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Effects of a brief psychotherapeutic intervention on resilience and behavior in patients with drug-resistant mesial temporal lobe epilepsy and late seizure recurrence after surgery

Maria Helena Brandalise [a], Gerardo Maria de Araujo Filho [a,b,*], Ricardo Silva Centeno [c], Elza Marcia Targas Yacubian [c], Andrea Parolin Jackowski [a]

[a] Universidade Federal de Sao Paulo (UNIFESP), Department of Psychiatry, Brazil
[b] Faculdade de Medicina de Sao Jose do Rio Preto (FAMERP), Department of Psychiatry and Medical Psychology, Brazil
[c] Universidade Federal de Sao Paulo (UNIFESP), Department of Neurology and Neurosurgery, Brazil

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ABSTRACT

Seizure recurrence (SR) after epilepsy surgery in patients with medically resistant temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) can compromise medical treatment and quality of life (QOL). However, there is a scarcity of interventions specifically addressing this issue in the literature. We aimed to evaluate the impact of a four-week psychotherapeutic intervention on the levels of resilience, behavioral symptoms, and QOL of patients with drug-resistant TLE-MTS who underwent corticoamygdalohippocampectomy (CAH) and who presented with late SR. Fifty patients who had been diagnosed with TLE-TMS, undergone CAH, and presented with late SR were included. The study instruments included a clinical and sociodemographic questionnaire and the Brazilian versions of the Connor–Davidson Resilience Scale (CD-RISC-10), the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), the Interictal Dysphoric Disorder Inventory (IDDI), and the Quality of Life in Epilepsy Inventory (QOLIE-31). Significant reductions in the IDDI ($p < 0.001$) and NDDI-E ($p < 0.001$) scores, improvements in the CD-RISC-10 ($p < 0.001$) and QOLIE-31 ($p < 0.001$) scores, and positive correlations between resilience levels and QOL ($p < 0.01$), as well as a negative correlation between depressive symptoms and resilience ($p < 0.01$) and QOL ($p < 0.01$), were observed after the psychotherapeutic intervention. Improvements in the resilience levels and QOL, with concomitant reductions in depressive symptoms, were observed in patients with TLE-MTS and late SR after a brief psychotherapeutic intervention. Since there is a lack of studies that measured the impact of interventions in this patient subpopulation, these results may support the development of treatment strategies for this specific group.

1. Introduction

Temporal lobe epilepsy with mesial temporal sclerosis (TLE-MTS), one of the most common drug-resistant epilepsies, is also one of the most frequent surgically remediable epilepsy syndromes. For these patients, corticoamygdalohippocampectomy (CAH) has been considered a safe and efficient surgical procedure [1–3]. However, studies with longer follow-ups have disclosed that only a group of 50–60% of patients who underwent CAH remained seizure-free, highlighting the phenomenon of seizure recurrence (SR) [4–6]. Defined as the return of seizures after a period in which the patient became seizure-free after surgery, SR has been considered a potentially serious adverse event in the population of patients with TLE-MTS that is already impacted by higher rates of social issues such as exclusion, unemployment, low educational level, and more cognitive dysfunction [7–10].

The ability to cope with SR can be a very important issue to consider for any intervention in patients who can have such potentially severe adverse events. Resilience is a psychological concept defined as the ability to address problems and overcome obstacles that are consequences of adverse situations [11,12]. Recently, as has occurred in studies on quality of life (QOL) [7–9], aspects associated with resilience have been assessed objectively using standardized instruments. At the moment, however, there is a scarcity of studies measuring the impact of treatments on the resilience levels in patients with TLE-MTS who presented with SR. Based on these premises, the main objective of this prospective study was to measure the impact of a psychotherapeutic intervention on the resilience levels and QOL of patients with TLE-MTS who underwent CAH and had late SR, which occurred at least six months after surgery with the aim of providing evidence for this therapeutic approach for this specific subpopulation of patients. A correlation

* Corresponding author at: Av. Brigadeiro Faria Lima, 5416 – Nova Redentora, São José do Rio Preto, SP CEP: 15090-000, Brazil.
E-mail address: filho.gerardo@gmail.com (G.M. de Araujo Filho).

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analysis between resilience levels and the presence of behavioral (depressive and dysphoric) symptoms was also performed with the aim of measuring the possible impact of the intervention on those symptoms and their correlation with the resilience scores.

2. Methods

2.1. Participants

At the time of the study, 425 patients with TLE-MTS had been surgically treated by CAH in a tertiary epilepsy center (the epilepsy clinic of Universidade Federal de São Paulo - UNIFESP) from 2004 to 2017, and 127 (29.8%) presented with SR. Of these, 32 (25.2%) had early SR, and 95 patients (74.8%) had late SR. The inclusion criteria were as follows: age of 18 to 65 years, presurgical diagnoses of TLE-MTS confirmed through video-electroencephalography (VEEG), clear magnetic resonance imaging (MRI) findings consistent with MTS, and follow-up for at least one year. The diagnosis of TLE was performed in accordance with the International League Against Epilepsy (ILAE) classification [13]. Exclusion criteria were cognitive impairments affecting the ability to answer questionnaires, presence of other epileptic syndromes at the neurological investigation, and inability to attend all four weekly meetings.

The recruitment period occurred between September 2017 and February 2018 and involved chart reviews of all patients with TLE-MTS and SR. Ninety-five patients met the inclusion criteria and no exclusion criteria, and all of them were invited through phone calls and at routine visits to participate in the study. After informed consent was assigned, 50 (52.6%) attended the four weekly meetings. The major reason for the exclusion of the other 45 patients was the inability to attend all the meetings, as was the case for 35 patients (77.7%). The other reasons noted by patients were all related to practical difficulties, such as transportation costs and/or the lack of availability of caregivers. Of the ten remaining (22.3%) excluded patients, five had developed an epilepsy syndrome other than TLE-MTS, and five did not have the cognitive condition to answer the questionnaires. The steps for patient inclusion are illustrated in Fig. 1.

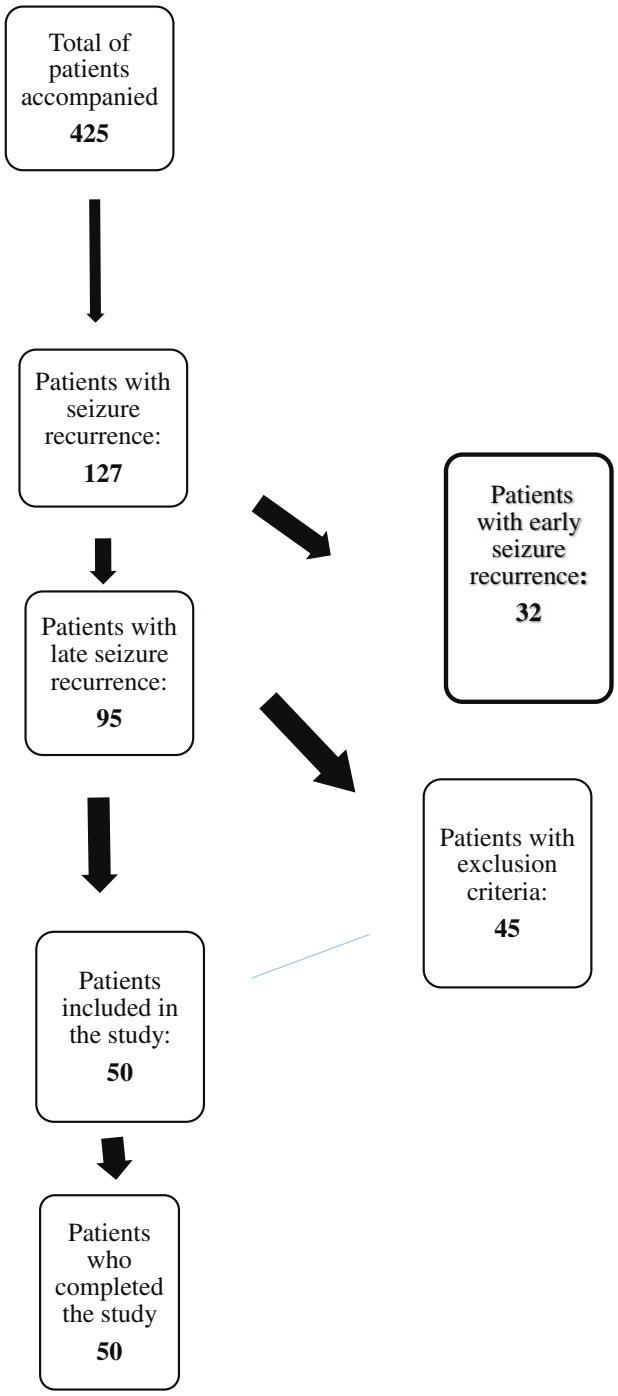

Fig. 1. Steps for patient inclusion.

2.2. Procedures

After local ethical committe approval, all participants signed the Informed Consent Form. The 50 patients included in the study performed a presurgical evaluation that consisted of 2–6 days of continuous VEEG monitoring with a 32-channel EEG recording; electrodes were placed according to the 10–10 system on the temporal lobe. Mesial temporal sclerosis was diagnosed if atrophy was present as an increased T2-weighted signal and disrupted internal structure or if there was atrophy of the hippocampus/amygdala complex upon visual inspection of the MRI images. Resistance to pharmacological treatment was defined as when seizures persisted after the utilization of at least two first-line medications for focal seizures at the highest tolerated doses for at least six months [14]. Clinical and sociodemographic data were obtained through chart review and/or through patient/family information. The dosages of antiepileptic drugs (AEDs) did not change during the study.

The psychological intervention occurred between March and August 2018 and consisted of four weekly individual sessions with the same psychotherapist. Each meeting was semistructured and focused on addressing specific aspects of SR, such as the introduction of the participant and psychotherapist; understanding the phenomenon of SR; identification of moods and thought distortions (e.g., guilt, frustration and anger) associated with SR; and preparing for life situations the patient might encounter after the intervention. All sessions were delivered by the same experienced psychologist (MHB). During the intervention, participants were highly encouraged to change negative behaviors associated with SR and to report the advances in their behaviors in the later session. More specific details are described in Table 1.

2.3. Instruments

The following instruments were used to obtain the data:

A) Clinical and sociodemographic questionnaire: all patients answered a semistructured questionnaire with the aim of collecting sociodemographic and clinical data;
B) Interictal Dysphoric Disorder Inventory (IDDI) [15]: this instrument was developed to diagnose interictal dysphoric disorder (IDD), which is determined by the presence of eight key

Table 1
Evaluation and intervention process of a brief psychotherapeutic intervention on patients with TLE-MTS and late seizure recurrence.

Meeting number	Activity	Objectives	Procedures
1st	Initial evaluation and guidance	To evaluate clinical/socio-demographic characteristics, dysphoric/depressive symptoms, QOL and resilience scores.	Identification form, QOLIE-31, IDDI, CD-RISC-10, NDDI-E.
2nd	Devolution of initial evaluation and intervention	Feedback of the initial evaluation's results and intervention with participants	Supportive psychotherapy (understanding SR, recognizing emotions and feelings) Psychoeducation (counseling activities)
3rd	Intervention	Intervention based on psychoeducation	Psychoeducation (recognizing negative feelings and how to manage them)
4th	Final evaluation	Feedback from patients about the benefits of intervention, evaluate dysphoric/depressive symptoms, QOL and resilience	Feedback from patients, QOLIE-31, IDDI, CD-RISC-10, NDDI-E.

CD-RISC-10: Connor–Davidsom Resilience Scale, IDDI: Interictal Dysphoric Disorder Inventory, NDDI-E: Neurological Disorders Depression Inventory for Epilepsy, QOLIE-31: Quality of Life in Epilepsy Inventory-31, SR: seizure recurrence.

symptoms divided into three dimensions: depression symptoms (depressed mood, energy, pain, insomnia), affective symptoms (fear/panic, anxiety), and so-called "specific" symptoms (irritability and euphoria). The presence of at least three of the eight key symptoms, in any dimension, producing considerable social and occupational dysfunction to patients with epilepsy is sufficient to determine the diagnosis;

C) Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) [16]: this is a brief inventory (6 items) and was developed for rapid screening (approximately 3 min) of depressive episodes in patients with epilepsy. It has the advantage of minimizing the influence of factors associated with epilepsy, which can be confused with depressive symptoms, such as memory complaints and adverse effects of AEDs, which can include changes in sleep, fatigue, and impaired concentration. According to the developers of the inventory, a score greater than or equal to 15 showed high specificity and sensitivity for the diagnosis of major depressive disorder (MDD);

D) Connor–Davidson Resilience Scale (CD-RISC-10) [17]: a 10-item instrument that evaluates individuals' perception of their ability to adapt to change, to overcome obstacles, and to recover from illnesses, injuries or other difficulties, among others. The instrument is self-administered, and participants record their responses on a scale of 0 (never true) to 4 (always true). The results are calculated by adding the points indicated by the participants for each item and can vary between 0 and 40 points; high scores indicate high resilience;

E) Quality of Life in Epilepsy Inventory-31 (QOLIE-31) [9]: a 31-item instrument with the objective of measuring the QOL as related to health for people with epilepsy. The following domains are evaluated: concerns with epileptic seizures, emotional aspects, vitality, sociability, adverse effects of AEDs, cognitive aspects and global QOL.

2.4. Statistical analysis

Statistical analyses were performed using SPSS 24.0 software (IBM, Chicago, Illinois). The collected data were described as means and standard deviations (discrete variables) or according to their presence or absence (categorical variables). The results obtained through multiple comparisons were analyzed through analysis of variance (ANOVA) with Bonferroni as a post hoc test when necessary. The Wilcoxon test for paired samples was used for the comparing the data from before and after the intervention. Cohen's *d* was calculated to measure the effect size for each instrument. To verify possible correlations between the clinical and sociodemographic data and the resilience levels, QOL and behavioral (depressive and dysphoric) symptoms, a correlational analysis using Spearman's coefficient was performed. Values of $p < 0.05$ were considered significant.

3. Results

Of the 50 patients included, 41 (82.0%) were females. The mean age was 40.9 ± 10.4 years. Thirty-one patients (62.0%) had high school or college as their educational level, and 32 (64.0%) were married. All 50 patients stated a religious preference, and 36 (72.0%) participated in professional activities. Mesial temporal sclerosis occurred more frequently on the left side (29 patients; 58.0%). All patients had used at least two AEDs; carbamazepine (CBZ) was the most frequent AED, prescribed to 32 patients (64.0%). Benzodiazepines (BZD), particularly clobazam (CLB), were the most common adjunctive drugs and were prescribed to 23 patients (46.0%). The mean interval since surgery in this study was 2.5 ± 1.4 years, and the mean interval between surgery and SR was 1.2 ± 0.6 years. At the time of the study, 42 patients (84.0%) were classified as Engel class II, six (12.0%) as Engel class III, and two (4.0%) as Engel class IV.

At initial evaluation, the instrument results indicated that 16 patients (32.0%) had a diagnosis of IDD, with a mean of 2.06 ± 0.35 symptoms. Major depressive disorder was present in 18 (36.0%) patients, with a mean score of 13.32 ± 3.61. Before the psychotherapeutic intervention, Spearman's coefficient revealed significant positive correlations between resilience levels and QOL ($r = 3.8$; $p = 0.009$) and between the diagnoses of MDD and IDD ($r = 5.8$; $p < 0.001$). Negative correlations were also observed between depressive symptoms and resilience ($r = -3.4$; $p = 0.006$) and between depressive symptoms and QOL ($r = -4.2$; $p < 0.001$).

Comparing the scores before and after the four-week individual psychotherapeutic intervention with Wilcoxon's test, statistically significant reductions in the IDD (1.34 ± 0.28 symptoms and 9 patients; $p < 0.001$) and MDD (10.81 ± 2.14 and 10 patients; $p < 0.001$) scores and diagnoses, as well as in the main symptoms and scores, were observed. The number of patients with the symptoms of IDD before and after intervention is showed in Fig. 2. There were also significant improvements in the resilience ($p < 0.001$) and QOL ($p < 0.001$) scores. Table 2 describes the results obtained from the instruments for the 50 patients at both time points. The effect sizes were moderate to large for the analyses, varying from 0.33 to 2.25. In addition, the use of Spearman's coefficient revealed significant positive correlations between resilience levels and QOL ($r = 4.3$; $p = 0.008$), as well as negative correlations between depressive symptoms and resilience ($r = -2.6$; $p = 0.007$) and between depressive symptoms and QOL ($r = -2.4$; $p = 0.009$), after the psychotherapeutic intervention. When compared with patients with psychiatric comorbidities (MDD and IDD), patients without psychiatric disorders had significantly greater improvements in their resilience levels ($p = 0.03$) and QOL ($p = 0.02$).

4. Discussion

The purpose of this study was to assess the impact of a brief psychotherapeutic intervention on resilience levels, dysphoric/depressive

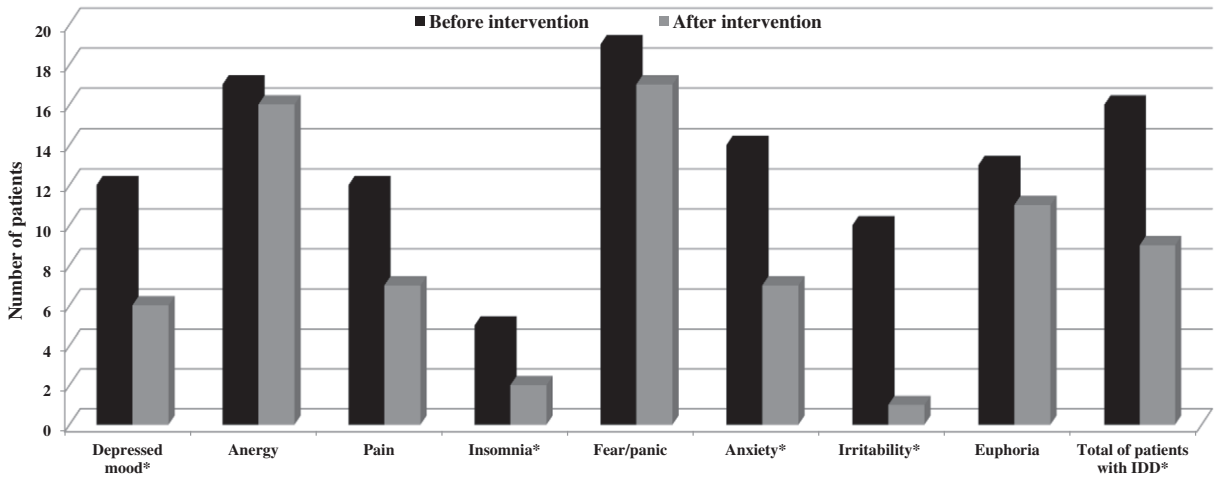

Fig. 2. Number of patients with the eight key symptoms of interictal dysphoric disorder before and after psychological intervention. IDD: interictal dysphoric disorder; *p < 0.05.

symptoms and QOL of patients with TLE-MTS who underwent CAH and presented with late SR and to provide evidence of this therapeutic approach for this specific subpopulation of patients. Correlation analyses between the levels of resilience and the clinical/demographic variables, as well as the presence of depressive and anxiety symptoms, were performed. Reductions in depressive symptoms with concomitant improvements in resilience levels and QOL were observed after the intervention. Positive correlations between the resilience levels and QOL, as well as a negative correlation between depressive symptoms and resilience and QOL, also occurred. To our knowledge, this is the first study that aimed to verify the impact of interventions in patients with SR after epilepsy surgery in this specific subpopulation.

Resistant TLE-MTS is one of the most frequent epileptic syndromes encountered in tertiary epilepsy centers. For these patients, CAH has been considered an important therapeutic option, with rates of seizure remission of up to 70% in the first year [1–3]. However, systematic reviews have observed that long-term seizure freedom (>5 years) is an important criterion to achieve for improving patients' QOL and functionality [10,18]. Although freedom from seizures has generally been associated with high levels of satisfaction, SR has been considered a consistent predictor of dissatisfaction with epilepsy surgery [10,18]. Studies have observed that SR may occur in up to 30–50% of patients who underwent CAH during long-term follow-up, with negative consequences [19–22]. The occurrence of SR has been considered a serious adverse event that can compromise patients' medical treatment and QOL [23,24]. Based on these findings, the negative emotional impacts on patients with late SR would therefore be even higher, since they have experienced a seizure-free period of at least six months [23,24]. Despite the scarcity of studies verifying the emotional aspects associated with early or late SR in patients with epilepsy after surgery, a recent study disclosed high levels of anxiety and depression in a sample of patients with resistant TLE-MTS who underwent CAH [5].

Resilience is a psychological concept defined as the ability to address adverse situations. It also consists of a process of making positive decisions to overcome adversities [11,12]. The development of higher resilience levels could allow appropriate behaviors to be achieved, providing opportunities to develop skills to overcome adverse situations [11,12]. The present results indicated reductions in depressive and dysphoric symptoms, with concomitant improvements in resilience levels and QOL after the intervention, possibly confirming previous results [11,12,24]. In addition, positive correlations between resilience levels and QOL, as well as a negative correlation between depressive symptoms and resilience and QOL, also occurred. It is believed that approximately 50–70% of patients with refractory epilepsy have some psychiatric comorbidities [25,26]. Mood (24–74%) and anxiety disorders (10–25%) have been the most frequent psychiatric comorbidities disclosed [26]. The presence of a psychiatric comorbidity has already been observed as a risk factor for worse surgery outcome, adversely affecting patients' QOL and possibly their patterns of coping and resilience [7–9,25,26]. In addition, it is already known that the presence of depression and anxiety symptoms have been associated with lower epilepsy surgery satisfaction and reduced QOL postsurgery [18]. A recent study also observed that resilience levels were negatively influenced by anxiety and depressive symptoms in patients with TLE-MTS and late SR [5].

Table 2
Scores of instruments before and after a psychotherapeutic intervention in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis with late seizure recurrence.

Instrument	Variable	Before intervention					After intervention					p-Value	Effect size
		Minimum	Maximum	Mean	SD	Presence of diagnosis	Minimum	Maximum	Mean	SD	Presence of diagnosis		(Cohen's *d*)
CD-RISC-10	Total scores	4	36	22.51	10.8	–	20	42	30.26	9.62	–	<0.001*,a	0.76
IDDI	Number of symptoms	0	8	2.06	0.35	16	0	7	1.34	0.28	9	<0.001*,a	2.25
NDDI-E	Total scores	6	24	13.32	3.60	18	6	20	10.81	2.10	10	<0.001*,a	0.88
QOLIE-31	Overall QOL scores	108	224	181.29	36.21	–	140	247	191.12	25.40	–	<0.001*,a	0.33

CD-RISC-10: Connor–Davidsom Resilience Scale, NDDI-E: Neurological Disorders Depression Inventory for Epilepsy, IDDI: Interictal Dysphoric Disorder Inventory, QOL: quality of life, QOLIE-31: Quality of Life in Epilepsy Inventory.
[a] Wilcoxon's test for paired samples.
* p < 0.05.

The results from the present study are therefore concordant with previous data in the literature and highlighted the benefits of these brief psychological interventions on resilience and behavioral and emotional aspects for this specific patient subpopulation. The effect sizes were moderate to large for the symptoms evaluated, showing the potential effectiveness of this intervention.

However, the present study has important limitations. First, the observed results should not be generalized to all patients with epilepsy and SR after surgery, since a specific population of patients with TLE-MTS and late SR was studied. Second, the inability of attending all four weekly meetings excluded a large percentage of patients, and this issue probably introduced major bias to the study. Despite the fact that only 39.3% of patients with TLE-MTS and SR who attended our tertiary center completed the intervention, the study participants represent 52.6% of the population that was potentially able to participate in this study (i.e., had late SR). In addition, the initial screening process could not distinguish clearly between the referenced practical difficulties and/or the lack of motivation to participate. Although only 32% of the patients fulfilled the criteria for IDD and 36% fulfilled the criteria for MDD according to the IDDI and NDDI-E assessments, respectively, the main purpose of using these instruments was to quantify symptoms in order to compare this population of patients before and after the intervention. Since we were not able to follow-up with patients for a period of time after the intervention due to the limitations of the outpatient clinic, we cannot assume that the positive changes observed persisted for a longer period, although therapy does not necessarily change all patients' issues. On the other hand, even in this four-session intervention, a positive effect could be observed. Based on the above limitations, the results observed may be overstated. Nevertheless, our findings were concordant with the scarce literature in this area and address a homogeneous population of patients with TLE-MTS and late SR after CAH.

In conclusion, the present study observed the positive effects of a four-week psychological intervention in patients with drug-resistant TLE-MTS with late SR after CAH who followed-up in a tertiary center and provided evidence of the efficacy of this brief intervention for this specific patient subpopulation. Due to the scarcity of data regarding nonpharmacological interventions in patients with late SR after epilepsy surgery, more studies on SR with a larger number of participants and a longer follow-up period are therefore highly necessary.

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