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Using multivariate data reduction to predict postsurgery memory decline in patients with mesial temporal lobe epilepsy

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ABSTRACT

Predicting postsurgery memory decline is crucial to clinical decision-making for individuals with mesial temporal lobe epilepsy (mTLE) who are candidates for temporal lobe excisions. Extensive neuropsychological testing is critical to assess risk, but the numerous test scores it produces can make deriving a formal prediction of cognitive change quite complex. In order to benefit from the information contained in comprehensive memory assessment, we used principal component analysis (PCA) to simplify neuropsychological test scores (presurgical and pre- to postsurgical change) obtained from a cohort of 56 patients with mTLE into a few easily interpretable latent components. We next performed discriminant analyses using presurgery latent components to categorize seizure laterality and then regression analyses to assess how well presurgery latent components could predict postsurgery memory decline. Finally, we validated the predictive power of these regression models in an independent sample of 18 patients with mTLE. Principal component analysis identified three significant latent components that reflected IQ, verbal memory, and visuospatial memory, respectively. Together, the presurgery verbal and visuospatial memory components classified 80% of patients with mTLE correctly according to their seizure laterality. Furthermore, the presurgery verbal memory component predicted postsurgery verbal memory decline, while the presurgery visuospatial memory component predicted visuospatial memory decline. These regression models also predicted postsurgery memory decline successfully in the independent cohort of patients with mTLE. Our results demonstrate the value of data reduction techniques in identifying cognitive metrics that can characterize laterality of damage and risk of postoperative decline.

1. Introduction

Comprehensive neuropsychological assessment using a large number of standardized tests is typically undertaken in individuals with intractable epilepsy who are candidates for a resection of their seizure focus. These tests are used to establish a patient's clinical profile and to assess risks of postsurgical cognitive decline [1]. In patients with mesial temporal lobe epilepsy (mTLE), many of these tests focus on memory performance, which is disrupted by temporal lobe dysfunction [1,2]. When epilepsy is unilateral, left-lateralized mTLE (L-mTLE) tends to disrupt verbal memory function, and left-lateralized temporal lobe resections can lead to a decrease in verbal memory function [3–5]. On the other hand, right-lateralized mTLE (R-mTLE) can affect visual and visuospatial memory, although the consistency with which performance is impacted by surgery is somewhat weaker [6–9].

Recently, much effort has been dedicated to the identification of reliable predictors of postsurgery memory decline in patients with mTLE. Among such predictors are patients' age at surgery and age at onset [10,11] and measures of medial temporal structural and functional integrity [12–15]. Baseline memory performance has also been identified as an important marker of risk for postsurgery memory decline: good presurgery verbal memory performance has been shown to predict significant verbal memory decline postresection in patients with L-mTLE [11,13,15–22], while individuals with R-mTLE with good baseline visuospatial memory have been shown to be at a greater risk of postsurgery visuospatial memory decline [3,12,13,23,24].

Many studies linking memory performance pre- and postsurgery typically rely on a single test score or on a few selected test scores assessed in separate analyses (for an exception, see [25]). Individual test scores can be influenced by measurement errors and by idiosyncratic factors that are unrelated to a patient's pathology. Also, parallel analyses conducted on test scores meant to capture similar cognitive functions

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(e.g., verbal memory) can lead to conflicting results that are difficult to interpret. Since neuropsychological assessments typically generate a rich collection of test scores, some of which clearly tap the same functional domains, data reduction techniques such as principal component analysis can be used to derive a smaller number of latent components that reflect these domains. Such components are more resilient to noisy fluctuations in individual test performance [26] and can be used as robust indices of memory in mathematical models predicting postsurgical change in cognitive performance.

With the current analysis, we used intelligence, verbal memory, and visuospatial memory neuropsychological test scores obtained from patients with left or right mTLE tested before and after they underwent a unilateral temporal lobe resection. We applied principal component analysis (PCA) to reduce these scores into a smaller set of latent components. We then used these components to discriminate between patients with L-mTLE and R-mTLE and to predict postsurgery changes in memory performance, both in the original cohort from which the components were derived and in an independent cohort of patients with mTLE. By cross-validating our model on an independent patient sample, we provide a rigorous assessment of whether the predictive power of the model can generalize to the general population of patients with unilateral mTLE identified as surgery candidates. Our goal was to assess whether we could derive simple yet powerful indices of verbal and visuospatial memory that could be used in both clinical and research settings.

2. Methods

2.1. Subjects

Neuropsychological, clinical, and demographic data were obtained from 56 patients with unilateral mTLE (28 L-mTLE, 28 R-mTLE) who had received epilepsy surgery at the Toronto Western Hospital between 1996 and 2011 (see Table 1). All patients provided informed consent for their anonymized data to be used for research purposes, according to a series of protocols approved by the University Health Network's Research Ethics Board. Forty-three patients underwent standard, en bloc anterior temporal lobe resection including surgical removal of the temporal pole, the amygdala, the anterior portion of the hippocampus, the rhinal and lateral temporal cortex, and portions of the parahippocampal cortex, while 13 patients underwent selective amygdalohippocampectomy including surgical removal of the amygdala, the anterior portion of the hippocampus, the rhinal cortex, and portions of the parahippocampal cortex. Patients had undergone a full neuropsychological assessment both preoperatively and postoperatively. The median interval between presurgical assessment and surgery was 14 months (1st quartile = 9 months; 3rd quartile = 21 months), and the median time interval between surgery and the postsurgical assessment was 9 months (1st quartile = 7 months; 3rd quartile = 12 months). All patients had a full scale intellectual quotient score greater than 70 on the Wechsler Abbreviated Scale of Intelligence (WASI; [27]) and had levels of English fluency appropriate for testing. Additional clinical information for this patient cohort and demographic and neuropsychological data for the cross-validation patient sample (see Table S1) are available as online supporting information.

2.2. Neuropsychological tests

Mean scores for the tests selected for this analysis are presented in Table 1. Intelligence indices included the verbal (*VIQ*) and performance (*PIQ*) intellectual quotient from the WASI [27]. Verbal memory test scores included the raw score on the Warrington's Word Recognition Test (*WWord*; [28]) and two scores from the Rey Auditory Verbal Learning Test [29]: the total learning score (over 5 learning trials; *RAVLTtot*) and percent retained score (*RAVLT%*), which corresponded to the percentage of words recalled on the 5th learning trial that were retained after a 20-minute delay. Visuospatial memory test scores included the raw score on the Warrington's Face Recognition Test (*WFace*; [28]), the total learning score from the Rey Visual Design Learning Test (*RVDLT*; [30]), and the total number of trials to reach learning criteria from the Spatial Conditional Associative Learning task (*CAL*). Although the latter is not a standardized test, it has long been

Table 1
Demographic data and mean neuropsychological test scores per patient group.

	L–mTLE (n = 28)			**R–mTLE (n = 28)**		
Gender	16F/12M			20F/8M		
Years of education	13.8 (2.5)			13.4 (2.6)		
Type of surgery	6 selective/22 standard			7 selective/21 standard		
Handedness	2 left/25 right/1 mixed			4 left/24 right		
Hemi. language dominance	28 left/0 right			28 left/0 right		
Age of seizure onset (years)	12.3 (12.2)			17.0 (15.6)		
	Pre–Sx	**Post–Sx**	**Diff. Score**	**Pre–Sx**	**Post–Sx**	**Diff. Score**
Age at test (years)	37.5 (9.5)	39.9 (9.8)	n/a	38.4 (10.9)	40.7 (10.8)	n/a
Duration of epilepsy (years)	25.3 (16.1)	26.6 (16.2)	n/a	21.4 (12.0)	22.6 (12.1)	n/a
VIQ	**96.1 (11.1)**	**95.3 (10.6)**	−0.8 (6.0)	**101.6 (11.3)**	**102.5 (9.9)**	0.9 (7.8)
PIQ	100.4 (11.6)	105.3 (10.8)	4.9 (8.0)	96.8 (13.7)	100.4 (16.6)	3.7 (8.3)
RAVLTtot	44.3 (7.4)	**41.2 (7.7)**	**−3.1 (9.7)**	46.1 (6.6)	**49.2 (8.9)**	**3.1 (7.9)**
RAVLT%	**59.1 (20.2)**	**49.8 (25.6)**	**−9.3 (25.4)**	**80.9 (17.1)**	**82.2 (13.9)**	**1.3 (22.8)**
WWord	**45.4 (3.2)**	**41.7 (4.6)**	**−3.7 (5.2)**	**47.5 (1.9)**	**46.7 (4.2)**	**−0.9 (4.4)**
RVDLT	36.3 (11.0)	33.1 (11.8)	−3.3 (7.4)	35.5 (11.9)	32.8 (11.3)	−2.7 (8.6)
CAL	44.1 (20.6)	45.5 (19.1)	1.4 (29.5)	50.3 (18.7)	51.3 (21.6)	1 (24.7)
WFace	40.4 (4.7)	**41.3 (4.1)**	**0.9 (2.5)**	40.1 (5.3)	**37.4 (6.6)**	**−2.8 (5.3)**

Note: Standard deviation is between parentheses. Duration of epilepsy at postsurgery testing corresponds to the time lapse between age at seizure onset and age at surgery. Significant differences in test scores between the group with right and the group with left mTLE are shown in bold ($p < .05$ based on 2-tailed independent sample t-tests). Diff. Score = difference between postsurgery and presurgery test score. F = female, Hemi. = hemispheric, M = male, Sx = surgery.