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Decline in word-finding: The objective cognitive finding most relevant to patients after mesial temporal lobe epilepsy surgery

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ABSTRACT

Purpose: The purpose of this study was to investigate the following: i) the objective impairment in neuropsychological tests that were associated with the subjective perception of cognitive function decline in Brazilian patients who underwent mesial temporal lobe epilepsy (MTLE) surgery and ii) the predictive variables for those impaired objective neuropsychological tests.
Methods: Forty-eight adults with MTLE (27 right HS and 23 male) were divided according to their perception of changes (Decline or No-decline) of cognitive function domain of the QOLIE-31 questionnaire applied before and 1 year after the ATL. The mean (SD) of changes in the raw score difference of the neuropsychological tests before and after the ATL was compared between Decline and No-decline groups. Receiver Operating Characteristic curves, sensitivity, specificity, and predictive values were used to assess the optimum cutoff points of neuropsychological test score changes to predict patient-reported subjective cognitive decline.
Key findings: Six (12.5%) patients reported a perception of cognitive function decline after ATL. Among the 25 cognitive tests analyzed, only changes in the Boston Naming Test (BNT) were associated with subjective cognitive decline reported by patients. A reduction of ≥8 points in the raw score of BNT after surgery had 91% of sensitivity and 45% specificity for predicting subjective perception of cognitive function decline by the patient. Left side surgery and age older than 40 years were more associated with an important BNT reduction with overall accuracy of 91.7%, 95% predictive ability for no impairment, and 75% for impairment of cognitive function.
Significance: Impairment in word-finding seems to be the objective cognitive finding most relevant to Brazilian patients after mesial temporal lobe epilepsy surgery. Similar to American patients, the side of surgery and age are good predictors for no decline in the BNT, but shows a lower accuracy to predict its decline. If replicated in other populations, the results may have wider implications for the surgical management of patients with drug-resistant MTLE.

1. Introduction

Mesial temporal lobe epilepsy (MTLE-HS) is the most common form of surgically remediable drug-resistant epilepsy [1–3]. Diagnostic and therapeutic procedures in epilepsy surgery improved significantly in the last decades, and anterior temporal lobectomy (ATL) has become a safe and effective treatment for seizure control in patients with drug-resistant MTLE [1–3].

The small incidence of motor, psychiatric, and cognitive incapacitating sequelae related to ATL is largely counterbalanced by the quality of life (QOL) improvement reported by nonrandomized [1] and randomized–controlled studies [2,3]. A systematic review [4] showed that objective cognitive deficits detected by neuropsychological tests particularly with regard to verbal memory and language have been

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well-documented for left side and less frequently for right side ATL. Decline of IQ, executive function, and attention are uncommon after temporal lobe epilepsy surgery [4].

Emphasis on patient-centered outcome requires assessment of clinically important changes in individual patients' QOL after ATL [5,6] and a similar approach can also be applied to patients' perception of cognitive changes after surgery [7]. Interestingly, some studies demonstrated a poor correlation between the subjective perception of cognitive function changes after ATL and the objective changes demonstrated by neuropsychological tests in American and Canadian patients [8–10].

Here, we investigated: i) the objective impairment in neuropsychological tests that were associated with the subjective perception of cognitive function decline in Brazilian patients who underwent mesial temporal lobe epilepsy (MTLE) surgery and ii) the predictive variables for those impaired objective neuropsychological tests.

2. Methods

2.1. Patients and presurgical evaluation

Forty-eight consecutive adult patients with refractory MTLE-HS who underwent ATL were enrolled prospectively during their presurgical evaluation using a predetermined research protocol approved by our Research Ethics Committee (registration 365FR30969). Informed consent was obtained from all patients. The presurgical and postsurgical evaluations were done by the same team (neurosurgeon, neurologists, neurophysiologist, psychiatrist, neuropsychologist and nurse) at the Centro de Epilepsia de Santa Catarina (CEPESC) between October 2008 and November 2013. Drug-resistance was defined as failure to respond to at least 2 antiepileptic drugs in adequate trials, and seizures impairing awareness occurring at least once a month in the last 12 months. All patients had complete medical history, seizure semiology, neurological examination, psychiatric and neuropsychological evaluation, interictal and ictal video-EEG analysis, and MRI results consistent with MTLE-HS (see below) [5,11–18]. No patients underwent VEEG recording with semi-invasive or invasive electrodes.

The clinical picture consisted typical temporal lobe epilepsy with impaired awareness associated or not with epigastric, autonomic, or psychic auras [19]. The EEG showed focal unilateral or bilateral interictal slowing, spikes, and sharp waves over the anterior and mesial temporal regions on interictal scalp EEG. Unilateral hippocampal atrophy was observed by visual inspection of MRI (1.5 T) on T1 and FLAIR and increased hippocampal signal on T2 MRI and FLAIR sequences. Histopathology performed in 38 patients confirmed hippocampus sclerosis. Exclusion criteria were features that put the diagnosis of MTLE-HS in doubt: i) extrahippocampal lesions; ii) focal motor or sensory abnormalities on physical examination; iii) bilateral synchronous or extratemporal interictal spikes; or iv) impaired neurodevelopment. The presurgical clinical and demographic variables analyzed were gender, age, age at epilepsy onset, years of education, positive history of initial precipitating injury, epilepsy duration until surgery, monthly frequency of seizures impairing awareness, number and type of AEDs used at the time of surgery, and side of hippocampal sclerosis.

Video-EEG (VEEG) recording (Bio-logic, System Corp.) with scalp electrodes applied the international 10/20 system associated with temporal 10/10 system. Visual interictal analysis was assessed in a one-hour sleep sample (between 5:00 and 7:00 a.m.) and one-hour sample during wakefulness (between 8:00 and 10:00 a.m.) in the first, second, and third days of VEEG monitoring. Patients had at least one habitual seizure during VEEG investigation, and the electrographic findings were suggestive of ictal zone onset localized in the temporal lobe.

Presurgical diagnosis of psychiatric comorbidities associated with epilepsy was done by a psychiatrist (R.G.) with expertise in epilepsy as previously described [5,16,18,20]. Axis I disorders were diagnosed according to Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders 4th edition – DSM-IV – Axis I Disorders, Clinical Version (SCID I). Patients were allocated into the following major diagnostic groups: Axis I: 0 = no diagnosis; 1 = anxiety disorders; and 2 = depressive disorders. Two patients with postictal psychosis and two with dysthymia were classified as "no diagnosis". According to Axis II, the diagnosis of patients was defined as: 0 = no diagnosis; 1 = personality disorders or personality disorders traits. Axis II Personality Disorders (PD) were classified according to DSM-IV. We also considered an epilepsy-specific PD termed Gastaut–Geschwind syndrome (GGS), which was classified as "personality disorders" into Axis II of DSM-IV.

2.2. Neuropsychological and quality of life testing

The neuropsychological assessments were done by a neuropsychologist (M.E.R.O.T.) blinded to all clinical, neurosurgical, and laboratory variables. The neuropsychological test battery is shown in Table 1 [21,22]. Presurgical neuropsychological assessments started between 9 and 10 am on the second day of hospitalization for VEEG recording. The test duration ranged from 90 to 210 min with an average of 120 min. The cognitive assessments included: Letters and Category Fluency, Rey Auditory Verbal Learning Test (RAVLT-Total, RAVLT-Retention, RAVLT-Delayed and RAVLT-Recognized), Wechsler Memory Scale III (VMS-III) subtests Logical Memory First Recall (LM 1st), Logical Memory I (LM I), Logical Memory II (LM II), Paired Associates I and II (PA I and PA II), Wechsler Adult Intelligence Scale III (WAIS-III) subtests Vocabulary, Similarities, Information, Block Design, Digit Span, Matrix Reasoning and Picture Completion, Rey-Osterrieth Complex Figure (ROCF-Copy, ROCF-Delayed), Five Points test, and Boston Naming Test (BNT). Language dominance was not accessed by WADA or fMRI, and hand dominance was reported during the cognitive evaluation based on the neuropsychologist interview.

Quality of life was assessed by the VEEG nurse (C.P.) as previously described [5,16] on the first day of VEEG recording using the Brazilian version of QOLIE-31 that shows good reliability, validity, and constructs validity [5,23,24]. Scores were determined according to the QOLIE-31 scoring manual [5,16,25], and the cognitive function domain scores were used to analyze the patients' subjective perception (see below).

2.3. Surgical procedure and postsurgical follow-up

Epilepsy surgery was done by the same neurosurgeon (M.N.L.) as previously described [5,12,26]. The temporal lobe resection included the middle and inferior temporal gyri extending up to 4 cm posterior from the temporal pole. After assessing the mesial temporal region, at least 2/3 of the amygdala were resected including its basal and the lateral nucleus. After the amygdala resection, the hippocampus was removed "en bloc". Routine follow-up and seizure outcome evaluation was done by two experienced epileptologists (R.W. or K.L.) 1, 3, 6, and 12 months after surgery. After surgery, AED treatment remained in the same schedule as before surgery and treatment adherence was strongly reinforced to all patients and their caregivers.

Twelve to fourteen months after surgery, all patients underwent the same neuropsychological, psychiatric, and quality of life evaluation as applied in the presurgical workup. These evaluations were done at the outpatient epilepsy clinic by the same neuropsychologist and nurse, blinded to all clinical, neurosurgical, and laboratory variables including the seizure control after surgery.

2.4. Patients' perception of cognitive changes after the ATL

The patients' subjective perception about their cognitive function before and 1 year after the ATL was determined using the subscale of cognitive function domain of the QOLIE-31 questionnaire that asks about difficulties with reasoning and solving problems (Question 12), difficulties or troubles with memory (Questions 15, 16 and 26), and concentration problems (Questions 17 and 18). The final score of the

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