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# Temporal lobe asymmetry in FDG-PET uptake predicts neuropsychological and seizure outcomes after temporal lobectomy

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ABSTRACT

*Objective:* The objective of this study was to determine whether preoperative [$^{18}$F]fludeoxyglucose (FDG)-positron emission tomography (PET) asymmetry in temporal lobe metabolism predicts neuropsychological and seizure outcomes after temporal lobectomy (TL).
*Methods:* An archival sample of 47 adults with unilateral temporal lobe epilepsy who underwent TL of their language-dominant (29 left, 1 right) or nondominant (17 right) hemisphere were administered neuropsychological measures pre- and postoperatively. Post-TL seizure outcomes were measured at 1 year. Regional FDG uptake values were defined by an automated technique, and a quantitative asymmetry index (AI) was calculated to represent the relative difference in the FDG uptake in the epileptic relative to the nonepileptic temporal lobe for four regions of interest: medial anterior temporal (MAT), lateral anterior temporal (LAT), medial posterior temporal (MPT), and lateral posterior temporal (LPT) cortices.
*Results:* In language-dominant TL, naming outcomes were predicted by FDG uptake asymmetry in the MAT ($r = -0.38$) and LPT ($r = -0.45$) regions. For all patients, visual search and motor speed outcomes were predicted by FDG uptake asymmetry in all temporal regions (MPT, $r = 0.42$; MAT, $r = 0.34$; LPT, $r = 0.47$; LAT, $r = 0.51$). Seizure outcomes were predicted by FDG uptake asymmetry in the MAT ($r = 0.36$) and MPT ($r = 0.30$) regions. In all of these significant associations, greater hypometabolism in regions of the epileptic temporal lobe was associated with better postoperative outcomes.
*Conclusions:* Our results support the conclusion that FDG uptake asymmetry is a useful clinical tool in assessing risk for cognitive changes in patients being considered for TL.

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## 1. Introduction

Temporal lobectomy (TL) is an effective treatment for seizures in patients with medically intractable temporal lobe epilepsy [1]. While seizure outcomes are good, post-TL cognitive decline is frequently reported [2,3]. In their meta-analysis of neuropsychologic outcomes following TL, Sherman and colleagues [3] found significant postoperative declines in verbal memory were present in up to 63% of left- and 34% of right-TL patients. Postoperative decline in naming was present in up to 54% of patients following left-sided resections. Despite the relatively common incidence of post-TL cognitive change, only a small fraction of patients (about 9%) perceive a decline following epilepsy surgery, and nearly twice as many report improvement in cognition [3]. For most patients, cognitive decline may go unnoticed in their routine daily activities, as these tasks are unlikely to overtax commonly affected abilities, such as memory and naming skills [4]. However, decline may be more conspicuous to those hoping to pursue more cognitively demanding activities after TL, such as attending school or obtaining employment in skilled professional settings [5]. Thus, while many patients do not perceive cognitive changes following TL, accurately assessing the likelihood of decline is critical for making informed clinical decisions on an individual level.

Predicting postoperative outcomes is a complex process, as certain factors confer more or less risk based on the outcome being predicted. For example, factors such as low preoperative intelligence quotient (IQ), left hemisphere resection, and older age at the time of surgery are all associated with increased likelihood for cognitive decline, but not poorer seizure outcomes [6]. Structural abnormalities consistent

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with mesial temporal sclerosis (MTS) on magnetic resonance imaging (MRI) is a positive prognostic indicator for both cognitive and seizure outcomes [6,7], but some 20–30% of patients with temporal lobe epilepsy may have no MRI evidence of MTS [8,9]. [$^{18}$F]Fludeoxyglucose PET (FDG-PET) may be informative in predicting seizure outcomes for patients with normal preoperative MRIs [10]. However, the relationship between preoperative PET and post-TL cognitive change remains uncertain, as there are less than a handful of relevant published studies, and findings have been inconsistent [11,12].

Griffith et al. [13] studied the relationship between preoperative FDG uptake and post-TL memory outcomes in 27 left- and 22 right-TL patients by visually analyzing the difference in FDG uptake between the right and left temporal lobes and grouping patients by "none/mild" or "moderate/severe" uptake asymmetry. They found that left-TL patients with no or mild asymmetries had greater postoperative verbal memory decline than those with moderate to severe asymmetries. Leeman, Leveroni, and Johnson [11] conducted a similar study, but used an automated technique for identifying anatomical structures, which allowed for quantification of the tracer uptake in temporal lobe regions. In their pilot study of 14 left-TL patients, FDG uptake asymmetry within the hippocampi (their region of interest) was not found to be a statistically significant predictor of postoperative changes in verbal memory. However, the relationship between temporal lobe asymmetry and verbal memory outcomes was close to statistical significance ($p = 0.06$), hinting at similar findings to those of Griffith et al. [13].

This report provides an analysis of temporal lobe asymmetries in FDG uptake and post-TL outcomes, using semiquantitative tools for PET image analysis and empirically based methods for quantifying the degree of pre- to postoperative cognitive change. Using automated methods for quantification of FDG uptake avoids reliance on descriptors such as "mild" or "severe" asymmetry, which—although useful starting points—do not capture the bidirectional nature of asymmetry. For instance, "mild asymmetry" could result from mild hypermetabolism or mild hypometabolism in the epileptic temporal lobe. In the present study, the terms "relative hypometabolism" or "relative hypermetabolism" are used to specify the relationship between baseline FDG-uptake in the epileptic compared to the nonepileptic temporal regions. We tested the following predictions: 1) a greater degree of relative hypometabolism in the medial temporal region would be associated with better verbal memory and naming outcomes for patients who underwent language-dominant TL, and 2) a greater degree of relative hypometabolism in the medial temporal region would be associated with better seizure outcomes for all patients. Lastly, we explored FDG correlates of outcomes of simple visual search and motor speed, executive functioning, and verbal fluency; however, since only a few studies have evaluated such outcomes following TL, no specific predictions were made for these measures [3].

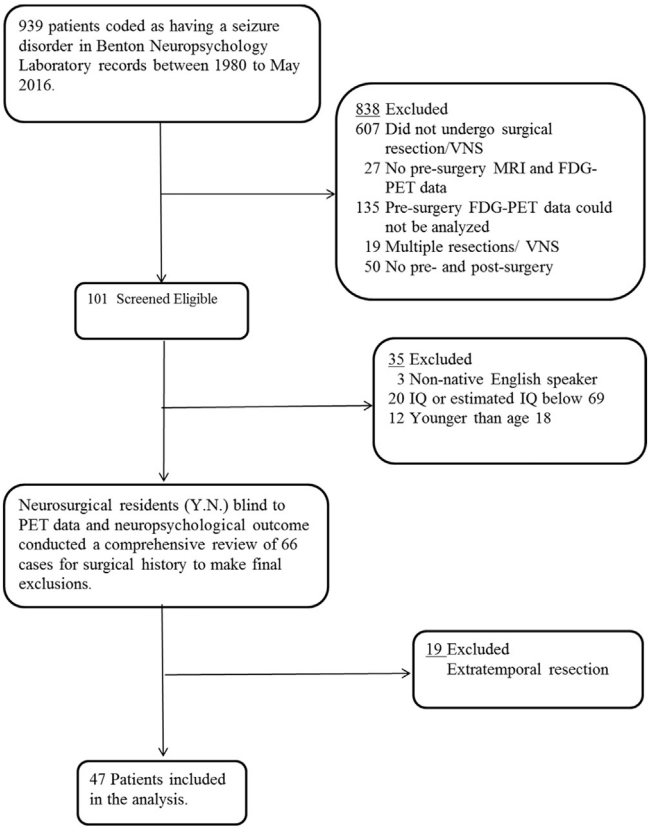


**Fig. 1.** Flow chart of participant selection.

## 2. Methods

### 2.1. Subjects

An archival sample of 47 patients with unilateral temporal lobe epilepsy who underwent surgical resection of the language-dominant (29 left-TL, 1 right-TL) or nondominant (17 right-TL) temporal lobe from the years 2004 to 2016 were selected from the Patient Registry of the Division of Neuropsychology and Cognitive Neuroscience at the University of Iowa. Fig. 1 presents a flow chart of case ascertainment, inclusion/exclusion, and information regarding patients examined for eligibility, confirmed eligible, and ultimately included in the study. All met the following criteria: unilateral temporal lobe epilepsy, no MRI abnormalities other than atrophy consistent with MTS, age18 years or older, and an IQ or an estimated IQ (based on the reading subtest of the wide range achievement test, $N = 5$) of 69 or greater. For patients ($N = 7$) in which the preoperative evaluations were not consistently concordant with unilateral temporal lobe epilepsy (or suggested temporal-plus epilepsy), an evaluation was conducted using intracranial electrodes to confirm the localization of the epileptogenic zone. All patients had video-EEG monitoring, high-resolution MRI, FDG-PET, and pre/post-TL neuropsychological testing. Language dominance was determined by intracarotid amobarbital testing in all but five patients (2 left- and 3 right-TL). Left hemisphere language dominance was assumed for these individuals, all of whom were right-handed. One patient (who underwent right-TL) demonstrated right hemisphere dominance for language; accordingly, this patient was placed in the "language-dominant TL" group. All patients provided written, informed-consent for the use of their data for the purposes of this study, as approved by the Institutional Review Board at the University of Iowa.

### 2.2. Surgery

All patients underwent corticoamygdalohippocampectomy (CAH), involving resection or disconnection of the temporal pole and temporal neocortex with resection of the amygdala and hippocampus. All surgeries were performed by one of two neurosurgeons experienced in epilepsy surgeries. The extent of the lateral neocortical disconnection/resection, measured from the anterior tip of the temporal pole, ranged from approximately 4 cm in the language dominant hemisphere to 6 cm in the nondominant hemisphere. For CAH of the dominant hemisphere, language areas were mapped with a standard electrical stimulation protocol [12]. The superior temporal gyrus was preserved in some of the dominant hemisphere cases. The extent of hippocampal resection was tailored based on intraoperative electrocorticography and ranged from approximately 1 to 4 cm measured from the head of the hippocampus. The extent of the lateral and mesial resection or disconnection was also tailored by findings from intraoperative electrocorticography in all cases.