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ARTICLE

Older adults with epilepsy: memory complaints and objective neuropsychological performance

Idosos com epilepsia: queixa de memória e desempenho neuropsicológico objetivo

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ABSTRACT

Introduction: People with epilepsy frequently complain of poor memory. **Objective:** To assess the occurrence of memory complaints in older adults with epilepsy (OAE) and whether it is associated with clinical variables, objective cognitive performance, and quality of life (QoL). **Methods:** The Memory Complaint Questionnaire (MAC-Q) was related to objective cognitive performance, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), the Quality of Life in Epilepsy Inventory (QOLIE-31), and the clinical characteristics of 83 OAE. **Results:** OAE showed worse cognitive performance and higher MAC-Q scores when compared to a similar control group (n=40). Impairment in multiple cognitive domains occurred in 34 (41%) OAE and was associated with older age and lower educational level. Memory complaints (MAC-Q≥25) were reported by 45 (54.2%) OAE and associated with older age, lower educational level, onset at ≥60 years, higher NDDI-E scores, lower QOLIE-31 scores, and impairment in multiple cognitive domains. **Conclusions:** OAE presented worse cognitive performance and greater memory complaints. Episode onset at ≥60 years of age was associated with complaints, but not with objective cognitive deficit. We found an association between subjective and objective cognitive performance, with aspects of epilepsy and worse QoL scores.

Keywords: Epilepsy; Memory; Aged.

RESUMO

Introdução: A queixa de memória fraca é frequente em pessoas com epilepsia. **Objetivo:** Avaliar a ocorrência de queixas de memória em idosos com epilepsia (IE) e se há associação com variáveis clínicas, desempenho cognitivo objetivo e qualidade de vida (QV). **Métodos:** O questionário de queixa de memória (*memory complaint questionnaire* — MAC-Q) foi relacionado ao desempenho cognitivo objetivo, o inventário de depressão de transtornos neurológicos para epilepsia (*neurological disorders depression inventory for epilepsy* — NDDI-E), o QOLIE-31 e com as características clínicas de 83 IE. **Resultados:** Houve desempenho cognitivo inferior e maiores escores no MAC-Q em IE quando comparados aos de um grupo controle similar (n=40). Comprometimento de múltiplos domínios cognitivos ocorreu em 34 (41%) IE e associou-se a maior idade e menor escolaridade. Queixas de memória (MAC-Q≥25) foram observadas em 45 (54,2%) IE e associadas a idade mais elevada, menor escolaridade, início das crises aos ≥60 anos, maiores escores no NDDI-E, menores escores no QOLIE-31 e comprometimento de múltiplos domínios cognitivos. **Conclusões:** Pior desempenho cognitivo e maiores queixa de memória ocorreram em IE. Crises com início aos ≥60 anos foram associadas a queixas, mas não a déficit objetivo cognitivo. Houve associação entre desempenho cognitivo subjetivo e objetivo, com aspectos da epilepsia e pior QV.

Palavras-chave: Epilepsia; Memoria; Idoso.

INTRODUCTION

Memory complaints are frequent in the older population and may be associated with emotional aspects and cognitive deficits in neuropsychological tests[1]. Studies suggest that these complaints may be predictors of cognitive decline in highly educated older adults[2].

Cognitive impairment in epilepsy is common, associated with clinical variables and repercussions on the quality of life (QoL), suggesting a complex relationship between cognition and pathophysiological mechanisms, as well as biological and psychosocial factors[3,4,5,6,7,8,9,10,11].

In adults with epilepsy, some clinical variables, such as early age of onset and depressive symptoms, are associated with greater cognitive complaints[12,13]. However, the relationship between objective and subjective cognitive performance is sometimes inconsistent, or the correlation is weak[6,7,8].

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The literature has described cognitive deficits in older adults with epilepsy (OAE)[10,11]; nonetheless, the presence of subjective complaints and their relationship with impairment in neuropsychological tests is little known, and the literature still has gaps regarding whether these variables are associated with subjective cognitive impairment in OAE.

Thus, this research is justified by the need to expand the knowledge of memory complaints in OAE and the associated neurophysiopathological, clinical, and emotional aspects, since the clinical valuation of cognitive complaints can contribute to a better understanding of the interface between cognition and epilepsy.

This study aimed to assess the occurrence of memory complaints and whether there is an association between objective cognitive performance, clinical characteristics of epilepsy, depression, and perceived QoL in OAE.

METHODS

Participants

This study included 83 consecutive outpatients (age≥60 years) diagnosed with epilepsy (OAE), treated at the neurology outpatient clinic at the Hospital of the Pontifícia Universidade Católica de Campinas, São Paulo, Brazil. The inclusion criteria were: (1) diagnosis of epilepsy according to the International League Against Epilepsy (ILAE) Classification of Epilepsies and Epileptic Syndromes criteria[14]; (2) signing an informed consent form to undergo the procedures.

Based on the ILAE criteria, 61 (73.4%) cases presented focal structural epilepsy, and 22 had epilepsy of unknown etiology. In 18 (21.6%) cases, the individuals were diagnosed with temporal lobe epilepsy with hippocampal sclerosis (TLE-HS), not submitted to surgery. At the time of the survey, 48 (57.8%) OAE were taking a single antiepileptic drug (AED), and 35 (42.1%) were on 2 or more AEDs. A total of 45 (54.2%) participants reported having no seizures in the previous year. The electroencephalogram (EEG) revealed epileptiform activity (EA) laterality in the right cerebral hemisphere in 35 cases, in the left hemisphere in 31 cases, and no EA in 17 cases.

The exclusion criteria were: difficulties in understanding the instrument questions due to a lower educational level or mental disability; history of neurosurgery, neurological and psychiatric diseases, or any other progressive chronic diseases.

The control group (CG) consisted of individuals who did not have neurological or psychiatric diseases or other progressive chronic diseases, preferentially recruited from family members. The individuals who agreed to participate in the research were interviewed to collect their sociodemographic and clinical data, and then submitted to the specific protocol. Thus, the CG comprised 40 individuals similar to the patients in age, gender, and socioeconomic conditions.

The study was approved by the Human Research Ethics Committee of the Pontifícia Universidade Católica de Campinas, protocol number 73249517300005481. All participants were informed of the research protocol and signed the consent form.

The OAE who agreed to participate in the study were submitted to a clinical assessment and to the research instruments, presented individually, in a quiet and well-lit room, in the neurological clinic of the hospital. This assessment was performed in a single session on the day the person had a medical appointment.

Procedures

The OAE were submitted to:

- A questionnaire on sociodemographic data (age, gender, educational level).
- A neurological investigation, including the individual's detailed medical history and the collection of clinical data on epilepsy (age of onset, seizure type and frequency, duration of epilepsy, and number of AEDs taken).
- Digital EEG to assess the location and the EA laterality.
- Memory Complaint Questionnaire (MAC-Q)[15]: consisting of 5 questions that assessed the individual's current performance in daily activities and 1 question that compared their perceived current memory to how it was when they were 18–20 years old (better, worse, or much worse). The cut-off score established to indicate a memory complaint was >25.
- Mini-Mental State Examination (MMSE)[16] as a brief screening measure of cognition. The maximum score was 30 points. The cut-off scores for the Brazilian population were established by Bruck et al.: 23 for 1–4 years of schooling; 26 for 5–9 years; and 27 for 10 years or more[17].
- Brief Cognitive Battery-Education (BCB-Edu)[18] to assess cognitive performance, encompassing the identification of ten common pictures (naming) and immediate recollection (incidental memory). Subsequently, the pictures were presented again, and the subject was asked to memorize them for 30 seconds and then recall them (immediate memory). This procedure was repeated one more time (learning). Next, the participants completed the semantic verbal fluency (SVF) test (animal pictures in one minute) and the clock drawing test[19]. After, they were asked to recall the pictures presented earlier (delayed recall). Finally, those ten pictures were presented alongside ten distracting pictures, and the participant had to identify the ones originally presented (recognition). For immediate memory, learning, delayed recall, and recognition, the cut-off scores were respectively <5, <7, <6, and <9. For the SVF test, the cut-off score was 9 for illiterate individuals and individuals with

<8 years of schooling; and 13 for individuals with more than 8 years of formal education[20].

- Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)[21]. The NDDI-E is an epilepsy-specific self-rating questionnaire developed to rapidly screen the symptoms of depression in the two weeks prior to a medical appointment at epilepsy clinics. It consists of six items reflecting depressive symptoms. Each item is assigned a score of 1–4, from "never" to "always/often". The total score ranges from 6 to 24, and higher scores correspond to greater depression severity. In Brazil, the cut-off score for more severe depressive symptoms was set at >15.
- Quality of Life in Epilepsy Inventory (QOLIE-31)[22], an epilepsy-specific QoL inventory. This inventory includes the total score and the following dimensions: seizure worry, overall QoL, emotional well-being, energy/fatigue, cognitive functioning, medication effects, social functioning. The overall score ranges from 1 to 100. Higher scores indicate higher levels of QoL.

The CG individuals were submitted to a questionnaire on sociodemographic data, an EEG, the MMSE, and the BCB-Edu.

Data analysis

MAC-Q scores of the OAE were compared to those of the CG. Data obtained from the MAC-Q were compared with the objective cognitive performance. In the OAE group, we assessed the association between memory complaints (MAC-Q>25), objective cognitive performance, clinical variables (age of onset, number of AEDs taken, seizure frequency and type), sociodemographic aspects (age, educational level), and the NDDI-E and QOLIE-31 scores.

Based on the cognitive performance in the MMSE and the BCB-Edu, OAE were categorized into: 1): subjects with intact cognition and minimally impaired when compared to individuals in the CG; and 2): subjects with impairment in multiple cognitive domains (changes in memory, language, and attention in the BCB-Edu and scores below the cut-off point in the MMSE, according to their educational level)[16,17,18,19,20].

Categorical variables were expressed as absolute values and percentages, and continuous variables as mean and standard deviations. Student's *t*-test, analysis of variance (ANOVA), and Pearson's chi-square test were used to compare continuous and categorical variables. Pearson's correlation coefficient measured the degree of association among quantitative variables.

The influence of sociodemographic and clinical variables (age, educational level, age of onset, number of AEDs taken — 1 or ≥2), cognitive aspects (impairment in multiple cognitive domains — yes or no), and NDDI-E scores regarding subjective memory loss (MAC-Q>25) was assessed using logistic regression, with stepwise selection criteria. A logistic regression analysis was also performed to identify which factors influence impairment in multiple cognitive domains (no or yes).

We used the Statistical Package for the Social Sciences, version 22, for statistical analysis. Statistical significance was set at $p<0.05$ in all tests.

RESULTS

MAC-Q: OAE, CG

No significant differences were found in terms of gender, educational level, and age between OAE and individuals in the CG. OAE had lower cognitive performance scores and higher MAC-Q scores compared to the CG (Table 1).

Subjective memory loss (MAC-Q>25) was higher in OAE than in individuals of the CG — chi-square test; 54 (65%) vs. 18 (45%); p=0.034. Controls showed no difference regarding the occurrence of MAC-Q>25 according to gender, age, and education level.

Table 1. Sociodemographic, clinical, and cognitive aspects and Memory Complaint Questionnaire, Neurological Disorders Depression Inventory for Epilepsy, and Quality of Life in Epilepsy Inventory scores of older adults with epilepsy and individuals in the control group.

	OAE (n=83)	CG (n=40)	p-value
Gender: female/male	39/44	23/17	0.275a
Age (years)	68.4 (±7.0)	68.5 (±4.1)	0.974b
Educational level (years)	3.9 (±3.3)	4.2 (±2.3)	0.534b
MMSE (total score)	22.7 (±4.1)	24.9 (±3.0)	0.004b*
BCB-Edu			
Identification	9.6 (±1.0)	9.9 (±0.1)	0.050b
Naming	9.4 (±1.5)	9.8 (±0.4)	0.029b*
Incidental memory	5.2 (±1.5)	5.9 (±1.5)	0.022b*
Immediate memory	6.6 (±1.7)	7.7 (±1.6)	0.001b*
Learning test	7.1 (±1.8)	8.0 (±1.3)	0.010b*
Delayed recall	6.4 (±1.3)	7.6 (±2.0)	0.001b*
Recognition	8.1 (±2.5)	9.2 (±2.2)	0.017b*
Clock drawing test	4.7 (±2.8)	6.3 (±2.6)	0.003b*
SVF test	10.4 (±4.6)	12.9 (±5.1)	0.010b*
MAC-Q	25.9 (±5.4)	24.0 (±3.9)	0.034b*
Age at first seizure (years)	46.8 (±23.4)		
Average epilepsy duration (years)	21.7 (±20.9)		
Seizure onset: <60/≥60 years	54/ 29		
QOLIE-31 (total score)	67.7 (±16.8)		
NDDI-E	10.9 (±4.6)		
NDDI-E>15	13 (15.6%)		

OAE: older adults with epilepsy; CG: control group; MAC-Q: Memory Complaint Questionnaire; MMSE: Mini-Mental State Examination; BCB-Edu: Brief Cognitive Battery-Education; SVF test: semantic verbal fluency test; QOLIE-31: Quality of Life in Epilepsy Inventory; NDDI-E: Neurological Disorders Depression Inventory for Epilepsy; [a]: chi-square test; [b]: Student's *t*-test; *p<0.05.

MAC-Q: clinical variables and cognitive performance

Table 2 shows the values of the correlations between age, age at first seizure, MAC-Q and NDDI-E scores, and cognitive tests of OAE.

Table 2. Correlation between clinical and sociodemographic data, Memory Complaint Questionnaire and Neurological Disorders Depression Inventory for Epilepsy scores, and objective cognitive performance.

	Age	Age at first seizure	MAC-Q	NDDI-E
MAC-Q	0.331*	0.260*		
NDDI-E	0.284*	0.141	0.268*	
MMSE	-0.224*	-0.086	-0.316*	-0.219*
Clock drawing test	-0.218*	0.064	-0.140	-0.141
SVF test	-0.054	-0.113	-0.212	-0.137
Identification	-0.343*	-0.233*	-0.102	-0.335*
Naming	-0.228*	0.083	0.039	-0.395*
Incidental memory	-0.432**	-0.256*	-0.312*	-0.240*
Immediate memory	-0.530*	-0.189	-0.280*	-0.295*
Learning test	-0.440*	-0.267*	-0.290*	-0.332*
Delayed recall	-0.305*	-0.102	-0.205	-0.181
Recognition	-0.426*	-0.156	-0.244*	-0.186

MAC-Q: Memory Complaint Questionnaire; NDDI-E: Neurological Disorders Depression Inventory for Epilepsy; MMSE: Mini-Mental State Examination; SVF test: semantic verbal fluency test; Pearson's correlation; *: p<0.05; **: p<0.001.

Subjective memory loss (MAC-Q>25) was identified in 45 (54.2%) cases. Higher age, lower educational level, onset of seizures after 60 years of age, greater NDDI-E scores, lower QOLIE-31 scores, and impairment in multiple cognitive domains were associated with a MAC-Q>25 score. We found no significant association between memory complaints and other clinical and electroencephalographic aspects (Table 3).

Some impairment was detected in multiple cognitive domains of 34 (41%) OAE. Table 3 presents sociodemographic aspects and clinical variables, as well as NDDI-E and QOLIE-31 scores, according to MAC-Q.

In the logistic regression analysis, the only predictive factor for a MAC-Q>25 score was age, while age and education were predictive factors for impairment in multiple cognitive domains. Other clinical aspects were excluded from the equation (Table 4).

DISCUSSION

The results of this study provide evidence that OAE have significantly more complaints of memory loss and cognitive impairment than individuals in the CG.

Cognitive deficit in OAE was associated with clinical aspects, similar to other studies[10,11]; however, little is understood about the impact of chronic epilepsy or early onset of seizures on the cognition of older adults.

Table 3. Sociodemographic and clinical aspects, Neurological Disorders Depression Inventory for Epilepsy and Quality of Life in Epilepsy Inventory scores according to the Memory Complaint Questionnaire, and the occurrence of impairment in multiple cognitive domains.

	MAC-Q			Cognitive impairment		
	≤25 (n=38)	>25 (n=45)	p-value	No (n=49)	Yes (n=34)	p-value
Gender: female/male	14/24	25/20	0.089[a]	23/26	16/18	0.991[a]
Age (years)	65.8 (±4.9)	70.5 (±7.8)	0.002[b*]	66.2 (±5.2)	71.5 (±8.0)	0.001[b*]
Educational level (years)	4.6 (±3.1)	2.9 (±2.5)	0.013[b]	4.6 (±3.1)	2.4 (±2.0)	<0.000[b*]
Age at first seizure (years)	40.2 (±22.7)	52.3 (±22.7)	0.018[b*]	42.8 (±20.8)	52.5 (±25.9)	0.077[b]
Seizure onset: <60/ ≥60	29/9	25/20	0.048[a]	36/13	18/16	0.054[a]
Epilepsy duration (years)	25.6 (±21.8)	18.4 (±19.8)	0.120[b]	23.5 (±20.4)	19.0 (±21.8)	0.345[b]
Seizures in the previous year: yes/no	20/18	18/27	0.205[a]	24/25	14/20	0.510[c]
EA laterality: right/left	16/15	19/16	0.828[a]	23/18	12/13	0.614[a]
Number of AEDs taken: 1/≥2	19/19	29/16	0.265[c]	25/24	23/11	0.176[c]
Structural epilepsy/unknown etiology	27/11	34/11	0.803[a]	32/17	29/5	0.048[a*]
QOLIE-31						
Emotional well-being	76.8 (±16.7)	62.3 (±26.3)	0.010[b*]	64.0 (±24.7)	74.6 (±21.6)	0.080[b]
Cognitive functioning	79.0 (±19.4)	61.1 (±25.2)	0.002[b*]	65.6 (±26.9)	72.4 (±20.0)	0.259[b]
Total score	74.1 (±11.7)	63.6 (±18.4)	0.007*	65.7 (±17.1)	70.9 (±16.1)	0.219[b]
NDDI-E	9.5 (±4.4)	12.1 (±4.8)	0.013[b*]	9.8 (±4.2)	12.5 (±5.2)	0.014[b*]
Cognitive impairment: no/yes	27/11	22/23	0.047[a*]			

MAC-Q: Memory Complaint Questionnaire; EA: epileptiform activity; AED: antiepileptic drug; NDDI-E: Neurological Disorders Depression Inventory for Epilepsy; [a]: chi-square test; [b]: *t*-test; [c]: Fisher's exact test; *p<0.05.

Table 4. Logistic regression to determine the factors that contribute to impairment in multiple cognitive domains and a Memory Complaint Questionnaire score >25 in 83 older adults with epilepsy.

	Predictor	Odds ratio	95%CI	p-value
Impairment in multiple cognitive domains	Age	1.11	1.10 1.22	0.016*
	Educational level	0.78	0.62 0.64	0.016*
MAC-Q	Age	1.12	1.04 1.23	0.005*

MAC-Q: Memory Complaint Questionnaire; OAE: older adults with epilepsy; 95%CI: 95% confidence interval; *p<0.05.

An association between impairment in multiple cognitive domains and subjective memory complaints was identified, revealing a complex mechanism involving different anatomical-pathophysiological aspects and neuropsychological factors in the perceived cognition of OAE. In contrast, other studies of OAE do not describe these findings[10]. The association between objective and subjective cognitive impairment has been reported in several cases of adults with epilepsy, using different cognitive tests[8,13,23,24].

This study found an association of subjective complaints with sociodemographic aspects (age and education), onset of seizures after 60 years of age, and other aspects of epilepsy. Other studies of OAE did not find associations between cognitive complaints and clinical aspects of epilepsy[10].

Depressive symptoms were associated with subjective memory complaints, suggesting that depressive symptoms can manifest as poor perceived health, multiple somatic complaints, and an exacerbated perception of cognitive impairments. Recent studies have indicated that the affective status contributes to subjective memory complaints in adults with different types of epilepsies[6,7,9,13,23,24,25,26,27], OAE[10], and healthy adults[3].

Memory complaints, but not the objective cognitive deficit, were related to worse QoL (emotional well-being, cognitive functioning, and total score), suggesting that QoL is a complex, subjective perception of multiple abilities[28].

This study has some limitations. The epilepsy clinic used in this article is in a university hospital but not a tertiary epilepsy center. This is a cross-sectional study with a relatively small sample, and the instruments used are mostly cognitive screening tests and depression in epilepsy screening test. The sample size of the control group is small. The groups were formed by individuals with lower educational levels, which can make cognitive assessment difficult and limit the generalization of the findings.

In summary, OAE reported more memory complaints and had worse cognitive performance levels than individuals in the CG. Memory complaints were associated with sociodemographic and clinical variables, depression, and lower cognitive performance. A better perception of QoL was related to lower memory complaints.

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