risks and benefits of potential treatment options (e.g., surgery, changes in AED regimen). One should recognize when it is possible that brain reorganization appears likely (e.g., naming and verbal memory deficits are observed in a patient with right TL seizure onset and normal visual memory) or when it is possible that ongoing seizures are likely disrupting distal brain regions (e.g., executive dysfunction in TL patients with no other findings of FL abnormality) and work these hypotheses into the final summary of results. Recommendations should be provided for interventions that may be required prior to surgery, such as completion of a Wada or fMRI study or a referral for psychotherapy in someone with untreated psychiatric issues or a high risk of developing PNES events. Recommendations for follow-up testing and referral for cognitive rehabilitation should be made as appropriate as well.

Clinical Vignette

The following brief case study is intended to highlight several of the principles from the current chapter, including a description of the process of examining the neurocognitive results for lateralizing or localizing patterns for use in confirming seizure focus, integrating other medical findings, considering the impact of latent variables upon neurocognitive performance (e.g., subclinical epileptiform activity), and prediction of outcome.

Background

Mr. Jones is a 42-year-old, right-handed, married, Caucasian male who was referred for neuropsychological assessment while undergoing video-EEG monitoring as part of a presurgical evaluation for possible epilepsy surgery. The patient has a reported history of measles encephalitis at the age of 5 and later developed complex partial seizures at the age of 14. The patient's seizures are characterized by unresponsiveness and lip smacking, but there is no evidence of motor involvement, loss of bowel or bladder control, or tongue biting. The patient believes that he experiences clusters of spells every 1–3 months. Medical records suggest that he has experienced rare secondary generalization of seizures, all in the context of medical noncompliance or subtherapeutic AED levels. Mr. Jones has no history of birth injury, developmental delay, febrile seizures, or head trauma. He denied any personal or familial history of psychiatric disturbance. Current medications included sodium valproate (1,250 mg TID), gabapentin (600 mg TID), and mephobarbital (200 mg BID). The patient completed high school and junior college and has been employed as a technician for the telephone company for the past 15 years. He and his wife have been married for more than 20 years and have two children together.

Results of Other Relevant Medical Procedures

MRI of the brain revealed the presence of left mesial temporal sclerosis and mild, diffuse volume loss. Video-EEG results were unavailable at the time of our evaluation. However, we would later learn that the patient was experiencing frequent left anterior TL spikes throughout the monitoring, as well as several subclinical events during our clinical interview and testing.

Neuropsychological Findings

Mr. Jones' neuropsychological test scores appear in Table 4.7, including his initial presurgical evaluation completed during inpatient video-EEG monitoring and a brief follow-up that was completed when he came back to undergo the Wada procedure. As will become clear, his initial testing appeared to be impacted by subclinical epileptiform activity, which actually contributed to our ability to confirm the seizure focus, yet also transiently disrupted his performance resulting in an underestimation of his actual baseline abilities. We first suspected that his performance was affected by some latent variable when he produced a genuine impairment profile on a performance validity test, as well as severely impaired memory scores on multiple measures of complex auditory/verbal learning and memory. This pattern suggested that Mr. Jones was either severely amnestic/demented (which was not consistent with his presentation, which included a good recent work history) or that some unknown factor was creating noise in his profile. When we met as a group to discuss the surgical cases for the week, it was discovered that the patient had experienced subclinical epileptiform discharges involving the left TL almost continuously throughout our evaluation. Neither the patient nor his examiners had suspected that his performance was altered. However, by completing additional testing when the patient returned approximately 6 weeks later to undergo the Wada procedure, the patient exhibited average performances in these domains, presumably when not experiencing such activity. AED regimen was unchanged at follow-up assessment. This confirmed our suspicions that the patient's inpatient performance was likely disrupted secondary to epileptiform activity and also afforded us the opportunity to better document his baseline ability. As the test sessions were very close together, we decided to use alternate forms of measures or similar tests thought to tap the same neurocognitive domains of interest. Of note, an underestimation of a patient's baseline performance can affect the neurosurgeon's approach to their case, as they could assume that an impaired memory performance means that there is nothing to lose secondary to surgery. Likewise, an underestimation of baseline performance could also lead to erroneous conclusions in outcome studies or research using neurocognitive scores as an end point (e.g., we might falsely determine that there was no decline or even an improvement following surgery, when instead the patient may have actually gotten worse).

As can be seen from examining his initial assessment results in Table 4.7, Mr. Jones exhibited a pattern of performance that suggested left frontotemporal lobe dysfunction, including severely impaired performances on most tasks of auditory/verbal learning and memory and visual confrontational naming ability despite average to high-average visual memory performance. Mr. Jones also exhibited mild deficits involving aspects of executive functioning, including problems with generative fluency, response inhibition, and mental flexibility. Of note, however, as performance on semantic fluency (impaired) was much worse than letter fluency (low average), this pattern could again suggest primarily TL dysfunction. It is also important to recognize that despite the acute epileptiform activity, the patient still exhibited many scores that were average or better on tasks involving visual memory, general intellectual functioning, remaining executive skills, and most aspects of language processing. Overall, this pattern was suggestive of dominant (presumably left) TL dysfunction, with possible disruption of FL regions as well. The latter finding could be conceptualized as perhaps reflecting dysfunction of the broader temporofrontal lobe networks secondary to ongoing seizures, a finding that we have noted is often observed in TLE patients (see earlier coverage of the nociferous cortex hypothesis).

An examination of Mr. Jones' follow-up testing from approximately 6 weeks later when he returned for the Wada procedure demonstrated that the initial findings during video-EEG monitoring were suboptimal for him. We felt confident that these results reflected the transient impact of epileptiform activity that was not present on the day of the Wada. While the same performance pattern was present, the patient's baseline ability was clearly far better than our initial assessment

Table 4.7 Select results of neurocognitive testing during video-EEG monitoring and 1 month later at time of Wada procedure

Tests administered	Results during video-EEG stay	Results on day of Wada
General IQ	WAIS-III FSIQ = 99, VIQ = 104, PIQ = 91	WASI FSIQ = 108, VIQ = 110, PIQ = 102
Performance validity testing	Failed 3/3 effort measures from the Word Memory Test (oral version) but produced a genuine impairment profile	Passed all performance validity tests, including the Medical Symptom Validity Test and the Word Memory Test (oral version)
Boston Naming Test	Raw = 39/60, impaired	Raw = 48/60, mildly impaired
Semantic fluency (animals)	Raw = 9, <1st percentile	Raw = 14, 4th percentile
Letter fluency (COWA)	Raw = 18, 2nd percentile	Raw = 24, 4th percentile
Screen of auditory comprehension and repetition	Normal	Normal
Complex list learning	Rey Auditory/Verbal Learning Test Trial 1 = 4/15, 6th percentile Trial 5 = 6/15, 1st percentile Trial 5 total = 27/75, 1st percentile Immediate = 0/15, <1st percentile Delayed = 2/15, 1st percentile Recognition = 3/15, <1st percentile	Verbal Selective Reminding Test (Form 1) LTS = 108, 44th percentile CLTR = 74, 23rd percentile Delayed = 11/12, 51st percentile Recognition = 12/12 normal
WMS-III Logical Memory Immediate recall	Raw = 41, 50th percentile	N/A
Delayed recall	Raw = 17, 25th percentile	
Verbal Paired Associates	WMS-III	WMS-I
Immediate	Raw = 2, 1st percentile	Raw = 16, 21st percentile
Delayed	Raw = 0, 1st percentile	Raw = 9, 12th percentile
Face recall	WMS-III faces	N/A
Immediate	Raw = 34, 25th percentile	
Delayed	Raw = 40, 75th percentile	
Recall of designs	WMS-III Visual Reproduction	N/A
Immediate Delayed	Raw = 76, 16th percentile Raw = 77, 75th percentile	
Recognition	Raw = 44, 50th percentile	
Trail Making Test	Part A = 29 s, 23rd percentile Part B = 129 s, 1st percentile	Part A = 26 s, 37th percentile Part B = 68 s, 30th percentile
Finger Tapping Test Dominant hand	Raw = 49, 21st percentile	Raw = 54, 50th percentile
Nondominant hand	Raw = 46, 30th percentile	Raw = 48, 45th percentile
Grip strength Dominant hand	Raw = 45, 18th percentile	Raw = 45, 18th percentile
Nondominant hand	Raw = 43, 18th percentile	Raw = 43, 18th percentile
Category test	13 errors, normal	N/A

IQ intellectual quotient, *WAIS-III* Wechsler Adult Intelligence Scale (3rd edition), *FSIQ* full-scale IQ, *VIQ* verbal IQ, *PIQ* performance IQ, *WASI* Wechsler Abbreviated Scale of Intelligence, *COWA* Controlled Oral Word Association Test, *LTS* long-term storage, *CLTR* continuous long-term retrieval, *WMS-III* Wechsler Memory Scale (3rd edition), *WMS-I* Wechsler Memory Scale

had suggested. This latter performance was also more in keeping with the patient's reported daily functioning. As can be seen from examining Table 4.7, the patient continued to exhibit mild deficits in auditory/verbal learning and naming ability during the second evaluation, yet these results were much better than the severely impaired performances initially observed during monitoring. It is interesting to note the dissociation between the contextual memory test and the list-learning and associative-learning tasks, as the former did not appear to be affected by the subclinical epileptiform activity. This finding highlights the dissociation that occurs between tests of memory and is supportive of the position that the latter tasks are more dependent on mesial TL structures. The patient also exhibited mild gains on some of the attentional measures and overall IQ, although it is difficult to disentangle practice effects and differences between measures for these smaller changes.

Mr. Jones did not exhibit any significant emotional distress during clinical interview or on formal measures of mood, although he did report some mild anxiety and concern over the effect of ongoing seizures and what he viewed as transient disruptions in his ability to function at work and at home. He did not have any risk factors for developing PNES events and did not exhibit somatizational tendencies on formal personality assessment.

Mr. Jones' Wada results demonstrated left hemispheric language lateralization and demonstrated that his right cerebral hemisphere was independently capable of encoding novel information. Therefore, he was scheduled for surgical resection. Based on the constellation of findings from neurocognitive performance and the other available data, we predicted that he would be at risk for further auditory/verbal memory decline with surgery. Primarily, this is because he had grossly intact baseline naming and verbal memory functioning (i.e., something to lose), and the resection was to be performed on his dominant cerebral hemisphere. Seizure onset was during his teen years, although there was really no indication of any brain reorganization based on available preoperative data. For example, he was exhibiting baseline deficits in naming and verbal memory (i.e., the areas that we were examining for evidence of a possible reorganization), and these deficits were enhanced by experiencing epileptiform activity involving the left TL (i.e., suggesting that they are still mediated by this region). The one factor arguing against a decline with surgery, and which we mentioned could possibly mediate the effects of surgery, was the presence of MTS. The patient decided to have surgery and was counseled regarding the potential risks of decline that he might face. These risks have to be balanced against the impact of ongoing seizures, which obviously contribute to transient disruptions of functioning and for some individuals likely contribute to more permanent changes in brain functioning over time. The patient will ultimately be scheduled for a 1-year postsurgical follow-up with our service, at which time we will repeat most of the initial battery of tests.

Direction of Future Practice and Research

Clinical neuropsychology in the epilepsy surgical setting already holds a solid position as a means of confirming the epileptic seizure focus, establishing a baseline level of functioning for the patient, and providing natural end points for outcome studies and other research. The ongoing effort to improve our ability to localize and lateralize functions should continue in the future, with an emphasis on developing improved techniques for assessing the extratemporal epilepsies. This will include further establishing the validity and usefulness of current measures for testing FL subregions and posterior cortical epilepsies, as well as developing new tests and paradigms. The assessment of FL function in particular will likely benefit from efforts to examine broader test patterns (e.g., teasing out the relative contribution of non-frontal lobe functions to executive control processes). Establishing collaborative efforts across centers (such as the NIH Common Data Elements Initiative) will also be critical for obtaining adequate sample sizes to explore many pertinent questions with these less common epilepsy syndromes. Another area of needed growth in the neuropsychology of epilepsy involves developing and implementing better methods of assessing functional capacity and monitoring a wider array of outcome variables (e.g., vocational success, avoidance of disability, marital statistics). Although not emphasized in the current chapter due to coverage elsewhere in this book, the need for neuropsychologists to be actively involved in broader assessment paradigms such as cortical stimulation mapping, Wada evaluations, and development of fMRI paradigms for language lateralization and other purposes is greatly encouraged. The future also holds a place for combining neuropsychological data with many of the emerging technologies, such as structural volumetric analysis, diffusion imaging, magnetoencephalography, dense array EEG, and virtual reality paradigms for the purposes of better understanding brain functioning and developing new means for assessing presurgical function and preventing postsurgical decline.

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