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Atypical neuropsychological profiles and cognitive outcome in mesial temporal lobe epilepsy

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ABSTRACT

Patients with left mesial temporal lobe epilepsy (MTLE) have deficits in verbal memory processes, while patients with right MTLE have visuospatial memory impairment. However, atypical cognitive phenotypes among patients with MTLE may occur. In this study, we analyzed preoperative memory deficits in a cohort of 426 right-handed patients with unilateral MTLE. We also evaluated the cognitive outcome after anterior temporal lobectomy (ATL) of patients with atypical profiles in comparison with those with typical memory profile. We found that 25% of our patients had a typical cognitive profile, with verbal memory deficits associated with left side hippocampal sclerosis (HS) and visuospatial memory deficits associated with right side HS. However, 75% of our patients had atypical memory profiles. Despite these atypical profiles, patients submitted to right ATL had no significant cognitive deficit after surgery. In patients submitted to left ATL, the higher the presurgical scores on verbal memory and naming tests, the higher the cognitive decline after surgery.

1. Introduction

Anterior temporal lobectomy (ATL) is the most common surgical procedure used to treat mesial temporal lobe epilepsy associated with hippocampal sclerosis (MTLE-HS), the most common epilepsy syndrome surgically treated in adolescents and adults [1]. The rate of seizure freedom is 60–70%, and the prevalence of neurological complications is low and mostly mild or transient [1]. It has been shown that unilateral resection of mesial temporal structures can result in reduced memory function in patients with MTLE-HS. A recent systematic review reported that 16 to 80% of patients submitted to left ATL may have significant additional verbal memory deficits after surgery. On the other hand, patients submitted to right ATL have a 3 to 42% risk of significant visual memory loss [2]. Most studies reporting cognitive outcome in patients with MTLE-HS group all patients together. However, even patients with a relatively uniform epilepsy syndrome, such as unilateral MTLE-HS, may have differences on cognitive performance before surgery. For example, studies have shown that patients with unilateral left MTLE-HS may have normal memory scores before surgery, which could significantly impact on cognitive outcome after surgery [3]. In addition, few studies have reported cognitive outcome in patients with discordant or bilateral neuropsychological findings. As the presurgical evaluation team needs to discuss the risk of cognitive deficits with their patients, studies are needed to identify those with a higher risk of memory loss according to specific neuropsychological profiles.

Here, we analyzed the neuropsychological profile of 426 right-handed patients with unilateral MTLE-HS. Four groups of patients with MTLE-HS with atypical memory profiles were identified. These "atypical" memory profiles were as follows: (1) bilateral memory deficits despite unilateral MTLE, (2) normal memory performance, (3) memory deficit contralateral to the side of MTLE-HS, and (4) severe memory impairment associated with low IQ. We also report the cognitive outcome in each memory profile subgroup and compared with those with a typical memory profile.

2. Patients and methods

2.1. Patient selection

The study was conducted at the Ribeirao Preto Epilepsy Center, University of São Paulo, Brazil. We retrospectively reviewed charts of 984 patients submitted to epilepsy surgery from 1996 to 2010. Patients satisfying the following inclusion criteria were selected to participate: (1) have drug-refractory TLE with unilateral MTLE-HS and

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were submitted to anterior temporal lobectomy; (2) aged 18 years or older at evaluation; (3) have IQ scores higher than 60; (4) have histopathological evidence of hippocampal sclerosis, with neuronal loss in CA1, CA3, and prosubiculum and relative sparing of CA2; (5) right-handed according to the laterality questionnaire [4]; and (6) were submitted to both presurgical neuropsychological assessment and postsurgical neuropsychological assessment (Fig. 1). We excluded patients with temporal or extratemporal lesions other than HS and those patients with bilateral HS based on the review of preoperative MRIs by experienced radiologists.

2.2. Neuropsychological assessment

The neuropsychological evaluation in our center comprises a standard battery of psychometric tests that assesses various cognitive functions, such as attention, executive functions, memory, visuospatial processing, language, and intellectual abilities. For the purposes of this study, we specifically selected the ones that are described below. For IQ evaluation, we used the Wechsler Adult Intelligence Scale Revised (WAIS-R) [5] or the 3rd edition (WAIS-III) [6,7]. For the assessment of cognitive functions mediated by the dominant temporal lobe, we chose the Logical Memory Delayed Recall (LM-DR) from Wechsler Memory Scale Revised (WMS-R) [8] and the Rey Auditory Verbal Learning Test Delayed Recall (RAVLT-DR) [8–10] to assess verbal memory; and the Boston Naming Test (BNT) from Boston Diagnostic Aphasia Examination [8,10,11] to assess naming abilities. For the assessment of cognitive functions mediated by the non-dominant temporal lobe, we chose the Visual Reproduction Delayed Recall (VR-DR) from WMS-R [8], the Rey Visual Design Learning Test Delayed Recall (RVDLT-DR) [9,10], and Delayed Recall of Rey–Osterrieth Complex Figure (RF-DR) [12–14].

2.3. Classification of atypical neuropsychological profiles

Typically, patients with TLE on the dominant hemisphere have verbal memory and language (naming) impairment [15–17], while patients with TLE on the non-dominant hemisphere have visual memory impairment [18]. We focused on verbal memory tests (LM-DR and RAVLT-DR) for the dominant hemisphere and visual memory tests (VR-DR and RF-DR) for the non-dominant hemisphere as representative of temporal lobe functions [10,19].

Each psychometric test described above was analyzed according to its normative data. As indicative of impairment on dominant temporal function, it was required that a patient had to have a score of two standard deviations below the norm in one test or one standard deviation below the norm in both tests (LM-DR and RAVLT-DR). To indicate impairment on non-dominant temporal function, it was required that a patient had to have a score of two standard deviations below the norm in one test or one standard deviation below the norm in both tests (VR-DR and RF-DR).

2.4. Group classification

Considering that we included only right-handed patients, the results obtained on neuropsychological evaluation before surgery, and the operated side (left-dominant hemisphere or right-non-dominant hemisphere), the groups were divided as follows: IPSILATERAL (cognitive deficits compatible with the side of HS), NORMAL (without functional deficits despite the unilateral HS), BITEMPORAL (involvement of dominant and non-dominant hemispheres, regardless of the side of unilateral HS), Global Cognitive Impairment — GCI (severe involvement of dominant and non-dominant memory functions associated with an IQ lower than 70), and CONTRALATERAL (cognitive deficits contralateral to the side of EH).

To assess cognitive outcome after surgery, we performed another neuropsychological evaluation one year after surgery, with the same battery performed before the surgery. All patients were interviewed regarding any events that could affect cognition between surgery and the neuropsychological examination.

2.5. Presurgical evaluation protocol

2.5.1. Video-EEG monitoring

At least two events similar to the patients' habitual seizures were recorded. If no seizure was registered in the first 24 h, antiepileptic drugs (AEDs) were progressively tapered until seizures were recorded. The laterality of ictal onset zone was independently assessed on ictal video-EEG by two investigators [20,21].

2.5.2. Neuroimaging

Most patients were scanned in a 1.5-T magnet (Magnetom Vision; Siemens AG, Erlangen, Germany) MRI machine, with 25-mT gradient coils of circular polarization. Since 2007, patients underwent high-resolution MRI in a 3-T scanner eight-channel head coil with a similar acquisition protocol. The sequences performed were a gradient echo 3D T1-weighted, axial T2, coronal and axial FLAIR (fluid attenuation

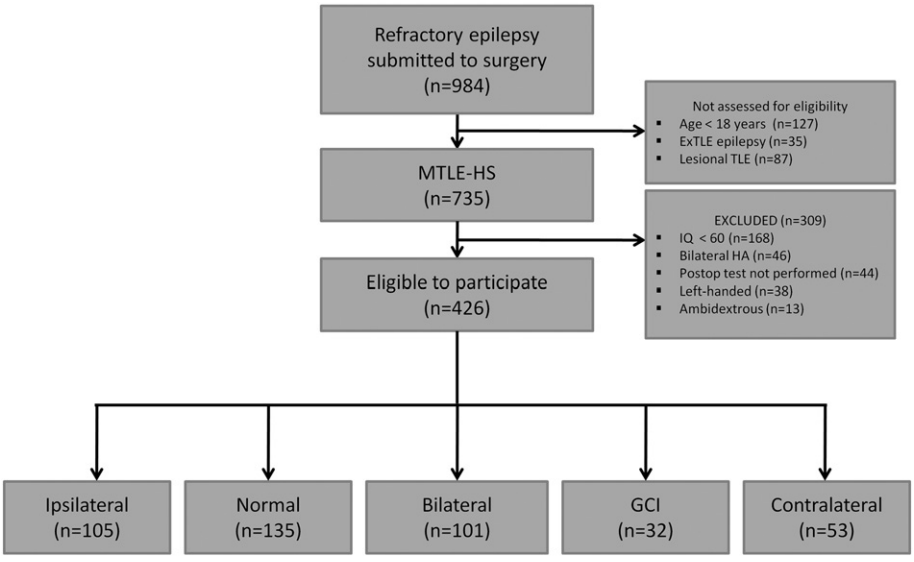

Fig. 1. The flow diagram shows the process of recruiting study participants.