

## Depressive and Anxiety Symptoms Exert Negative Impact on Resilience to Stressful Events in Patients with Refractory Temporal Lobe Epilepsy with Late Seizure Recurrence after Surgery

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### Abstract

Seizure recurrence after cortico-amygdalohippocampectomy (CAH) in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) is a potentially serious event, which can compromise their medical treatment and quality of life. However, any purpose of intervention among these patients should be based on specific parameters, and among them their levels of resilience to stressful events. The objective of this study was to evaluate the levels of resilience in patients with refractory TLE-MTS submitted to CAH who presented late seizure recurrence after surgery through a structured instrument (*Quest\_Resiliencia*), as well as to measure the possible negative impact of anxiety and depressive symptoms to the presence of resilience levels to stressful events. Methods: Sixty patients with age between 18 and 65 years, followed-up at the Outpatient Clinic of epilepsies of Universidade Federal de Sao Paulo, with clinical and electrographic diagnoses of TLE-TMS, who had been submitted to CAH and presented seizure recurrence at the time of the study were included. The instruments included a clinical and socio-demographic questionnaire, *Quest\_Resiliencia*, Beck Depression Inventory (BDI) and State and Trait Anxiety Inventory (STAI). Results: Satisfactory levels of resilience to stressful events were observed, suggesting that these patients may benefit from stress-coping interventions. However, significant negative correlation of anxiety ( $p < 0.01$ ) and depressive ( $p < 0.01$ ) symptoms were observed. Since there is a research gap in literature on studies that aimed to verify the resilience levels in patients with TLE-MTS, studies that may support the development of resilience resources are thus necessary.

**Keywords:** Surgical outcome; Resilience; Seizure recurrence; Quality of life; Depression; Anxiety

### Introduction

Temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS), one of the most common epileptic syndromes with refractory seizures, is the most frequent 'surgically remediable' syndrome. Cortico-amygdalohippocampectomy (CAH) has been considered a safe and efficient surgical procedure for patients with refractory TLE-MTS [1-5]. However, a recent study has shown that 55.2% of patients become seizure-free since surgery with a follow-up of 5.4 years [6]. Seizure recurrence after epilepsy surgery can be classified as either early or late depending on the recurrence time after operation (before or after six months), and has been considered as a potentially serious adverse event in this population already so impacted by higher rates of problems such as social inclusion, unemployment, lower educational level and more cognitive dysfunction secondary to the presence of seizures and/or chronic use of medication [7-13].

Any purpose of intervention for these patients should be based on specific parameters, and among them their ability to cope with these adverse events. Resilience is a psychological concept originally borrowed from physics, defined as the ability to deal with problems, to overcome obstacles or to resist the pressure of adverse situations. It consists in a process of making restorative decisions when there is an unfavorable environment, in order to overcome the adversities [14]. It can also be considered a strategy that enables the cope with stress, presenting a methodology that enables the resignification of beliefs. The development of resilience allows achieving appropriate behaviors, innovating the way of thinking, providing opportunities to develop skills in overcoming the challenges and obstacles facing the adverse situations, such as: relationship difficulties, anxiety,

marital conflicts, lack of ability to concentration and stress [15]. Recently, as occurs in studies involving QOL, the aspects related to resilience have been analyzed more objectively, through the use of instruments. The principle of the methodology consists to verify, by means of standardized instruments, which current beliefs need to be restructured, favoring changes through the review of eight areas of life where seeks excellence: context analysis, self-confidence, self-control, empathy, interpersonal relationships, body scan, optimism and a sense of life. The *Quest\_Resiliencia* scale was developed with the objective of mapping out the beliefs that organize the resilient behavior through the analysis of Models of Determinant Beliefs (MDB) [16]. The objective of this study was to measure the resilience levels of patients with TLE-MTS submitted to CAH who presented late seizure recurrence through the analysis of MDB (*Quest\_Resiliencia*). In addition, a correlation study between the resilience levels and the presence of depressive and anxiety symptoms was performed, aiming at measuring the impact of such symptoms in resilience indices.

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## Participants and Method

### Participants

Sixty patients between 18 and 65 years, followed-up at the Outpatient Clinic of Epilepsy of the Universidade Federal de São Paulo, who presented clinical and electrographical diagnosis of TLE-MTS, who had been submitted to CAH and had recurrent seizures at the time of the study were included after signing the Informed Consent Form. Data collection was carried out from April to July 2013.

### Instruments

The following instruments were used in obtaining the data.

**Clinical and socio-demographic questionnaire:** All patients answered a semi-structured questionnaire with the aim of being collected sociodemographic and clinical data;

**Quest\_Resiliencia:** The evaluation of the resilience indices was performed through the resilience scale *Quest\_Resiliencia*. The scale is available online and accessed through the website of Brazilian Society of Resilience (SOBRARE) [www.sobrare.com.br](http://www.sobrare.com.br). For the present study, the SOBRARE afforded 60 copies of the instrument, with logins and passwords for access to the site. The scale *Quest\_Resiliencia* is one of the tools of the methodology of “Resilient Approach” which objectively maps the eight MDB that structure behavior and shape the resilience to stressful events [16]. The 72 items of the scale are grouped together in each of the eight MDB, which are: Context analysis, Self-reliance, Self-control, Attract and keep People, Empathy, Body reading, Optimism with life, Meaning of life [16]. The definition of each MDB is showed in Table 1. The instrument configures each MDB in three ways: firstly, as a balance between the possibilities of “accept” or “reject” the stress; secondly, intensity attributed to beliefs with predominance for the “suffering” and “absorb” the impacts that stress causes, and third; the allocation of intolerance to the beliefs given the high stress and that configures a behavior of rejection of stress. Within the behavioral pattern, the patient may find himself in a condition of low, good, strong or excellent resilience in face of stressful situations and adversities to which he is subject [16];

**Beck depression inventory (BDI):** Consists of a 21-item questionnaire of self-report to measure the presence and severity of depressive symptoms [17,18];

**State/trait anxiety inventory (STAI):** Consists of a dimensional 20-item questionnaire with the objective to identify the possible presence of anxiety traits (STAI I), which are more stable anxiety characteristics frequently associated with anxiety disorders; and/or states (STAI II), which are anxiety characteristics associated with life circumstances [18].

### Statistical analysis

Statistical tests (chi-square, t-Test, Fisher’s Exact Test, Analyze of Variance–ANOVA and/or Kruskal-Wallis) were applied to investigate possible differences between subgroups of the sample. The quantitative data on the *Quest\_Resiliencia* were obtained through four levels of response: often, a few times, many times, almost always. The participants answered the statements by means of criteria of subjective intensity, measuring the level of agreement or disagreement. The responses gathered from the questionnaires were coded and interpreted by the SOBRARE database through established parameters for each of the resilience models analyzed. In order to reduce the number of elements of the study and to facilitate the statistical analysis of results, data were organized in a clustering analysis. Correlation analyses were performed through Spearman’s test. The statistical analysis was performed taking into account the 95% confidence interval ( $p < 0.05$ ).

### Results

Of the 60 patients included, 41 were female (68.3%). The mean age was of  $40.9 \pm 10.4$  years. Regarding educational level, 61.7% had a high-school or college. In relation to marital status, 63.3% were married. All patients have stated some kind of religious confession and 73.3% exerted some type of professional activity. Regarding the source of support obtained in the more critical periods of the disease, 58.3% obtained from parents, 18.7% from the spouse, 1.7% from their children, 5.1% from friends and 16.7% from other people. The mean interval since surgery to the present study was of  $3 \pm 2.1$  years, and the main interval between surgery and seizure recurrence was of  $2 \pm 0.9$  years. Regarding Engel’s classification, 44 patients (73.3%) were Engel class II, 12 (20%) Engel class III and 4 (6.67%) Engel class IV at the moment of the study.

The results of the application of BDI showed that 20 patients (33%) presented no depressive symptoms, whereas 14 (23%) presented mild, 16 (27%) moderate and 10 (17%) severe depressive symptoms, respectively. Regarding the results of STAI-I, 30 patients (50%) presented with slight anxiety, whereas 27 (45%) moderate and 3 (5%) with high anxiety traits. The results of STAI-II showed that 13 patients (22%) presented with slight anxiety, whereas 35 (58%) moderate and 8 (13%) with high anxiety state.

The results obtained for the eight MDB analyzed through *Quest\_Resiliencia* are shown in Figure 1. The clustering analysis allowed the distribution of patients in three classes accordingly their resilience levels to face with stressful situations: Cluster 1 (18 patients; 30%) showed moderate resilience levels; Cluster 2 (32 patients; 53.3%) showed good resilience levels; and Cluster 3 (10 patients; 16.7%) showed a strong or

MDB <sup>1</sup>	DEFINITION
Self-control	Organize the control of emotions
Body reading	Identify bodily reactions in themselves and in the other to organize in situations of high stress
Context analysis	Identify tracks and signs in the environment and assume consequences of facts and decisions
Optimism for life	Looking at life in a positive way, creative and hopeful
Self-reliance	Confidence in himself and in others to find solutions in the resolution of problems
Attract and keep people	Competence to initiate and maintain relationships to ensure protection in the environment
Empathy	Competence to identify and communicate with each other with reciprocity by consolidating the necessary interpersonal communication
Meaning of life	Competence to find and construct his/her meaning for life

<sup>1</sup>MDB: Model of Deteminant Beliefs

**Table 1:** Definition of each model of deteminant beliefs of *Quest\_Resiliencia* scale.

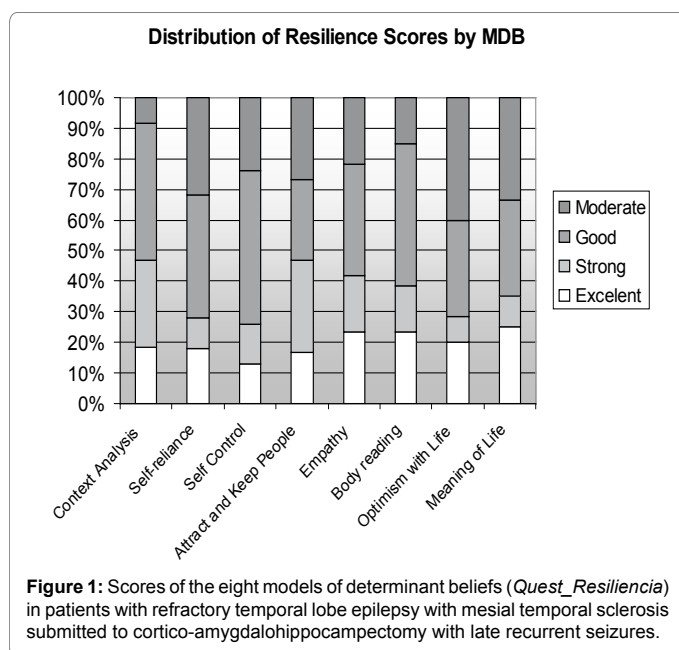
excellent resilience levels. The results of clustering analysis are showed in Table 2.

A correlation study (Spearman's test) was performed between the scores obtained in the analysis of MDB and demographic and clinical data, as well as the scores of anxiety and depressive symptoms obtained through the assessment with STAI-I/II and BDI. Overall, negative correlations were observed between the degree of resilience levels in the majority of MDB and the presence of depressive and anxiety symptoms. In addition, there was a negative correlation between the resilience

indices to stressful situations and the severity of seizure recurrence, measured through the Engel's classification, in the MDB "Optimism for life", "Self-reliance" and "Meaning of life". There was also a negative correlation between age and the resilience levels in the MDB "Meaning of life". There were no statistical significance between the resilience levels and other demographic and clinical variables. The results of correlations between the variables investigated are showed in Table 3.

## Discussion

The objective of this study was to identify the resilience levels to stressful situations in patients with TLE-MTS submitted to CAH who presented late seizure recurrence through the analysis of the eight MDB that compose the *Quest\_Resiliencia* instrument. In addition, a correlation analysis between the levels of resilience and clinical/demographic variables, as well as the presence of depressive and anxiety symptoms performed aiming at measuring the possible negative impact of these symptoms on the resilience indices. Refractory TLE-MTS is one of the most frequent epileptic syndromes, whereas CAH has been considered an important therapeutic option, with rates of remission of seizures in up to 70% in the first year [1-5]. Systematic revisions in literature have observed that seizure freedom, and particularly long-term seizure freedom (>5 years), are important criteria to achieve improvements on patients' QOL and functionality [12,13]. Despite the fact that epilepsy surgery satisfaction is considered a multidimensional construct, varying according to the type of question asked and the number of response options provided, seizure freedom has been generally associated with high levels of satisfaction, and postoperative neurologic deficits have been observed as a consistent predictor of dissatisfaction with epilepsy surgery [13]. In addition, the presence of post-surgical depression and anxiety, post-surgical lack of employment, patient perception that expectations of surgery were not met (such as the remaining AED use and the lack of ability to drive) were also associated with lower epilepsy surgery satisfaction and post-surgical reduced QOL [19].



	Cluster 1 N=1		Cluster 2 N=32		Cluster 3 N=10		Total N=60	
	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation
Context Analysis	-0.57	3.07	2.34	3.13	5.88	4.14	2.06	3.89
Self-reliance	1.19	4.46	3.28	4.11	9.92	5.84	3.76	5.33
Self control	-1.32	3.06	2.91	3.13	8.26	6.14	2.53	4.87
Attract and keep people	-1.35	3.13	3.13	3.84	6.21	3.37	2.93	4.55
Empathy	-1.79	4.33	0.68	3.50	7.21	5.10	1.03	4.98
Body reading	0.24	4.16	2.54	3.22	5.53	4.89	2.35	4.14
Optimism with Life	-3.87	4.64	3.89	3.81	9.95	5.06	2.57	6.37
Meaning of Life	-0.66	3.49	3.56	3.95	13.14	3.77	3.89	5.89

**Table 2:** Clustering analysis of the eight models of determinant beliefs (*Quest\_Resiliencia*) in patients with refractory temporal lobe epilepsy with mesial temporal sclerosis submitted to cortico-amygdalohippocampectomy and with recurrent seizures.

MDB <sup>1</sup>	BDI <sup>2</sup> r(p)	STAI-I <sup>3</sup> r(p)	STAI-II <sup>4</sup> r(p)	AGE r(p)	ENGEL r(p)
Self-control	-0.24 (0.034*)	-0.20 (0.061)	-0.24 (0.036*)	0.05 (0.340)	-0.19 (0.073)
Body reading	-0.29 (0.012*)	-0.20 (0.061)	-0.16 (0.110)	0.07 (0.278)	-0.13 (0.151)
Context analysis	-0.34 (0.004*)	-0.41 (0.001*)	-0.25 (0.027*)	-0.04 (0.356)	-0.10 (0.273)
Optimism for life	-0.37 (0.002*)	-0.29 (0.001*)	-0.18 (0.082)	-0.04 (0.370)	-0.29 (0.001*)
Self-reliance	-0.34 (0.004*)	-0.46 (<0.001*)	-0.19 (0.072)	-0.15 (0.118)	-0.25 (0.027*)
Attract and keep people	-0.27 (0.020*)	-0.08 (0.251)	-0.17 (0.100)	0.19 (0.073)	-0.09 (0.378)
Empathy	-0.25 (0.027*)	-0.21 (0.047*)	-0.22 (0.047*)	0.13 (0.151)	-0.13 (0.151)
Meaning of life	-0.47 (<0.001*)	-0.37 (<0.001*)	-0.35 (0.003*)	-0.26 (0.025*)	-0.36 (0.003*)

<sup>1</sup>MDB: Model of Determinant Beliefs; BDI: Beck Depression Inventory; STAI-I: State/Trait Anxiety Inventory (trait); STAI-II: State/Trait Anxiety Inventory (state); r: Spearman's rho; \*(<0.05).

**Table 3:** Results of a Spearman's correlation analysis between age, Engel's classification, beck depression inventory, strait/trait anxiety inventory and the eight models of determinant beliefs of *Quest\_Resiliencia* scale.

Literature studies have observed that seizure recurrence may occur in up to 30-50% of the patients submitted to CAH during the long-term follow-up and may cause negative emotional consequences [20-23]. In addition, seizure recurrence has been considered as a potentially serious adverse event which can compromise patients' medical treatment and QOL. Studies reporting measures of QOL, patient's preferences and disability in epilepsy have shown an important magnitude of the adverse effects of seizure recurrence after surgery [11-13]. Thus, the negative emotional impacts among patients with late seizure recurrence would be even higher, since they experienced a seizure-free period [24]. On the other hand, the intensity of negative experiences associated with unsuccessful medical interventions can be associated with a number of characteristics before procedures, such as the social dynamics and perceived stigma, presence of negative emotions, resilience and ability to use coping strategies, hope and optimism, and the presence of psychiatric symptoms [25].

The present results observed that most (70%) of patients included in the study presented a good, strong or excellent resilience to stress in the eight MDB analyzed. Although few studies have investigated the patient experience of unsuccessful medical interventions, particularly in the epilepsy surgery field [24], this finding would be of importance since any purpose of intervention focused on these patients should be based on specific parameters, among them their ability to deal with adverse events. The presence of high resilience levels would enable patients to develop new skills and to overcome challenges and adverse situations [16,24]. It was observed, however, a negative correlation between the presence of anxiety and depressive symptoms and the resilience indices. It is believed that approximately 10-20% of patients with epilepsy have some psychiatric comorbidities, and this prevalence increases to 50 to 70% in patients with refractory epilepsy [26-28]. Mood disorders, particularly depression, are the most frequent (24-74%), followed by anxiety disorders (10-25%), psychoses (2-7%) and personality disorders (1-2%) [26]. The presence of psychiatric comorbidities have already been observed as a risk factor for a worse surgery outcome, adversely affecting patients' QOL and possibly their patterns of coping and resilience [4,5,26-28]. Therefore, the relatively high psychiatric comorbidities observed in surgical candidates and the surgical's potentially negative impact on post-surgical seizure outcomes require a careful pre- and post-surgical psychiatric evaluation of surgical candidates with TLE-MTS with a focus on clinical, sociodemographic and psychiatric factors [27,28].

A negative correlation between the resilience indices to stressful situations and the severity of seizure recurrence, measured through the Engel's classification, was also observed. This observation occurred particularly for the MDB "Optimism for life", "Self-reliance" and "Meaning of life". Although there is a paucity of studies measuring patients' satisfaction after medical procedures, and particularly in the epilepsy surgery field, seizure freedom has been consistently associated as a predictor of post-surgical satisfaction [12,13,19,20,24]. Consequently, seizure recurrence would be considered as an important factor of lower epilepsy surgery satisfaction, with a possible negative impact on resilience levels [24]. There was also a negative correlation between age and resilience levels in the MDB "Meaning of life", possibly denoting a decrease in importance of this component associated with aging process.

Studies have investigated the possible association of sociodemographic variables (such as gender, age, level of education and social support) and the resilience levels [29,30]. The main findings have showed that other factors, such as self-efficacy, low levels of negative

mood and lower functional independence were associated with higher levels of resilience, instead of sociodemographic factors. Other variables like social support and low severity of secondary conditions also trended to significance. However, other sociodemographic and injury variables did not contribute significantly for resilience levels [29,30]. After statistical analyses, sociodemographic variables were not associated with resilience levels in the present study, maybe supporting these previous literature findings.

The present findings need to be analyzed considering a number of limitations. Firstly, the cross-sectional methodology performed after surgical procedure did not allow evaluating the impact of surgical procedure itself on patients' resilience. In addition, specific evaluation of patients' expectations before surgery, as suggested in more recent studies [13,19] were not performed. Since this study aimed to perform an exploratory evaluation of the resilience levels in patients with late seizure recurrence, we did not evaluate patients who achieved seizure freedom or those with early seizure recurrence (<six months after surgery). Despite these limitations, to our knowledge this is the first study that measured resilience levels in patients with refractory TLE-MTS who presented late seizure recurrence after CAH, correlating resilience levels to the presence of depressive and anxiety symptoms.

To conclude, the present study observed relatively elevated indices of resilience to stressful situations in patients with TLE-MTS submitted to CAH and late seizure recurrence. However, a significant negative impact of anxious and depressive symptoms in the presence of resilience was observed. Given the scarcity of research on the resilience levels in patients with epilepsy, studies that deal with this subject, as well as the ability to cope with stress, may support the development of treatment strategies which are necessary to improve their QOL. In this context, the analysis of MDB would be useful for defining such strategies. As several questions remain, continued investigation through prospective studies with larger follow-up periods is highly recommended.

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