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## Naming ability after tailored left temporal resection with extraoperative language mapping: Increased risk of decline with later epilepsy onset age

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### Abstract

Standard temporal resection in the left hemisphere carries the risk of postoperative naming ability decline, especially with later epilepsy onset age/absence of hippocampal sclerosis. Language mapping has been performed routinely at some centers to minimize postoperative primary language impairment, but its effect on changes in naming performance has not been explored. This study examined naming outcome in 24 patients with nonlesional epilepsy who had left temporal resection after extraoperative language mapping. The mean decline in Boston Naming Test (BNT) score was 7.8, and 13 (54%) patients had a BNT decline greater than the Reliable Change Index. Simple correlations found significant relationships between BNT score decline and: later onset age, higher preoperative BNT score, and resection of isolated language sites. A multiple regression analysis showed that onset age was the best predictor of BNT decline. Although naming ability in patients with early onset age is stable with language mapping, there is still a risk of decline for those with later onset age.

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### 1. Introduction

Anterior temporal lobectomy (ATL) in the hemisphere dominant for language carries risks for impairing language function, specifically naming ability, after surgery, even in the absence of gross aphasic symptomatology [1-11]. Other aspects of language function such as fluency and comprehension seem to be spared [1,12]. Reports of the results for naming following ATL have shown that although group comparisons often demonstrate no or modest decline [2,3,6], a subgroup of patients is at risk for decline. A risk factor for decline is

later epilepsy onset age and/or absence of hippocampal sclerosis (HS).

Mapping of language areas has been used as a technique to minimize the risk of producing primary language dysfunction after surgery in the dominant hemisphere. Mapping may be intraoperative [13-15] or extraoperative [16,17], the latter allows ictal EEG monitoring so that the procedure is then tailored to maximize the resection while preserving functional areas. Mapping has revealed that language sites can be quite variable in distribution, and not confined to the classic well-demarcated language areas [13-15]. Some studies have suggested that tailored resections may also result in naming decline, and again, although group comparisons suggest no or modest risk [4,5,16], there is evidence that for these cases to a subgroup is at risk. [8,18].

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We examined naming outcome in patients undergoing tailored left temporal resection with language mapping. The resection was based on cortical mapping of primary language cortex with the objective of avoiding postoperative aphasia. We hypothesized that, if these patients undergo a naming decline, the same risk factor (i.e., onset age) may be relevant as for standard resection. This study was a retrospective analysis.

## 2. Material and methods

The patient sample was taken from a population of patients with intractable epilepsy undergoing left, language-dominant temporal resection after placement of a subdural electrode grid with extraoperative mapping of language cortex. The following criteria were required: left hemisphere dominance for language as evaluated with an intracarotid amobarbital procedure; pre- and postoperative neuropsychological testing including the Boston Naming Test (BNT); full scale IQ (FSIQ) > 69; and no lesion on magnetic resonance imaging (MRI) apart from changes consistent with HS. MRI volumetry or spectroscopy was not performed. Seven patients had MRI evidence of HS. Onset age refers to onset of unprovoked seizures.

### 2.1. Neuropsychological testing

Neuropsychological testing was performed preoperatively and 6 to 8 months postoperatively. A comprehensive battery of tests was administered, including tests of language function, intelligence, and memory. For the purposes of this study the 60-item BNT was used [19].

### 2.2. Language mapping technique

Language mapping was performed extraoperatively via a subdural electrode array. A minimum of two sessions were scheduled following clarification of the area of the ictal onset. The objective of the mapping was to locate areas that, when stimulated, consistently produced language errors. The stimulation procedure involved engaging the patient in ongoing speech tasks such as counting, reciting a nursery rhyme, and naming the months of the year, and noting any errors that occurred when the stimulation was applied. Errors ranged from complete speech arrest to paraphasic responses or errors of sequencing. More recent cases were administered a more formal language protocol that tested automatic speech, naming; auditory comprehension, reading, and repetition on every stimulation trial. Data from this protocol were available for 12 patients. For the purposes of this study, language sites were then identified on the basis of consistent stimulation interruption of any one of these modalities.

### 2.3. Surgical technique

The craniotomy was always performed with general anesthesia. At the first procedure, a subdural grid was placed on the convexity of the hemisphere to ensure good coverage of frontal and temporal convexity cortex. In addition, subdural strip electrodes were placed beyond the edges of the grid to cover subtemporal, anterior frontal, and subfrontal areas. Recording and stimulation studies were then undertaken over the following days. The second procedure was performed after completion of language mapping and delineation of the area of ictal onset. The aim was to resect areas identified as significant for ictal onset and to spare the temporal language area. This area was defined as a cluster of sites where consistent language errors were demonstrated in response to stimulation. Occasionally isolated single language error sites, or sites where errors were inconsistently recorded, were identified. These sites were typically surrounded by large areas of silent cortex and we have considered them anomalous and not essential for language function. Thus, they were not spared in the resection if they were within the area of ictal onset.

Surgically, the lateral temporal cortex was resected first, and, unless memory function was considered to be at risk, mesial structures were then resected by aspiration. The fragments of the mesial structures were submitted for histopathological examination which did not allow detailed study of neuronal loss within specific sectors of Ammon's horn. Mesial structures were not resected in seven cases.

### 2.4. Data analysis

Simple bivariate correlations (Pearson  $r$  for continuous variables and Spearman  $\rho$  for noncontinuous variables) were used to examine relationships between BNT score change and predictors. Variables considered were: onset age, chronological age, FSIQ, preoperative BNT score, extent of lateral temporal resection, distance from the edge of the resection to the closest language site, distance from the temporal pole to the most anterior temporal language site, resection of any isolated language sites, resection or preservation of hippocampus, and presence of any language sites on the edge of the grid. Presence/absence of HS was not included in the analysis because the imaging certainly underestimated the number of patients with HS, and we did not have histopathological confirmation of hippocampal pathology.

Meaningful change in the BNT score was evaluated with the reliable change index (RCI). RCIs provide an index of reliable alteration in test performance, changes that cannot be attributed to common sources of measurement error inherent in test-retest designs (e.g., practice effect, regression to the mean). These indexes are

derived from the assessment of epilepsy patients who were tested twice but did not undergo surgery. The decline necessary to exceed the 90th %centile, of the RCI is 5 for the BNT [20].

Finally, a multiple regression analysis with backward entry of variables was undertaken. The dependent variable was change in BNT score and the independent variables were those found to have significant relationships with BNT decline.

Seizure outcome was evaluated according to the classification of Engel et al. [21].

### 3. Results

Twenty-four patients were identified who met the inclusion criteria. Details are given in Table 1. None was clinically dysphasic postoperatively.

#### 3.1. Mapping findings

The mean number of temporal language sites was 6.5. For males the mean was 7.7, and for females, 4.1 (*t* test of independent samples, NS). There was no significant correlation between the number of language sites and age of epilepsy onset ( $r = 0.01$ , NS). Also, there was no significant correlation between distance from the temporal pole to the most anterior language site and age of onset ( $r = -0.04$ , NS).

#### 3.2. Naming outcome

The mean change in BNT score was -7.8. Significant correlations were found between . BNT decline and preoperative BNT score ( $r = -0.57$ ,  $P < 0.01$ ), onset age ( $r = -0.54$ ,  $P < 0.01$ ), and resection of isolated

Table 1

Patient data: Continuous variables, mean (SD)

N	24
Sex M/F	15/9
Seizure outcome: Engel class I	15 (63%)
Chronological age (years)	28.0 (11.89)
Onset age (years)	13.8 (10.55)
FSIQ	93.1 (14.02)
BNT score before surgery	41.5 (11.62)
BNT score change	-7.8 (12.60)
Extent of lateral resection (cm)	5.6 (1.63)
Distance from resection edge to closest language site (cm)	0.9 (0.93)
Number of temporal language sites	6.5 (4.68)
Distance from temporal pole to most anterior language site (cm)	6.5 (1.40)
Patients with any isolated language sites resected	5
Language sites on edge of grid	17
Resection of hippocampus	17
MRI evidence of HS	7

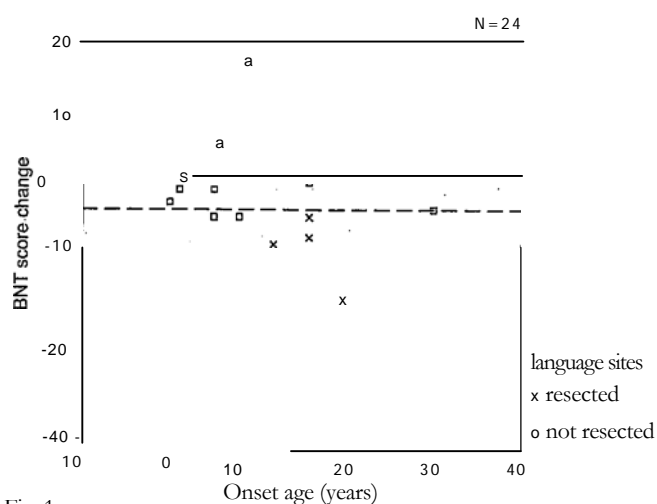


Fig. 1. Scattergraph of pre- to postoperative change in BNT score versus epilepsy onset age.

language sites ( $p = -0.48$ ,  $P < 0.05$ ). BNT decline was associated with higher preoperative BNT scores, later onset age, and resection of isolated language sites. The pre- to postoperative change in BNT score by onset age for individual patients is shown in Fig. 1. No significant correlation was found between BNT score change and: chronological age, number of temporal language sites, extent of lateral temporal resection, FSIQ, distance from the resection edge to the closest language site, distance from the temporal pole to the most anterior language site, or presence of language sites on the edge of the grid:

Thirteen (54%) patients had a BNT decline greater than the RCI. Decline was associated with higher preoperative BNT score, later epilepsy onset age, and resection of isolated language sites. For those undergoing RCI decline and those who did not, mean preoperative BNT scores were 48.6 and 33.1 (*t* test of independent samples,  $P < 0.01$ ), mean onset ages were 19.1 and 7.5 years (*t* test of independent samples,  $P < 0.01$ ), and mean numbers of isolated language sites resected were 0.7 and 0 (Fisher exact test,  $P < 0.05$ ).

A multiple regression analysis with BNT score change as the dependent variable and preoperative BNT score, onset age, and resection/preservation of isolated language sites as independent variables revealed preoperative BNT score to be the only significant predictor of BNT score decline ( $R^2 = 0.38$ ,  $F = 4.23$ ,  $P < 0.05$ ). However, as preoperative BNT score and BNT score change were highly correlated ( $r = -0.57$ ), higher preoperative BNT score being associated with greater BNT decline, and this is consistent with the absence of the syndrome of mesial temporal lobe epilepsy (MTLE) [22,23], the analysis was repeated omitting preoperative BNT score as an independent variable. Epilepsy onset age was then found to be the only significant

predictor of BNT score decline ( $R^2 = 0.23$ ,  $F=5.53$ ,  $P<0.05$ ).

The median onset age was 14 years. The mean BNT 'change for onset age < 14. years was -9, and for >14 years, the mean change was -14 (*t* test of independent samples,  $t = 3.5$ ,  $P < 0.05$ ). For onset age < 14 years, the number undergoing BNT RCI decline was 3 (27%), and for onset age > 14 years, the number undergoing RCI decline was 10 (77%) ( $\chi^2 = 5.92$ ,  $P < 0.05$ ).

The BNT score-change for patients rendered seizure free, was -4.07, and for those not seizure free, -14.2 (*t* test of independent samples, NS). RCI decline in those rendered seizure free occurred in 6 of 15 (40%), and in those not seizure free, in 7 of 9 (78%) (Fisher exact test, NS).

### 3.3: Seizure outcome

Fifteen patients (63%) were in Engel class 1 at 1 year after surgery, five were in class 2, and three were in class 4.

## 4. Discussion

The present study finds evidence for decline in naming ability, as measured by a confrontation naming task, after tailored temporal resections performed with extraoperative language mapping. Relevant to the naming decline were higher preoperative BNT score and later age of epilepsy onset. While resection of isolated language sites initially appeared to be correlated with naming decline, subsequent analysis revealed that this was no longer a significant predictor. Other mapping-associated factors such as the extent of the lateral temporal resection and the location of language sites in relation to the resection were not associated with naming decline.

Standard anatomical resections such as ATL and selective amygdalohippocampectomy do not entail language mapping, but remove fairly well-defined anatomical structures (menial temporal structures) that have been implicated in epileptogenesis by a combination of the results of imaging studies and EEG monitoring. For ATL, the resection is conservative with respect to lateral temporal lobe, usually 4 to 4.5 cm posterior to the pole, and this is based on the assumption that this will be anterior to the typical location of language sites.

The aim of the tailored resection is to maximize the resection of epileptogenic cortex while preserving functional cortical areas. Proponents of language mapping emphasize that language sites are not only variable in location but also can be anteriorly placed on the temporal lobe [14,16,24,25]. The approach to the surgical treatment of a patient with temporal lobe onset seizures will differ according to the philosophy of the particular epilepsy surgery center.

### 4.1. Naming after standard temporal resection

Reports of the effects of ATL on naming have been conflicting, and while group comparisons often show no or modest decline [2,3,6,7], it is possible to identify a subgroup that may be at risk, the size of this subgroup depending on the method used to identify meaningful decline [8,10,12]. Hermann et al. employed as a criterion a test-retest decline exceeding the greatest decline for a right, nondominant resection, and found that about 7% of the patients undergoing left, dominant ATL exceeded this value [8]. Langfitt and Rausch, using the BNT, considered a change in language performance exceeding one standard deviation as meaningful, and found that 25% of left ATL patients exhibited such a decline [10]. Using RCI values as indicators of meaningful decline, Davies et al. found that 39% of patients exceeded this on the BNT and 17% on the Visual Naming subtest of the Multilingual Aphasia Examination [12]. RCIs are indices derived from the assessment of epilepsy patients who have been tested twice but did not undergo surgery and provide an index of reliable alteration in test performance that cannot be attributed to common sources of measurement error inherent in test-retest designs, such as practice effect and regression to the mean [20,26]. This is, of course, not synonymous with a clinically significant decline, which has not been established. In fact, there is evidence of no clear relationship between postoperative change in confrontation naming and subjective change in naming abilities [27]. It is possible that an auditory naming task may be a more accurate measure of subjective difficulties [28,29].

Published studies have shown that the subgroup at increased risk for naming decline will tend to have later epilepsy onset age [8,30], absence of early risk factors (\*5 years) for epilepsy [1,11], and absence of HS [12], all features of the absence of the syndrome of MTLE [31,32]. MTLE is defined by early onset age of recurrent seizures and/or early risk factors for epilepsy (e.g., febrile convulsions) and by MRI findings suggestive of HS (unilateral atrophy) or with frank HS on histopathological examination. Typical onset ages have been found to be 7 years for those patients with HS and 20 years for those without HS [33]. Thus, for standard ATL without mapping, the presence of the syndrome of TLE confers stability, an association that applies not only to naming but also to memory [34]. The implication is that the absence of sclerosis indicates the presence of functioning structures, including -hippocampus, and their removal results in loss of function.

Also of interest is a report by Bartha et al. of naming decline after selective amygdalohippocampectomy, a standard resection procedure that spares lateral temporal cortex. These authors also showed a decline in naming ability in some patients, and later epilepsy onset age was a risk factor [35].

#### 4.2. Naming after tailored resections

Some studies have reported declines in naming ability after tailored resections. Swanson et al. [18], using the same criterion as Hermann et al. [8], found a naming decline in 8% of patients after resection with language mapping, a figure similar to that for the standard ATL. Furthermore, in a multicenter comparison of naming outcome in patients who had had standard temporal resection (with sparing or resection of superior temporal gyrus) versus those who had language mapping and tailored resection (with intra- or extraoperative mapping), there was no difference with respect to naming outcome. [30]. All groups underwent a similar RCI decline. The predictors of decline for all groups were later age of onset and more extensive resection of lateral temporal cortex. These findings suggest that for tailored resections, factors apart from language mapping maybe relevant for naming outcome.

In the present study we initially found significant relationships between BNT score decline and higher preoperative BNT score, later epilepsy onset age, and resection of isolated language sites. The multiple regression analysis initially showed that preoperative BNT score was the only significant predictor of BNT score change. However, higher preoperative BNT score is consistent with absence of the syndrome of MTL, as reported previously [22,23], and these patients are known to undergo greater BNT declines. When the analysis was repeated omitting preoperative BNT score as an independent variable, onset age emerged as the only significant predictor of BNT score change. Resection of isolated language sites was no longer a significant predictor. We believe that this supports our interpretation of these sites as not essential for language integrity, although the study of additional cases is necessary to fully evaluate the significance of these sites.

#### 4.3. Mechanism of naming decline after temporal resection

Naming has classically been considered to be dependent on lateral temporal neocortical function [36], although localization of the naming function has proved to be quite elusive. Some studies have demonstrated relationships between naming and hippocampal structure and function [37-40]. It has not been clear whether the naming decline after ATL is due to resection of mesial structures directly involved in naming, or whether earlier onset of epilepsy may result in intrahemispheric reorganization of language in the lateral temporal lobe, with the decline in naming then following the lateral temporal resection. Functional imaging studies have suggested a contribution of the mesial temporal lobe to naming; Spitzer et al. showed left mesial temporal activation. with a picture naming task [39], and Sawrie

et al. demonstrated with MR spectroscopy that the language-dominant hippocampus is a component of the visual confrontation naming network [37]. The report of Bartha et al., showing naming decline after selective amygdalohippocampectomy and greater decline with later onset age, also supports the view that mesial temporal structures and/or their connections are involved in the mediation of naming [35].

Support for intrahemispheric reorganization of language function comes from mapping studies that show a relationship between epilepsy onset age and the location of language sites in the temporal lobe. Devinsky et al. [24] and Schwartz et al. [25] found that patients with earlier onset age tended to have more anteriorly placed sites, potentially within the 'resection line of a standard ATL. This is the reverse of what may be expected if these sites are essential to language function: typically, patients with earlier onset age remain stable with respect to naming after ATL. It is, however, possible that these sites represent duplication of function, as a consequence of reorganization of function secondary to an early insult. The present study did not find such a relationship: we found no significant correlation between onset age and the distance of the most anterior language site from the temporal pole.

We have found decline in naming ability in a group of patients undergoing temporal resection after language mapping. Higher preoperative BNT score and epilepsy onset age were important in predicting this decline. These results underscore the unique nature of the naming function in relation to spontaneous expressive speech, repetition, and auditory comprehension. Naming, whether in response to visual or auditory stimuli, appears to represent a different level of language processing that may require integration of lateral temporal and mesial temporal functions anatomically distinct from primary language cortex. Thus, while tailored resection continues to be a valuable technique in the management of focal epilepsy by permitting maximum resection-and minimizing risk to primary language functions, it is not useful in predicting the degree of naming difficulty postoperatively.

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