A critical evaluation of the lateralizing significance of material-specific memory deficits in patients with mesial temporal lobe epilepsy with hippocampal sclerosis

Malcolm K. Jeyaraj [1], Ramshekhar N. Menon [1], Sunitha Justus, Aley Alexander, P. Sankara Sarma, Kurupath Radhakrishnan *

R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India

ARTICLE INFO

ABSTRACT

To critically assess the value of material-specific memory deficits in lateralizing temporal lobe dysfunction preoperatively, we compared the neuropsychological data of 50 consecutive patients with unilateral mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS; right: 31, left: 19) with those of 50 age- and education-matched healthy control subjects. On case-control comparison, both the subcohorts with left and right MTLE-HS performed poorly on intelligence tests, in addition to individual memory tests. However, comparison of the verbal and visual memory functions between subcohorts with right and left MTLE-HS revealed that learning trials and delayed word list recall were the only tests that hypothesized left temporal lobe dysfunction. We conclude that material-specific memory deficits are largely test driven, but there is a lateralizing role for task-specific deficits in left MTLE-HS. Although neuropsychological data help to define baseline neuropsychological impairment, caution should be exercised in interpreting the lateralizing value of material-specific memory deficits prior to surgery.

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1. Introduction

A majority of patients with mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) tend to be resistant to antiepileptic drugs (AED) [1]. Anterior temporal lobectomy (ATL) is the standard treatment for AED-resistant MTLE-HS, resulting in seizure remission in over two-thirds of patients [2,3]. Presurgical evaluation strategies in patients with MTLE-HS aim to identify those with high chance of post-ATL seizure freedom and low risk of neuropsychological deficits. While concordance of the interictal and ictal electroencephalographic (EEG) abnormalities to the magnetic response imaging (MRI)-identified HS is a well-established strong predictor of favorable post-ATL seizure outcome [2–4], the value of neuropsychological tests in lateralizing temporal lobe dysfunction preoperatively and in predicting post-ATL memory outcome is less certain [5–8].

The material-specific memory hypothesis implies that learning of verbal materials is dependent more on the left (dominant) than the right (nondominant) mesial temporal structures, whereas the capacity to learn visual materials relies more on the right than the left mesial

temporal structures [9]. This concept, proposed more than fifty years ago based upon postoperative memory deficits, still forms a cornerstone of presurgical decision-making. However, only a comparatively small proportion of studies have strongly agreed with the lateralized model of material-specific memory deficits, and in the majority of studies, the material specificity hypothesis has only been weakly supported or not supported at all, especially with regard to lateralization to right hemisphere [5–8]. The reasons for these inconsistent results could be many. First, patients with temporal lobe epilepsy (TLE) are heterogeneous with regard to the extent and nature of pathological substrates, demographic characteristics, and epilepsy-related variables such as age at onset/duration of the epilepsy syndrome, interictal epileptiform discharges (IED), seizure burden, AED usage and psychiatric comorbidities [1,10,11]. Second, neuropsychological tests utilized have often been too varied and restrictive in their objectives and thereby overlooked far more diffuse impairments [12,13]. Furthermore, most of the tests employed have not been validated for the populations on whom they have been administered, and tests validated on patient populations with large cerebral lesions such as infarctions and neoplasms are often less sensitive to the small substrates such as HS associated with focal epilepsy [14]. Third, extrapolating the hypothesis based on postoperative observations to presurgical patients has limitations because while the resection beyond the diseased hippocampus in ATL could exaggerate the neuropsychological dysfunction in postoperative patients, abolition of IEDs and seizures and reduction in AEDs following ATL could have a favorable influence.

* Corresponding author at: Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum 695 011, Kerala, India. Fax: +91 471 2446433.
E-mail address: krk@sctimst.ac.in (K. Radhakrishnan).
[1] Both the first and second authors have made equal contributions.

With this background, we asked the following question: Prior to ATL, do verbal and visual memory deficits help to conclusively lateralize left and right temporal lobe dysfunction? We hypothesized that preoperatively patients with left MTLE-HS would have lower scores on verbal memory tests, whereas patients with right MTLE-HS would have lower scores on visual memory tests. To test this hypothesis, we assembled a uniform cohort of patients with unilateral MTLE-HS, administered a comprehensive battery of tests to assess verbal and visual learning and recall, and compared their results with those of healthy control subjects. We also compared the memory test results of the subcohorts with left and right MTLE-HS.

2. Methods

2.1. Study subjects

For this prospective study, we recruited 50 consecutive patients who underwent presurgical evaluation at the R. Madhavan Nayar Center for Comprehensive Epilepsy Care, Trivandrum, India, from March through September 2011 and fulfilled the following criteria: 1) right hand dominance, 2) full-scale intelligence quotient (IQ) ≥70, 3) MRI findings consistent with unilateral HS defined as the presence of both volume loss and T2 hyperintensity of the hippocampus on visual inspection and no other lesions, and 4) all seizures and ≥75% of IED ascertained by long-term video-EEG monitoring using scalp/sphenoidal electrodes verified as originating from the side of HS. We have described our MRI and long-term video-EEG protocols in detail elsewhere [15,16]. The handedness was determined by the Edinburgh Handedness Inventory [17]. We excluded patients who had initial precipitating injury like encephalitis, meningitis or head trauma, early age of onset of habitual seizures without a latent period following initial precipitating injury, auditory or vertiginous auras, early head version and facial jerks, secondary generalization of more than 25% of seizures, and midtemporal or posterior temporal IED because these features were indicative of neocortical temporal lobe epilepsy or temporal plus syndromes [18,19]. We also excluded those with active psychosis that interfered with the neuropsychological examination. We used a detailed seizure scoring system to define the seizure burden [20]. The diagnosis of unilateral MTLE-HS was concluded after a thorough discussion in the multidisciplinary patient management conference based upon the concordance between clinical, EEG, and MRI findings. We selected 50 healthy right-handed subjects from the relatives of the patients attending the general neurology clinic and hospital staff. The controls were matched with patients with respect to age and education.

2.2. Neuropsychological testing

All the patients and controls were administered a comprehensive battery of neuropsychological tests by a trained psychologist (SJ) and were supervised by a senior neuropsychologist (AA). The algorithm of neuropsychological assessment and the tests administered are provided in Fig. 1. The testing of patients was done during the video-EEG monitoring either prior to onset of seizures or at least 48 h after the last seizure. Following the intelligence quotient (IQ) assessment, a questionnaire was administered to rule out any psychiatric illnesses that could interfere with the administration or interpretation of the neuropsychological tests before proceeding with the verbal and visual memory function assessments. The testing methods, interpretations, and references are provided in Appendix A.

2.3. Statistical methods

Statistical analyses were performed using SPSS statistics 17.0 (Chicago, IL, USA). We summarized the quantitative data as mean ± standard deviation (SD) and categorical data as percentages (%). To examine the difference in the neuropsychological data between different groups of subjects, we used the following comparisons: between percentages of subjects with test scores less than 2 SDs of the normative scores and between group means ± 2 SDs, using receiver–operator curves (ROCs). While Fisher's exact tests were used to compare categorical data, Mann–Whitney U tests were used to compare the scores between subcohorts with right and left MTLE-HS. A P value of <0.05 was considered significant. The discriminating capacity of the variables that were statistically significantly different between the subcohorts with left and right MTLE-HS was subjected to ROC analysis, with lower scores being taken as supportive of left lateralization. The area under the ROC curve and Youden's index were used to derive the optimal cutoff levels to lateralize.

3. Results

3.1. Demographic and clinical characteristics

The 50 patients with MTLE-HS (27 females, 23 males) consisted of 31 with right HS and 19 with left HS. Their mean age at the time of evaluation was 27.4 ± 12.4 years and the mean duration of epilepsy prior to evaluation was 15.0 ± 8.4 years. We have provided the characteristics of patients in Table 1. The subcohorts with right and left MTLE-HS did not differ from each other in terms of age at evaluation, age of onset of seizures, duration of epilepsy, average seizure score,
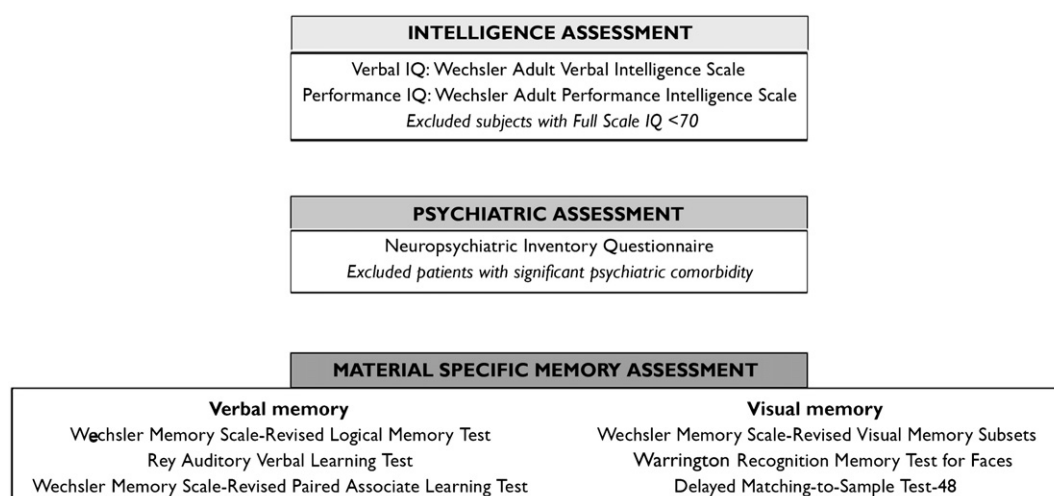
INTELLIGENCE ASSESSMENT

Verbal IQ: Wechsler Adult Verbal Intelligence Scale
Performance IQ: Wechsler Adult Performance Intelligence Scale
Excluded subjects with Full Scale IQ <70

PSYCHIATRIC ASSESSMENT

Neuropsychiatric Inventory Questionnaire
Excluded patients with significant psychiatric comorbidity

MATERIAL SPECIFIC MEMORY ASSESSMENT

Verbal memory	Visual memory
Wechsler Memory Scale-Revised Logical Memory Test	Wechsler Memory Scale-Revised Visual Memory Subsets
Rey Auditory Verbal Learning Test	Warrington Recognition Memory Test for Faces
Wechsler Memory Scale-Revised Paired Associate Learning Test	Delayed Matching-to-Sample Test-48

Fig. 1. Neuropsychological testing algorithm and tests used.