Prediction of neuropsychological outcome after resection of temporal and extratemporal seizure foci

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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. (<http://thejns.org/doi/abs/10.3171/2012.1.FOCUS11340>)

KEY WORDS • neuropsychology • memory • postsurgical outcome • epilepsy

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 medically intractable epilepsy. Of individuals who undergo unilateral ATR, the most common form of surgery for intractable epilepsy, between 66% and 70% achieve seizure freedom.⁵⁹ Of patients with seizures originating from the frontal lobe, approximately 57% are seizure free 1 year after surgery and 30% 5 years after surgery.³² Resection not only has the potential to cure intractable epilepsy, but also can significantly improve health-related quality of life⁵⁷ and independence in activities of daily living,³⁵ increase the likelihood of return to work,¹⁷ and improve cognitive functioning.⁵⁸ Problematically, in a subset of patients, resection can contribute to postoperative neurocognitive impairment and emotional disturbance.^{44,58} In this review article, we

provide a summary of the neurocognitive outcome 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.²⁵ 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.⁵⁸ In contrast, between 10% and 34% of patients show improvement in verbal memory after right ATR.⁵⁸ 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,⁶ the absence of structural MRI abnormalities such as mesial temporal sclerosis,⁶³ a lack of significant asymmetry in temporal lobe activation on FDG-PET,²² and intact presurgical verbal memory ability on neuropsychological⁹ or Wada testing.³ 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.⁵⁴

Abbreviations used in this paper: ATR = anterior temporal lobe resection; fMRI = functional MRI.

Postsurgical verbal memory loss after left ATR is also predicted by poor seizure control after surgery,⁵³ more extensive resection,²⁶ male sex (hypothesized to result because women have a more bilateral representation of memory),⁶² and older age at surgery.³⁰ The latter finding is presumed to reflect reduced plasticity or lower compensatory reserve in older adults.¹ 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 compensatory reserve.⁸ 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.¹⁵ 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,³¹ a relatively larger right hippocampus compared with the left hippocampus,⁶³ later age at seizure onset,²¹ and intact presurgical visual memory ability on neuropsychological²⁰ or Wada testing.⁴² Other predictors include side of surgery (nondominant temporal lobe),¹⁵ larger right lateral neocortex and mesial temporal excision,³⁷ poor postoperative seizure control,¹⁶ and pathology of the resected tissue (atypical hippocampal sclerosis).⁶⁵ Besides visual memory, right ATR is found to impair olfactory discrimination, identification, and recognition memory abilities.⁴⁵

Language After Left ATR

Word-finding difficulties also occur after ATR to the language-dominant hemisphere. The most common ap-

proach 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.⁵⁸ Postoperative word-finding difficulties are more likely to occur with more extensive resection of lateral temporal cortex,²⁹ which is one area that stores semantic knowledge.²⁴ Other predictors of postoperative word-finding difficulties include an absence of hippocampal sclerosis or other imaging abnormalities before surgery,¹¹ MR tractography showing more lateralized white matter tracts in the language-dominant hemisphere,⁴⁸ fMRI temporal lobe laterality index,⁵¹ the absence of risk factors for seizures (for example, febrile seizures in childhood),⁵⁶ cessation of language in tissue to be resected during intraoperative electrical stimulation mapping,²³ and better presurgical naming ability.¹⁰ Semantic knowledge acquired later in life is the most vulnerable to loss after surgery.⁴

Later age at seizure onset is also a valid predictor of naming decline.⁵⁰ 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.⁵⁶ 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.¹⁴ 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 1: Predictors of memory outcome after ATR

Predictors of Verbal Memory Decline	Predictors of Visual Memory Decline
dominant, lt ATR	nondominant, rt ATR
greater pre-ATR lt temporal lobe fMRI activation	greater pre-ATR rt temporal lobe fMRI activation
absence of hippocampal sclerosis	larger rt hippocampus
good preop verbal memory	good preop visual memory
good preop Wada verbal memory w/ rt-side injection	good preop Wada visual memory w/ lt-side injection
no asymmetry in activation on PET scan	later age at seizure onset
later age at seizure onset	poor postop seizure control
poor postop seizure control	larger rt-lateral neocortex & mesial temporal excision
more extensive resection	pathology of resected tissue (atypical sclerosis)
male sex	
older age at op	
preop major depression	

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Fig. 1. Graph showing the reduction in naming ability (rounded to closest number of words) from before to after a left ATR stratified by age group (age at which patients began to have seizures). The results show that older age at seizure onset is a risk factor for greater naming decline (11-word decline or 19% reduction in performance) after left ATR. The bars represent the mean scores for the different age groups.

naming ability after left ATR (Fig. 2), whereas less than 5% in the same age at seizure onset group showed decline after right ATR. Follow-up analyses demonstrated that it was not that older surgical candidates were more likely to show a decline in naming after surgery but rather older age at seizure onset increased the risk of postsurgical decline.

Executive Function After Frontal Lobe Resection

The primary predictor of any impairment after frontal lobe resection is the location of surgery. Specific neurological deficits occur when resection involves the primary motor cortex, supplementary motor area, frontal eye fields, Broca area, dorsolateral prefrontal cortex, orbitofrontal cortex, or operculum. Motor and executive functioning impairments are the hallmark deficits associated with frontal lobe resection. Postoperative executive functioning declines following frontal lobe resection may include changes in attention and multitasking, fluency, response inhibition, concept formation, or problem solving.⁷ Left dorsolateral frontal lobe resection is associated with

Fig. 2. **Left:** Graph showing the percentage of individuals who underwent left ATR and experienced a significant decline in naming ability divided by age group (age that patients began to have seizures). Over 60% of patients with seizure onset later than 30 years of age had a significant decline in naming ability after left ATR. **Right:** Graph showing the results after right ATR.

postoperative phonemic fluency impairment, and right frontal lobe resection is associated with postoperative visual fluency impairment, particularly when the resection is extensive and includes frontal pole and orbitofrontal cortex.^{36,49} Resection that includes dorsolateral prefrontal cortex can also lead to working memory and multitasking deficits.⁴⁰ Left-sided resection of frontal premotor and supplementary motor areas is associated with transient expressive aphasia. Larger resections in either hemisphere also contribute to postoperative disinhibition and perseverative behavior.^{27,49} Odor identification and odor memory impairments occur following resection of orbitofrontal cortex.³⁸ 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.⁶⁰

Other predictors of executive impairments after frontal lobe resection include intact presurgical executive functioning,²⁷ continued seizures after surgery,²⁷ and presurgical depressed mood.¹³

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 temporo-occipital junction led to transient prosopagnosia, which resolved 7 days after the surgery.⁴⁶ Another case study described new-onset implicit visual memory and font-specific priming deficits after a right occipital lobe resection involving Brodmann areas 17 and 18 and a portion of area 19.^{19,64}

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.^{39,52} 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.⁴³

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.^{28,55}

Disclosure

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

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