Epilepsy affects approximately 1% of the US population. Thirty percent of patients who present to epilepsy specialty centers are diagnosed with intractable epilepsy and undergo a comprehensive evaluation for possible surgical intervention for seizure control. A diagnostic workup for surgical intervention includes medical and psychiatric history, neurological examination, video-electroencephalographic monitoring, structural MRI and other neuroradiological techniques, and neuropsychological testing. Neuropsychological assessment helps to identify patients at risk for cognitive decline following epilepsy surgery.

Resection of seizure foci is an effective treatment for the control of medically intractable epilepsy. However, cognitive morbidity can occur as a result of surgical intervention. This morbidity is dependent on several factors, including location and extent of resection, disease characteristics, patient demographic characteristics, and functional status of the tissue to be resected. In this review article, the authors provide a summary of the neurocognitive outcomes of epilepsy surgery with an emphasis on presurgical predictors of postsurgical cognitive decline.

Memory After Left ATR

Verbal memory decline is the most consistently found impairment after left ATR. Sections of the hippocampus and parahippocampal gyrus, removed as part of a standard ATR, are important for encoding and retrieval of verbal information for recent events. Between 22% and 63% of individuals who undergo left ATR experience a significant decline in verbal memory, while about 7% show improvement. In contrast, between 10% and 34% of patients show improvement in verbal memory after right ATR. The primary predictor of postsurgical verbal memory loss following left ATR is the presurgical functional status of the tissue to be resected. Functional integrity of the mesial temporal lobe can be estimated in a number of ways, including greater left medial temporal lobe activation during presurgical fMRI, the absence of structural MRI abnormalities such as mesial temporal sclerosis, a lack of significant asymmetry in temporal lobe activation on FDG-PET, and intact presurgical verbal memory ability on neuropsychological testing. Later age at seizure onset is also associated with greater risk for memory decline following ATR, because individuals who have seizures that began in adulthood have a greater likelihood of developing adequate verbal memory abilities prior to the onset of seizures.
Postsurgical verbal memory loss after left ATR is also predicted by poor seizure control after surgery, more extensive resection, male sex (hypothesized to result because women have a more bilateral representation of memory, and older age at surgery. The latter finding is presumed to reflect reduced plasticity or lower compensatory reserve in older adults. Finally, individuals with moderate depressive symptoms before surgery are at greater risk of verbal memory decline following left ATR; this finding is hypothesized to reflect reduced compensated reserve. Table 1 summarizes the presurgical predictors of postsurgical memory decline.

**Memory After Right ATR**

Visual memory impairments (for example, memory for faces or places) occur in approximately 6%–32% of individuals who undergo right ATR, depending on the type of visual memory. For example, a recent study showed that 1 in 5 individuals who underwent right ATR had a significant decline in face memory ability, whereas 1 in 4 individuals had a decline in memory for spatial locations. As with verbal memory decline after left ATR, postsurgical visual memory loss is predicted by estimating the presurgical functional status of the tissue to be resected. Postsurgical visual memory loss after right ATR is predicted by greater presurgical right medial temporal lobe activation in response to a nonverbal task on fMRI, a relatively larger right hippocampus compared with the left hippocampus, later age at seizure onset, and intact presurgical visual memory ability on neuropsychological or Wada testing.

Other predictors include side of surgery (nondominant, left ATR nondominant, right ATR), later age at seizure onset, poor postoperative seizure control, and pathology of the resected tissue (atypical hippocampal sclerosis). Besides visual memory, right ATR is found to impair olfactory discrimination, identification, and recognition memory abilities.

**Language After Left ATR**

Word-finding difficulties also occur after ATR to the language-dominant hemisphere. The most common approach to assessing word-finding difficulties, confrontation naming (also referred to as semantic memory), evaluates general facts and meanings acquired through experience. Between 29% and 54% of individuals who undergo dominant, left ATR show significant word-finding difficulties after surgery. Postoperative word-finding difficulties are more likely to occur with more extensive resection of lateral temporal cortex, which is one area that stores semantic knowledge.

Other predictors of postoperative word-finding difficulties include an absence of hippocampal sclerosis or other imaging abnormalities before surgery, MR tractography showing more lateralized white matter tracts in the language-dominant hemisphere, fMRI temporal lobe laterality index, the absence of risk factors for seizures (for example, febrile seizures in childhood), cessation of language in tissue to be resected during intraoperative electrical stimulation mapping, and better presurgical naming ability. Semantic knowledge acquired later in life is the most vulnerable to loss after surgery.

Later age at seizure onset is also a valid predictor of naming decline. Individuals who experience seizures beginning at a later age routinely have better presurgical naming ability, so they are at greater risk of naming difficulties after dominant ATR. Schwarz et al. found that individuals who had seizure onset at 15 years of age or older were more likely to experience word-finding difficulties than those whose seizures started earlier. It may be that individuals with earlier age at seizure onset have less to lose after surgery because naming ability is already impaired or, alternatively, that brain functions have had the opportunity to reorganize in individuals whose seizures began early in life.

We recently conducted a study to evaluate the risk of naming decline after surgery as a function of age across the lifespan. We divided a sample of 229 individuals who underwent unilateral ATR (118 left and 101 right) into 5 groups (age at seizure onset < 10, 10–19, 20–29, 30–39, or ≥ 40 years). Results showed that the risk of naming decline after left ATR increased as a function of patient age at seizure onset, especially in middle adulthood (see Fig. 1). Over 60% of patients who had disease onset beginning after the age of 40 years showed a significant decline in

<table>
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<th>TABLE 1: Predictors of memory outcome after ATR</th>
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<tr>
<td><strong>Predictors of Verbal Memory Decline</strong></td>
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<tr>
<td>dominant, lt ATR</td>
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<tr>
<td>greater pre-ATR lt temporal lobe fMRI activation</td>
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<tr>
<td>absence of hippocampal sclerosis</td>
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<tr>
<td>good preop verbal memory</td>
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<tr>
<td>good preop Wada verbal memory w/ rt-side injection</td>
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<tr>
<td>no asymmetry in activation on PET scan</td>
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<tr>
<td>later age at seizure onset</td>
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<tr>
<td>poor postop seizure control</td>
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<td>more extensive resection</td>
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<tr>
<td>male sex</td>
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<td>older age at op</td>
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<td>preop major depression</td>
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neurological deficits occur when resection involves the orbitofrontal cortex. There is also literature demonstrating executive dysfunction after ATR, which is hypothesized to result from a disconnection between frontal and temporal lobe networks.2 Interestingly, a recent case study found that right posterior inferior frontal lobe resection led to transient hemispatial neglect.

Other predictors of executive impairments after frontal lobe resection include intact presurgical executive functioning,27 continued seizures after surgery,27 and presurgical depressed mood.

Deficits After Occipital and Parietal Lobe Resection

There is a paucity of research evaluating the cognitive sequelae associated with resection of occipital and parietal lobe seizure foci, and most available studies are based on small samples of heterogeneous patient populations.5,7 Given this situation, we focus on summarizing neurological deficits that frequently accompany resections within the occipital or parietal lobes. Patients with occipital lobe epilepsy often have visual symptoms even prior to epilepsy surgery, including visual agnosia, visual hallucinations or illusions, and contralateral visual field defects.18,41,47 Visual-cognitive difficulties after occipital lobe resection are usually attributed to damage to optic radiations and other visual processing areas during surgery. A recent report indicated that 50% of patients had new visual deficits following occipital lobe resection with 17% developing quadrantanopia or hemianopia.61 In one study, 4 of 12 patients who underwent occipital lobe resection sustained new visual field cuts following surgery, and an additional 2 patients reported postoperative change in motion detection ability (that is, with damage to area V5/MT).33 In a case study involving a 23-year-old woman, right-sided resection at the inferolateral temporoparietal junction led to transient prosopagnosia, which resolved 7 days after the surgery.65 Another case study described new-onset implicit visual field cuts following surgery, and an additional 2 patients reported postoperative change in motion detection ability (that is, with damage to area V5/MT).65

Parietal lobe epilepsy is associated with visual perceptual and spatial-constructional impairments, agnosia, decreased tactile discrimination ability contralateral to the side of surgery, left-right orientation confusion, hemineglect, and visual illusions.12,34,52 Resection of the parietal lobe can also lead to anomia, agraphia, alexia, apraxia, acalculia, and face-perception difficulties in a small percentage of patients.5,7 One study demonstrated that resec-
tion within posterior temporal-occipital-parietal areas for treatment of epilepsy resulted in a postoperative decline in nonverbal IQ, but not verbal IQ, as nonverbal skills rely to a greater degree on visual processes.

Conclusions

Cognitive morbidity following resection for treatment of intractable epilepsy is associated with several factors, including location and extent of resection, disease characteristics, patient demographic characteristics, and functional status of the tissue to be resected. Preoperative neuropsychological assessment is useful for creating a risk-benefit profile when estimating the possible postsurgical decrements associated with excision of eloquent areas of the brain versus the benefits of seizure freedom. Presurgical counseling, as well as postsurgical rehabilitation referrals, could diminish any distress associated with deficits that may occur after resection of temporal and extratemporal seizure foci.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: both authors. Acquisition of data: both authors. Analysis and interpretation of data: Dulay. Drafting the article: both authors. Critically revising the article: both authors. Reviewed submitted version of manuscript: both authors. Approved the final version of the manuscript on behalf of all authors: Dulay. Statistical analysis: Dulay.

References

Neuropsychological outcome


