Epilepsy & Behavior xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Neuropsychological profile of mild temporal lobe epilepsy

Maria Grazia Vaccaro [a,1], Michele Trimboli [a,1], Cristina Scarpazza [b,c], Liana Palermo [d], Antonella Bruni [a], Antonio Gambardella [a], Angelo Labate [a,*]

[a] Department of Medical Sciences, Institute of Neurology, University Magna Græcia, Catanzaro, Italy
[b] Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, UK
[c] Department of General Psychology, University of Padua, Italy
[d] Department of Medical and Surgical Sciences, Magna Graecia University of Catanzaro, Italy

ARTICLE INFO

Article history:
Received 22 February 2018
Revised 25 May 2018
Accepted 7 June 2018
Available online xxxx

Keywords:
Mild temporal lobe epilepsy
Cognitive profile
Verbal memory
Prospective memory
Retrospective memory

ABSTRACT

Objective: In the current literature, whether patients with mild mesial temporal lobe epilepsy (mMTLE) have typical neurocognitive profile similar to patients with treatment-refractory seizures still remains unknown. The purpose of the present work was to analyze the neuropsychological profile in a group of consecutive patients with mMTLE.

Methods: Forty consecutive patients whose conditions were diagnosed with mMTLE and 30 healthy controls (HC) were evaluated with an extensive neuropsychological battery. In addition, self-report questionnaires were also administered to evaluate the subjective impairments in prospective and retrospective memories. Finally, the levels of depression and anxiety were evaluated using the Beck Depression Inventory II (BDI-II) and the State–Trait Anxiety Inventory — Form Y1 (STAI-YI e 2).

Results: Patients with mMTLE patients showed higher BDI-II scores (15.9 ± 13.9 vs 7.2 ± 6.7; p =, 002), and higher STAI-Y1 (41.2 ± 14.6 vs 32.6 ± 9.8; p =, 005) together with both objective and subjective memory deficits. Although BDI-II and STAI scores strongly correlated to the outcome in Rey Auditory Verbal Learning Test (RAVLT) and prospective and retrospective memory questionnaire (PRMQ) ($p < 0.0021$), these results did not change without depression scores.

Conclusion: We showed that a specific neurocognitive profile in patients with mMTLE exists. The neuropsychological features are mood depression, verbal memory immediate and delayed deficits, and subjective prospective and retrospective memory deficits.

1. Introduction

Temporal lobe epilepsy (TLE) is the most common type of partial epilepsy in adulthood [1]. According to the International League Against Epilepsy (ILAE) classification, two different TLE categories have been distinguished: mesial TLE (MTLE) and lateral TLE (LTLE). Mesial temporal lobe epilepsy represents the vast majority (more than 70%) and comprises two subtypes: mild mesial temporal lobe epilepsy (mMTLE) and refractory mesial temporal lobe epilepsy (rMTLE) [2–4]. Mild mesial temporal lobe epilepsy is defined as "benign" because it is characterized by at least 24 months of seizure freedom with or without antiepileptic medication, seizures that begin during adolescence up to middle age, and an average age of onset at around 34 years [5–7]. In more than 90% of patients, seizures are well-controlled with a single antiepileptic drug (AED) at low dosage, and some patients do not take medications. At long-term follow-up, seizures in one-third of patients with mMTLE will develop refractoriness to AEDs over time [7]. Although mMTLE and rMTLE share very similar electroclinical and neuroimaging features, a cognitive profile has been described only in rMTLE. A typical cognitive impairment in rMTLE (possible candidates to surgery) is characterized by memory deficits, impaired executive functions, language, processing speed, intelligence, and motor dexterity [8,9]. There are several studies investigating the relationship between patients with rMTLE and memory impairment; one of them suggests that hippocampal sclerosis influences verbal memory [10], and a second one found that the mood and memory disturbances are the most salient comorbid conditions in patients with rMTLE [11,12]. Conversely, a typical cognitive mMTLE profile has not been fully described so far. Only few studies with limited patients suggested that mMTLE shows verbal memory deficits [13–15]. Therefore, the aim of our study was to describe a cognitive profile using a large cognitive battery in a consecutive group of patients with mMTLE.

* Corresponding author at: Cattedra di Neurologia, Università degli Studi "Magna Graecia", Campus Universitario Germaneto, Viale Europa, 88100 Catanzaro, Italy.
E-mail address: labate@unicz.it (A. Labate).
[1] These authors contributed equally.

https://doi.org/10.1016/j.yebeh.2018.06.013
1525-5050/

2. Materials and method

2.1. Participants

In this study, 40 consecutive patients with a diagnosis of mMTLE were enrolled from February 2015 to June 2017. Patients were recruited from the Outpatients Epilepsy Centre of Magna Graecia University of Catanzaro, Italy. The mMTLE of all patients was diagnosed according to the ILAE classification of seizures [16] by two trained epileptologists (AG and AL). Exclusion criteria were as follows: patient age is less than 18 or more than 70 years; patient has other neurological, psychotic disorders (excluding depression and anxiety) or comorbidities; and patient has generalized epilepsy, other partial epilepsies, or rMTLE. We decided not to exclude patients with clinically relevant depression or anxiety as these psychiatric symptoms are often associated with epilepsy [17–20]. Thirty healthy individuals matched in age, gender, and level of education to the patients with mMTLE were also recruited. Healthy individuals with Mini Mental State Examination (MMSE) [21] score equal or less than 25/30, neurological or psychiatric diseases, and drug addiction were excluded. Both patients and healthy controls (HC) provided written informed consent to participate in the study. The study was approved by the local Research Ethics Committee in accordance with the Helsinki Declaration. In each patient, the diagnosis of MTLE was mainly based on typical temporal auras or interictal electroencephalographic (EEG) discharges with a maximum over the temporal lobes. Any suggestion of seizure onset outside the mesial temporal structures by semiology or EEG findings was an exclusion criterion. Lateralization was based on lateralized EEG discharges, with or without lateralized seizure features. Epileptiform discharges were diagnosed in the presence of focal spikes or sharp waves followed by slow waves, and they always involved the temporal regions.

All patients underwent 3-Tesla magnetic resonance imaging (MRI) test to evaluate the presence of abnormal temporal lobe features, mainly the presence of hippocampal sclerosis. Multiple scalp EEG recordings were used to detect interictal EEG abnormalities. At baseline, all participants underwent a battery of standardized neuropsychological (NPC) tasks and several neuropsychiatric interviews. All tests and questionnaires were administered by the same neuropsychologist expert (MGV) blinded to clinical information.

2.2. Neuropsychological battery

The general cognitive functions of all patients and HC were evaluated by a battery of standardized neuropsychological tests. The following tests were administered: MMSE [21] was used to screen cognitive impairment; the Controlled Oral Word Association Test (COWAT) was used as a measure of lexical stock, ability to access the lexicon, and cognitive flexibility [22–25]; Stroop Color and Word Test (Stroop) [26,27] evaluated attention with an interference procedure (times in s); the Modified Wisconsin Card Sorting Test (MWCST) [28] was a modification of the original Wisconsin Card Sorting Test, and it tested the abstract reasoning, decision making, planning, conceptual shifting, learning new rules, and the ability to change cognitive strategies depending on changes in environmental conditions [29]; the Digit Span: Forwards and Backwards task [30] was used to assess the short-term verbal memory; the Rey–Osterrieth Complex Figure Test (ROCFT) [31,32] was used to investigate visuospatial constructional functions, visuographic memory, and some aspects of planning and executive functions, with immediate and delayed recalls; the Rey Auditory Verbal Learning Test (RAVLT) [33,34], which includes measures of immediate and delayed recalls, was used to assess verbal learning and memory; and the Short Tale (ST) [35,31], which includes measures of immediate and delayed recalls, was used to assess the episodic memory. In addition, the self-reported prospective and retrospective memory questionnaire (PRMQ) [36] was used to measure the subjective impairment in daily life in prospective memory (PM) and retrospective memory (RM). It is a self-report questionnaire, and it is made up of sixteen items: eight asking about PM (i.e., the ability to remember to accomplish an intended action at some point in the future such as remembering to take a tablet after lunch) and eight about RM failures. Participants were asked to rate how often they believe to fail in daily life activities requiring PM or RM from very often (rated as 5 in a Likert scale) to never (rated as 1 in a Likert scale) [37,38]. In this way, the higher the PRMQ score is, the higher the subjectively perceived problems in PM and RM are. Although the PRMQ is widely used in literature [39–44], it has never been used to study the cognitive impairment in epilepsy. The Beck Depression Inventory Second Edition (BDI-II) [45] was used to evaluate depressive symptoms of both groups; the State–Trait Anxiety Inventory — Form Y1 (STAI-YI) provides scores for state anxiety; and State–Trait Anxiety Inventory — Form Y2 (STAI-YII) [46] provides scores for trait anxiety levels. The entire neuropsychological battery lasted around 60 to 90 min.

2.3. Statistical analysis

Categorical variables are expressed as count (percentage) and continuous variables as mean (SD) or median (range), as appropriated. Between-group differences were tested using the chi-square for categorical variables and the two independent samples *t*-test or the Mann–Whitney *U* tests for categorical and continuous variables, depending on whether the data were or were not normally distributed. The normal distribution of the data was tested using the Kolmogorov–Smirnov test (d-value) on each variable. The partial eta squared (η^2_p) was reported as an estimate of effect size [47]. Note that 0.2 is considered a small effect, 0.5 a medium effect, and 0.8 a large effect [47]. The results from the neuropsychological tests were corrected for multiple

Table 1
Demographic, clinical, and neuroimaging features of healthy controls (HC) and patients with mild mesial temporal lobe epilepsy (mMTLE).

	HC n = 30	mMTLE n = 40	p value
Gender (F)[a]	20 (66.6%)	27 (67.5%)	0.941
Age (years)[b]	43.4 ± 16.5	44.3 ± 12.9	0.790
Education (years)[c]	13 [5–17]	13 [5–17]	0.763
Duration of illness (years)[b]	–	15.8 ± 11.6	–
Febrile seizures, n	–	22	–
Simple partial seizures (e.g., dejàvù)/m (n), mean (CI)	–	0.7 (0.2–6.2)	–
Number of AEDs (mean ± SD)	–	1.1 ± 0.6	–
MRI evidence of hippocampal sclerosis (n)	–	8	–
BDI-II[b]	7.2 ± 6.7	15.9 ± 13.8	0.002
STAI-YI[b]	32.6 ± 9.8	41.2 ± 14.6	0.005
STAI-YII[b]	35.4 ± 11.4	41.6 ± 13.2	0.046

Results were expressed using row number percentage (a) for dichotomous variable and mean ± standard deviation (b) or median [range] (c) for continuous variables depending on whether or not the data were normally distributed. Statistical analyses were performed using chi-square (a) for dichotomous variable, two independent samples *t*-test (b) or Mann–Whitney (c) for continuous variables depending on whether or not the data were normally distributed. CI: confidence interval; m: month; n: number.

Please cite this article as: Vaccaro MG, et al, Neuropsychological profile of mild temporal lobe epilepsy, Epilepsy Behav (2018), https://doi.org/10.1016/j.yebeh.2018.06.013