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Intra-individual relative deficits in visual memory to lateralize seizure onset in temporal lobe epilepsy

Sloane Sheldon^a, Nahal Heydari^a, Jeffrey Cole^a, Marla J. Hamberger^a

^aDepartment of Neurology, Columbia University Medical Center, New York, New York, USA

Abstract

It is well established that presurgical neuropsychological assessment can assist in lateralizing and localizing focal epileptogenic regions. However, unlike verbal memory impairment, which is a robust and reliable finding in left temporal lobe epilepsy (LTLE) patients, nonverbal memory deficits are less consistently found among right TLE (RTLE) patients. This study aimed to determine whether memory assessment for spatial location in addition to visual content would differentiate RTLE and LTLE patients. We compared performances between 25 RTLE and 37 LTLE patients on the Wechsler Advanced Clinical Solutions-Faces (ACS-F) subscales (Faces I, Faces II, Content and Spatial), verbal-visual memory asymmetry scores, and IQ-visual memory difference scores. Results revealed no significant differences between RTLE and LTLE patients for any ACS-F memory score. By contrast, groups demonstrated significant differences in memory asymmetry scores ($p=.007$) and IQ difference scores ($p=.006$). Thus, visual memory scores in isolation failed to differentiate RTLE and LTLE groups; however, within-patient differences between visual memory and other cognitive abilities successfully differentiated the groups. These results highlight the importance of using an intra-individual model of neuropsychological assessment to identify relative weaknesses potentially associated with the epileptogenic region.

Keywords

Memory assessment; neuropsychology; non-dominant hemisphere; visual memory; temporal lobe; face memory

Address correspondences to: Sloane Sheldon, Ph.D. at The Neurological Institute, 710 West 168th Street, New York, NY 10032. U.S.A. sloane.sheldon@gmail.com.

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None of the authors have any conflict of interest to disclose.

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1. Introduction

Neuropsychological assessment plays an integral role in the presurgical evaluation of individuals with refractory, focal epilepsy, assisting in localization and lateralization of the epileptogenic region and estimating the potential risk of post-treatment cognitive decline. Accordingly, it is critical that cognitive measures and interpretive methods accurately reflect the functional integrity of specific neuroanatomical regions.

It is well established that verbal memory impairment is a robust and reliable finding among individuals with left (i.e., language dominant) temporal lobe epilepsy (TLE) [1,2]. Visual memory impairment, however, has been a less consistent finding among right (i.e., non-dominant) TLE (RTLE) patients [3,4]. It has been hypothesized that while critical verbal memory mechanisms are well localized to the left (dominant) mesial temporal region, visual memory processes are not as specifically localized to non-dominant mesial temporal structures. Additionally, it is challenging to test visual memory in its pure form, without contribution from verbal cuing to assist with visual encoding (e.g. “a big triangle with a dot in it” or “a young boy with blond hair”), thereby, engaging both dominant and non-dominant temporal regions, and both verbal and visual mnemonic processes on a presumably “visual” memory task. However, it has been suggested that while visual content can often be readily verbalized, memory for spatial location is less amenable to verbal cueing, and therefore, may be more sensitive to dysfunction associated with RTLE[5].

To test this hypothesis, we utilized the Wechsler Advanced Clinical Solutions Faces subtest (ACS-F) which assesses memory for both visual content and spatial positioning (detailed in Methods section). The goal of this retrospective analysis was to determine whether visual memory, as assessed by ACS-F, would differentiate between RTLE and LTLE. We predicted that, consistent with previous findings, groups would not differ in learning and recall of the content of the faces. By contrast, we hypothesized that RTLE patients would perform more poorly than LTLE patients in learning and recall of spatial positions of the faces on a grid, due to its purer assessment of visuospatial functioning (i.e., separate from visual content).

Additionally, in keeping with intra-individual models of neuropsychological assessment, we examined the utility of intra-individual verbal-visual memory performance differences. Although most clinicians interpret test results in this context conceptually, we applied a straightforward, empirical approach, calculating asymmetry scores between verbal and visual memory performance. We hypothesized that these memory asymmetry scores would differentiate RTLE and LTLE patients.

2. Methods

2.1 Participants

Sixty-two adults with RTLE (n=25) or LTLE (n=37) were included in this retrospective analysis. Table 1 provides patient characteristics and demographic information. Notably, the two groups did not differ significantly for any pertinent demographic factor. Inclusion criteria were as follows: (1) a diagnosis of RTLE or LTLE made by an epileptologist via a neurological work-up, including electroencephalography; (2) age $\geq$ 18 years; (3) native

English speaker or learned English by age 5; (4) FSIQ > 70 and (5) left hemisphere language dominance, identified by Wada procedure (n=21), post-ictal language assessment and right-handed (n= 24), cognitive performance consistent with left hemisphere language dominance and right-handed (n=12), left-handed but post-ictal language assessment and cognitive functioning consistent with left hemisphere language dominance (n=4), or fMRI (n=1).

2.2 Procedures

All patients completed measures of visual memory, verbal memory, and overall intellectual functioning during a comprehensive neuropsychological evaluation as part of their clinical care. This research was approved by the Columbia University Medical Center's Institutional Review Board and all patients provided written informed consent.

2.3 Measures

2.3.1 Visual Memory—ACS-F assesses learning and recall of novel faces and their locations on a grid [7]. The examinee is presented with a page of ten faces placed on a 4×4 grid. Following a 10-second exposure, the page is removed, and the examinee is asked to select the previously presented ten faces out of 20 possible face cards and place them in the previously presented location on a blank grid. This procedure is repeated with the same stimulus page over four learning trials to obtain an immediate recall score. After a 10–15-minute delay, the examinee is again presented with a blank memory grid and the 20 face cards, and is asked to place the previously presented 10 faces in the correct spatial position on the grid, resulting in a delayed recall score. The full set of scores include 1) Faces I: immediate recall of *both* the content of the faces and the spatial positioning of faces over the four learning trials, 2) Faces II: delayed recall of *both* the content and the spatial positioning of faces, 3) Content: accurate recall of the target faces across immediate and delayed recall trials, regardless of their spatial positioning, and 4) Spatial: accurate recall of the spatial positioning of the faces on a grid across immediate and delayed recall trials, regardless of the content. Of note, as the delayed recall (Faces II) score is an aggregate memory score for both the spatial positioning and content, we did not hypothesize how these scores in isolation would differentiate between RTLE and LTLE groups.

2.3.2 Verbal Memory—The Rey Auditory Verbal Learning Test (RAVLT) [8] was used to measure rote verbal memory. This test includes 5 learning trials of a list of 15 verbally presented words, followed by a learning trial of a distractor list, immediately before a short-delay recall trial, and delayed recall after a 30-minute delay. We utilized delayed recall scores in our analyses, as we believe this aspect of performance is most meaningful with regard to function.

2.4 Statistical Analysis

One-way multivariate analysis of variance (MANOVA) and chi-square analyses were used to assess demographic differences between RTLE and LTLE groups. MANOVA was also used to compare RTLE and LTLE group performances on the four ACS-F subscales, using scaled scores. Memory asymmetry scores were calculated by converting RAVLT verbal memory scores to scaled scores and then subtracting ACS-F delayed recall (Faces II) scaled score

from the verbal memory scaled score. Independent samples t-test was used to compare asymmetry scores between the groups.

3. Results

There were no significant differences between the RTLE and LTLE patients for Faces I [$F(1,60)=0.92$, $p=.34$], Faces II [$F(1,60)=2.92$, $p=.09$], Content [$F(1,60)=2.93$, $p=.09$] or Spatial [$F(1,60)=0.03$, $p=.88$] scores. By contrast, there was a significant difference in memory asymmetry scores for RTLE ($M=2.28$, $SD=4.38$) and LTLE ($M=-0.38$, $SD=3.08$) groups with a medium to large effect size, $t(60) = -2.81$, $p=.007$, $d=0.70$. Of note, on average, the RTLE group scored nearly a standard deviation lower on the visual memory task than they did on the verbal memory task.

We completed further exploratory analyses on difference scores between visual memory and overall level of intellectual functioning (i.e., FSIQ) to determine if visual memory as a relative cognitive weakness – not only memory asymmetries – would differentiate RTLE and LTLE patients. Difference scores were calculated by subtracting ACS-F delayed recall (Faces II) scaled scores from FSIQ scores (after transformation to scaled scores). Results showed a significant difference in these difference scores for RTLE ($M=3.48$, $SD=4.93$) versus LTLE ($M=0.40$, $SD=3.51$) with a medium to large effect size, $t(60)=-2.78$, $p=.006$, $d=0.72$. Here the RTLE group, on average, scored a standard deviation worse on visual memory compared to their overall intellectual functioning.

4. Discussion

Numerous measures of visual memory have been tried, without success, to identify non-dominant hemisphere dysfunction. As prior research has suggested that memory for spatial location, rather than visual content, might be more focally supported by the right temporal region,⁵ we speculated that spatial memory performance would differentiate RTLE and LTLE patients. However, at odds with our hypothesis, we found that neither “spatial” nor “content” memory scores differentiated RTLE and LTLE groups. It is possible that even for spatial location, patients utilized verbal cuing to encode the positioning on the grid (e.g. “two faces in the top row, three in the second row”), thereby relying partly on dominant hemisphere processing.

We also considered the possibility that visual weaknesses associated with RTLE are more subtle than the established verbal memory deficits found in LTLE. Therefore, while visual memory performances on their own did not inform lateralization, we investigated the utility of memory asymmetry scores in this regard. Consistent with our hypothesis, verbal versus visual memory asymmetry scores differentiated between RTLE and LTLE.

These findings add to existing practices of using asymmetry scores with epilepsy populations. For Wada procedures, memory asymmetries between the left and right hemisphere – compared to unilateral memory scores in isolation – are stronger predictors of post temporal lobe resection memory functioning [9,10]. Additionally, asymmetries between auditory and visual naming performances assist in localizing abnormalities to the anterior versus posterior temporal region[11]. With other neurological populations, such as dementia,

asymmetry scores – but not individual scores – have been shown to distinguish between preclinical and at-risk Alzheimer’s disease (AD) populations from healthy controls [12,13], and help better explain heterogeneity within AD [14,15].

Further analysis indicated that differences between visual memory scores and FSIQ also differentiated between RTLE and LTLE, underscoring that a single cognitive performance is best interpreted within the context of other cognitive abilities. Overall, the RTLE group scored close to a standard deviation lower on visual memory than both verbal memory and intellectual functioning, highlighting the clinical relevance of these findings. These results emphasize the importance of a comprehensive neuropsychological evaluation, even when the referral question is limited to concern in one particular domain (i.e. visual memory). This aligns with the common practice of clinical neuropsychology in considering the individual’s full cognitive profile in order to understand the meaning of individual scores, understanding that without full knowledge of a patient’s intellectual and cognitive functioning, clinicians may reach false conclusions.

Regarding limitations, the sample size did not allow for examination of the influence of potentially relevant clinical factors (e.g., age of seizure onset and presence of mesial temporal sclerosis) on memory performances within the lateralized groups. As these factors are known to affect cognitive functioning, findings may have been more robust in particular subgroups. Furthermore, our sample was not balanced for lateralization of epileptogenic zone, with more individuals with LTLE compared to RTLE, reflective of our clinical population. Finally, we unfortunately did not have post-operative data for the majority of our sample, which would have allowed us to determine the sensitivity of these tests in predicting post-operative cognitive changes.

There were some limitations regarding the tests, as well. The structure of the test’s subscales may have contributed to the poor lateralization of ACS-F. Specifically, the “content” and “spatial” scores are calculated by combining immediate and delayed memory trials, without providing separate “content” and “spatial” delayed recall scores. Perhaps a true spatial memory score, separate from content memory, would better lateralize RTLE versus LTLE. Lastly, the memory tests utilized were not co-normed, and therefore, differences in normative samples may have influenced the results. Ideally, all tests administered would be co-normed to allow for unbiased comparisons; however, this is often a challenge in a clinical context.

5. Conclusion

In conclusion, the current findings suggest that neither memory for content of novel faces nor spatial placement, as measured by the ACS-F, is effective in lateralizing cognitive dysfunction in an epilepsy population when analyzed in isolation. However, examining visual memory within the context of the patient’s other cognitive abilities with direct contrast scores is more consistent with clinical practice and more effective. These results emphasize the importance of an intra-individual approach to assessment in identifying a circumscribed, relative deficit associated with a focal epileptogenic region.

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References

- [1]. Alessio A, Bonilha L, Rorden C, Kobayashi E, Min LL, Damasceno BP, et al. Memory and language impairments and their relationships to hippocampal and perirhinal cortex damage in patients with medial temporal lobe epilepsy. *Epilepsy & Behavior* 2006;8:593–600. 10.1016/j.yebeh.2006.01.007. [PubMed: 16517214]
- [2]. Davies KG, Bell BD, Bush AJ, Wyler AR. Prediction of Verbal Memory Loss in Individuals After Anterior Temporal Lobectomy. *Epilepsia* 1998;39:820–8. 10.1111/j.1528-1157.1998.tb01175.x. [PubMed: 9701371]
- [3]. Barr W, Morrison C, Zaroff C, Devinsky O. Use of the Brief Visuospatial Memory Test—Revised (BVM-T-R) in neuropsychological evaluation of epilepsy surgery candidates. *Epilepsy & Behavior* 2004;5:175–9. 10.1016/j.yebeh.2003.12.010. [PubMed: 15123018]
- [4]. BARR WB, CHELUNE GJ, HERMANN BP, LORING DW, PERRINE K, STRAUSS E, et al. The use of figural reproduction tests as measures of nonverbal memory in epilepsy surgery candidates. *Journal of the International Neuropsychological Society* 1997;3:435–43. 10.1017/S1355617797004359. [PubMed: 9322402]
- [5]. Breier JJ, Plenger PM, Castillo R, Fuchs K, Wheless JW, Thomas AB, et al. Effects of temporal lobe epilepsy on spatial and figural aspects of memory for a complex geometric figure. *Journal of the International Neuropsychological Society* 1996;2:535–40. 10.1017/S1355617700001703. [PubMed: 9375157]
- [6]. Wechsler D Wechsler adult intelligence scale—Fourth Edition (WAIS—IV) Fourth Edition. San Antonio : NCS Pearson; 2008.
- [7]. Wechsler D Advanced clinical solutions for WAIS-IV and WMS-IV: Administration and scoring manual San Antonio: The Psychological Corporation; 2009.
- [8]. Schmidt M Rey auditory verbal learning test: A handbook Los Angeles: Western Psychological Services; 1996.
- [9]. Loring DW, Meador KJ, Lee GP, King DW, Nichols ME, Park YD, et al. Wada memory asymmetries predict verbal memory decline after anterior temporal lobectomy. *Neurology* 1995;45:1329–33. 10.1212/WNL.45.7.1329. [PubMed: 7617192]
- [10]. Wyllie E, Naugel R, Awad I, Chelune G, Lüders H, Dinner D, et al. Intracarotid Amobarbital Procedure: I. Prediction of Decreased Modality-Specific Memory Scores After Temporal Lobectomy. *Epilepsia* 1991;32:857–64. 10.1111/j.1528-1157.1991.tb05542.x. [PubMed: 1743157]
- [11]. HAMBERGER MJ, SEIDEL WT. Localization of cortical dysfunction based on auditory and visual naming performance. *Journal of the International Neuropsychological Society* 2009;15:529–35. 10.1017/S1355617709090754. [PubMed: 19573271]
- [12]. HOUSTON WS, DELIS DC, LANSING A, JACOBSON MW, COBELL KR, SALMON DP, et al. Executive function asymmetry in older adults genetically at-risk for Alzheimer's disease: Verbal versus design fluency. *Journal of the International Neuropsychological Society* 2005;11 10.1017/S1355617705051015.
- [13]. Jacobson MW, Delis DC, Bondi MW, Salmon DP. Do neuropsychological tests detect preclinical Alzheimer's disease: Individual-test versus cognitive-discrepancy score analyses. *Neuropsychology* 2002;16:132–9. 10.1037/0894-4105.16.2.132. [PubMed: 11949704]
- [14]. Demadura T, Delis DC, Jacobson M, Salmon D. Do Subgroups of Patients With Alzheimers Disease Exhibit Asymmetric Deficits on Memory Tests? *Journal of Clinical and Experimental Neuropsychology* 2001;23:164–71. 10.1076/jcen.23.2.164.1207. [PubMed: 11309670]
- [15]. FINTON MJ, LUCAS JA, RIPPETH JD, BOHAC DL, SMITH GE, IVNIK RJ, et al. Cognitive asymmetries associated with apolipoprotein E genotype in patients with Alzheimer's disease. *Journal of the International Neuropsychological Society* 2003;9:751–9. 10.1017/S1355617703950089. [PubMed: 12901781]

Highlights

- Memory for content and spatial positioning of novel faces in isolation fail to distinguish between right and left temporal lobe epilepsy adult patients.
- However, verbal versus visual memory asymmetry scores differentiate the groups.
- Additionally, overall IQ versus visual memory difference scores also distinguish between right and left temporal lobe epilepsy groups.

Fig. 1. RTLE and LTLE Memory and Contrast Score

Mean memory performances of left temporal lobe (LTLE) and right temporal lobe (RTLE) patients. Memory asymmetry = verbal memory performance-visual memory performance; IQ difference = FSIQ-visual memory performance. * $p < .01$.

Table 1.

Demographic characteristics for patients with LTLE and RTLE

Variable	Left TLE (n=37)	Right TLE (n=25)	P-value
Sex, <i>n</i> (%)	Male = 21 (56.8%) Female = 16 (43.2%)	Male = 14 (56.0%) Female = 11 (44.0%)	.95
Age (years), <i>m</i> (<i>SD</i>)	41.19 (15.68)	41.32 (15.30)	.97
Handedness, <i>n</i> (%)	Right= 32 (86.5%) Left= 4 (10.8%) Ambidextrous= 1 (2.7%)	Right= 22 (88.0%) Left= 3 (12.0%) Ambidextrous= 0 (0.0%)	.71
Onset age (years), <i>m</i> (<i>SD</i>)	26.17 (16.28)	25.62 (17.52)	.90
Education (years), <i>m</i> (<i>SD</i>)	15.14 (2.60)	15.92 (6.89)	.53
FSIQ, <i>m</i> (<i>SD</i>)	99.32 (14.47)	104.50 (21.30)	.25
MTS	Definite= 6 (16.2%) Non-Definite= 31 (83.8%)	Definite= 5 (20.0%) Non-Definite= 20 (80.0%)	.88

FSIQ=Full Scale IQ based on the WAIS-IV[6]; TLE=temporal lobe epilepsy; MTS=mesial temporal sclerosis