Monitoring Anesthetic Depth Using the Patient State Index in Electroconvulsive Therapy Improves Seizure Quality

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ABSTRACT

Objectives The determination of anesthetic depth has been used to assess the optimal moment for applying electrical stimuli in electroconvulsive therapy (ECT), as some of the anesthetics used can reduce its effectiveness. In this study, seizure quality was assessed using anesthetic depth measurement with the patient state index (PSI).

Methods A prospective experimental study was conducted with a control group, including a sample of 346 stimulations (PSI = 134; Control = 212) in 51 patients admitted and diagnosed with major depressive disorders. Seizure adequacy variables (seizure time in electroencephalogram [EEG] and motor activity, visual evaluation of the EEG, ECT-EEG parameter rating scale [EEPRS], seizure concordance, central inhibition, automated parameters, and autonomic activation) were assessed using linear mixed-effects models for continuous variables and generalized linear mixed-effects models for dichotomous variables.

Results The PSI group required lower stimulation energy. The use of the PSI was associated with longer seizure time, both motor and electroencephalographic, higher quality of the EEG recording, better seizure concordance, and higher values for the automated parameters of maximum sustained coherence and time to peak coherence.

Conclusions The use of the PSI to measure anesthetic depth may reduce the electrical stimulus charge required and improve seizure quality in ECT modified with propofol.

Introduction

Electroconvulsive therapy (ECT) is the most effective treatment for resistant and more severe affective and psychotic disorders [1]. Its therapeutic effect is achieved by inducing various grand mal seizures of adequate quality. On the other hand, seizures that lack that quality can lead to therapeutic failure [2]. Modified ECT involves the use of anesthetic agents such as propofol, which can increase the seizure threshold and, thus, make optimal seizure difficult [3]. Excessively deep anesthesia can reduce the antidepressant effect of ECT and increase cognitive side effects due to the need for higher stimulus energy [3].

Various strategies for improving seizure quality include: hyperventilation, modification of the stimulus parameters, changing the position of the electrodes, use of anesthetic agents with less anti-

convulsant activity, the addition of opiates such as remifentanil, use of oral theophylline or intravenous caffeine or flumazenil before applying the stimuli, delaying the moment of stimulation with respect to the anesthetic induction, or use of monitors of the depth of anesthesia [4–6]. Among the monitors, the bispectral index has been the most studied. It has been shown to be useful in determining a state of less profound narcosis when inducing seizures [6–8]. Other authors who used the Narcotrend™ monitor also found an association between higher values of the anesthetic depth index and higher seizure quality [9]. The SedLine™ monitor calculates the patient state index (PSI) based on the spectral analysis of four simultaneous channels of the electroencephalogram (EEG) with an algorithm that incorporates a high heterogeneity of the variance at different levels of sedation/hypnosis and takes into account the brain anterior-posterior axis, as well as the coherence between bilateral regions. It provides values on a scale from 0 to 100, with the latter corresponding to the waking state [10, 11].

The use of the PSI in ECT may provide advantages over the bispectral index, because while it has been shown to equally predict loss of consciousness, it is superior in detecting intraoperative awakening [12] and is less sensitive to sources of electrical interference [11, 13]. The proposed hypothesis was that patients monitored with the PSI would experience seizures of higher quality (in terms of duration, electroencephalographic expression, and automated parameters) compared to the group treated with the traditional clinical method.

Materials and Methods

This prospective experimental study was conducted with two groups. One group received ECT determining the moment of stimulation by measuring the anesthetic depth with the PSI (i. e., the PSI group); the other was a control group (application of ECT), in which the procedure was based on the clinical assessment of the patients.

Sample

The present study sample consisted of 51 patients who underwent a total of 346 sessions: 134 for the PSI group, and 212 for the control group. The patients were admitted to the Psychiatric Unit Benito Menni CASM-HGG and recruited between November 2017 and March 2023. The inclusion criteria were the diagnosis of major depressive disorders according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) [14] and the indication of ECT (i. e., intense inhibition, high suicidal risk, psychotic symptoms, intense anxiety or agitation, history of response to ECT, lack of response or intolerance to psychopharmacological treatment) [15]. The exclusion criteria were: the presence of epilepsy, a history of electroencephalographic alterations due to other pathologies or current treatment with anticonvulsants, active use in the context of substance abuse or dependence according to DSM-IV-TR in the previous 6 months, American Society of Anesthesiologists (ASA) criteria > 3, performance of ECT in the previous 6 months, or outpatient ECT.

Demographic and clinical characteristics are shown in ▶ **Table 1**. Four patients ended the study prematurely—three due to voluntary withdrawal and one due to a Coronavirus disease-2019 infection, although their sessions were included in the study. Of the initial sample of 360 sessions, 14 were excluded from the PSI group as their values fell outside the range considered for stimulation.

Study Variables

The variables assessed were those related to patients (age, sex, body mass index [BMI]); anesthetic risk level (ASA); episode and disorder (time, severity, and symptomatology, pharmacotherapy); session procedure (session number, oximetry, and heart rate, dose of propofol, atropine, and muscle relaxant); application of the stimuli (electrode placement and energy level used) (▶ **Table 1**).

▶ **Table 2** illustrates the variables that measure seizure quality, such as motor and EEG seizure times, and the quality and extent of the seizures, including heart rate variations. Seizures were considered adequate if the following criteria were met: (a) motor seizure time ≥ 20 s or ≥ 25 s in the EEG, (b) average seizure energy index > 3,500 microV^2; (c) postictal suppression index > 70 %, and (d) maximum sustained coherence (MSC) > 90 % (motor seizure Time, ASEI, postictal suppression Index and MSC (TAIM) criteria).

A method similar to that of Rattehalli [16] was used to assess the characteristic phases of the EEG. In the case of the ECT-EEG Parameter Rating Scale (EEPRS) [17], doubtful seizures were also considered inappropriate. Seizure concordance was included as a measure of central inhibition because it is less influenced by EEG artifacts than the postictal suppression index [18]. When seizure duration could not be obtained from EEG to assess the seizure duration, motor seizure time was used instead. Unregistered automated parameters were counted as missing values. As there is no single parameter to predict seizure quality, following Gasteiger [9] and Weiss [19], seizures were also classified as adequate if they met the TAIM criteria.

It was estimated that the dose of propofol in the restimulations was equivalent to half of that administered initially. The independent variables considered were the position of the electrodes, sex, age, BMI, dose of lorazepam, pre-stimulus oxygen saturation, dose of propofol, and stimulation energy. The dependent variables were those described for the assessment of seizure quality.

For the assessment of autonomic activation, only cases not treated with β-blockers were considered, including the following independent variables: position of the electrodes, sex, age, use of atropine, dose of propofol, and stimulation energy. Measures of mood (HDRS-17) [20], severity (CGI) [21], and cognitive status with the mini-cognitive examination (MEC) [22] were taken in alternating sessions. Clinical response was considered when the HDRS-17 scale score reached 75 % of the initial score. Clinical remission was defined as a score ≤ 7 on the HDRS-17 scale and/or a score < 4 on the CGI severity score.

Procedure

The present study followed the criteria of the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee of the General Hospital of Granollers, Spain (CEIC201073003). The patients or their relatives gave informed consent for both ECT treatment and participation in the study. Subsequently, the patients were randomly assigned to one of the two groups. They remained admitted to the hospitalization unit throughout the treatment. The antidepressant dosage remained unchanged throughout the course of

▶ **Table 1** Sociodemographic and ECT procedure characteristics.

	PSI	Control	Statistical analysis	
			test	p
Patients (n)	25	26		
Sex n (%)				
Male	8 (32)	12 (46.2)	$\chi^2 = 1.07$; df = 1	0.30
Female	17 (68)	14 (53.8)		
Age mean (SD)	62.16 (13.33)	64.59 (12.93)	Mann-Whitney U test = 279.5	0.39
BMI mean (SD)	24.70 (4.37)	24.77 (5.40)	Mann-Whitney U test = 315	0.85
Current episode in days mean (SD)	123.24 (104.03)	136.85 (146.39)	Mann-Whitney U test = 314	0.83
Years of illness mean (SD)	18.63 (14.36)	19 (17.60)	Mann-Whitney U test = 305	0.71
Previous episodes mean (SD)	2.08 (2.18)	1.69 (2.07)	Mann-Whitney U test = 267	0.37
HDRS-17 score at baseline mean (SD)	20.4 (6.58)	22,6 (5.75)	Mann-Whitney U test = 238.5	0.15
CGI (Clinical Global Impression) at baseline				
4	14 (56)	11 (42.3)	Fisher's exact = 2.29	0.54
5	6 (24)	9 (34.6)		
6	4 (16)	6 (23.1)		
7	1 (4)	0 (0)		
ASA				
I	1 (4)	1 (3.8)	Fisher's exact = 5.17	0.10
II	19 (76)	21 (80.8)		
III	5 (20)	4 (15.4)		
Sessions n	134	212		
Dose of lorazepam mg, mean (SD)	1.80 (1.25)	2.62 (1.42)	Mann-Whitney U test = 8145.5	0.007
Atropine use n (%)				
yes	6 (4.5)	26 (12.3)	$\chi^2 = 5{,}93$; df = 1	0.015
no	128 (95.5)	186 (87.7)		
Dose of atropine mg/kg, mean (SD)	0.0081 (0.0025)	0.0074 (0.0023)	Mann-Whitney U test = 62	0.44
Sat O_2 (%) pre-stimulus mean (SD)	98,77 (1.34)	99.13 (0.92)	Mann-Whitney U test = 8023.5	0.014
Dose of propofol mg/kg, mean (SD)	1.13 (0.32)	1.07 (0.30)	Mann-Whitney U test = 8756	0.074
Dose of succinylcholine mg/kg, mean (SD)	0.68 (0.23)	0.64 (0.13)	Mann-Whitney U test = 9544.5	0.52
Electrode placement n (%)				
BL	100 (74.6)	193 (91)	$\chi^2 = 17.05$; df = 1	0.000
RUL	34 (25.4)	19 (9)		
Stimulus energy mC, mean (SD)	218.47 (115.6)	254.22 (110.33)	Mann-Whitney U test = 10672.5	0.000

ECT: electroconvulsive therapy; BMI: body mass index; Sat O_2: oxygen saturation on pulse oximeter; SD: standard deviation.

the ECT. Lorazepam was used as a hypnotic or anxiolytic but was never administered immediately before ECT sessions. Antipsychotic or euthymizing drugs were withdrawn. Propofol was used as an anesthetic, succinylcholine as a muscle relaxant, and atropine to prevent asystole or treat bradycardia after the electrical stimulus. The anesthesiologist determined the dosage of each based on weight, aiming to repeat the same dosage in each session.

Stimulation was performed using the Thymatron SYSTEM IV™ device (Somatics LLC, Illinois, USA). The recording of constants was performed using an Omicrom™ Vision multiparameter monitor (RGB Medical Devices SA, Madrid, Spain), and the PSI was determined using the SedLine™ monitor (Masimo Corporation, California, USA). Electroencephalographic recording was performed by placing one electrode in a frontal position and two others in each mastoid region.

Oxygenation with flow ≥ 4 L/min was applied prior to anesthetic induction and until recovery of spontaneous breathing after the seizures. Blood pressure, heart rate, electrocardiographic recording, and pulse oximetry were monitored during treatment.

The stimulus dose was calculated according to the age-based method, using a 0.5 ms pulse width for bifrontotemporal (BL) ECT or 0.25 ms for right unilateral (RUL) ECT. The ECT application procedure was identical for both groups, except for the decision on the moment of application of the electrical stimulus.

In the PSI group, propofol was administered first, followed by succinylcholine, when the PSI index began to decrease. Electrical stimulation was applied when this index showed an upward trend between values of 50 and 70. In the case of re-stimulation, the same evolution of the PSI was awaited.

▶ **Table 2** Variables to assess seizure quality.

Motor seizure time	Adequate if ≥ 20 s
Electroencephalogram (EEG) seizure time	Adequate if ≥ 25 s
Characteristic phases in EEG	One point for each phase present (hypersynchronous polyspikes, polyspikes-slow waves, and postictal suppression), with a maximum of 3 points if all were present or the termination was clear and abrupt with subsequent flattening
EEPRS (ECT-EEG parameter rating scale)	Adequate if: bilateral high amplitude spike and wave phase (visual assessment, ASEI > 1000, MIA [ASEI/tEEG] > 26) > 13 s + abrupt endpoint of seizure + adequate postictal suppression (> 74 %) + bilateral seizure duration > 24 s
ASEI	Average seizure energy index
Postictal suppression index	Postictal suppression index
MSC	Maximum sustained coherence
MSP	Maximum sustained power
TtoPP	Time to peak power
TtoPC	Time to peak coherence
Seizure concordance	Motor seizure time/electroencephalographic seizure time
Central inhibition	Appropriate if seizure concordance was ≥ 0.8 or the postictal suppression index was ≥ 80 %
Maximal HR	Maximum heart rate during seizure
HR > 140 beats/min	Heart rate greater than 140 beats/min during the seizure
Maximal - pre-stimulus HR	The difference between the maximal heart rate during the seizure and that before the electrical stimulus
motor seizure Time, ASEI, postictal suppression Index and MSC (TAIM) criteria	Adequate seizure if it meets: (a) motor seizure time ≥ 20 s or in EEG ≥ 25 s; (b) ASEI > 3500 microV^2; (c) Postictal suppression index > 70 %; and (d) MSC > 90 %

In the control group, after the administration of propofol, the cessation of the palpebral reflex was awaited before administering succinylcholine. Electrical stimulation was applied when succinylcholine-induced fasciculations had ended, and the score was 6 on the Ramsay scale [23]. In cases of re-stimulation, the stimulus was not applied until 1 minute had passed since the previous seizure.

The PSI monitoring was not used in the control group and the Ramsay scale score was not applied to the PSI group.

In both groups, restimulation was performed when the duration of the seizures was less than 25 s in the EEG or 20 s at the motor level, increasing the energy by 50.4 mC (10 %) in the second stimulus, and by 504 mC (100 %) in the third, following the same guidelines. In cases of an MEC score < 23, the electrode position became RUL. It was changed from RUL to BL ECT if no improvement had been experienced after six sessions of starting treatment with the former. The frequency was two sessions per week. The patients ended the study when: they achieved clinical remission, if a stimulus of 504 mC of energy did not achieve adequate seizures, or if there was no clinical remission after 12 sessions.

Statistical Analysis

Descriptive statistics (i. e., mean, standard deviation, and frequency) were used to characterize the sample. A p-value < 0.05 was considered statistically significant. Graphical assessment and the Kolmogorov-Smirnov test were used to examine the distribution of the variables. The Mann-Whitney U-test was used to analyze quantitative variables, and the χ^2 test was used for the qualitative data. When the contribution of the PSI in the improvement of seizure quality was assessed, linear mixed-effects models were used for continuous variables and generalized linear mixed-effects models for dichotomous variables. The two models allowed for the analysis of fixed and random effects.

Due to the existence of collinearity between the variables age and energy, the analysis was performed separately for each of them, together with the rest of the independent variables. The statistical analysis was performed using SPSS (Version 23; IBM Corp., New York, USA) and R software [24]. The models were adjusted for all possible combinations of the covariates to discard those that were irrelevant. This way, the variable lorazepam dose was discarded. Following Rothman [25], it has not been deemed necessary to make corrections for multiple comparisons.

Results

▶ **Table 1** presents the characteristics of the ECT procedure. The control group received a higher dose of lorazepam during treatment, used a greater but non-significant amount of atropine, and also exhibited a better oxygen saturation prior to the stimuli. The PSI group was treated with significantly more sessions using the RUL position and with a lower mean stimulus energy. The mean PSI value before the application of the stimuli was 56.57 ± 6.51.

▶ **Table 3** illustrates the parameters of seizure quality for each study group. The PSI group obtained: a higher percentage of adequate seizures according to the scores of the three assessment methods (EEG phases, EEPRS, and TAIM criteria), longer seizure duration, both motor and electroencephalographic, and higher mean values in the automated parameters. This group also obtained better results in seizure concordance and central inhibition.

There were no significant differences between the two groups regarding clinical improvement (clinical response: $\chi^2 = 0.18$, df = 1, $p = 0.67$; clinical remission: $\chi^2 = 0.64$, df = 1, $p = 0.42$), nor on MEC scores at the end of the treatment ($t = -2.07$, df = 150.94, $p = 0.26$).

In the linear models that included age or energy as an independent variable for seizure quality, the use of the PSI was associated with better seizure quality according to the EEG phases. Age, stimulus energy, propofol dosage, electrode placement, and BMI were also associated with measures of seizure quality. Thus, in the age model, the RUL electrode position and older age were significantly associated with a worse score on the EEPRS and per the TAIM criteria. Conversely, in the energy model, the RUL electrode position was significantly related to poorer seizure quality according to the EEG results and the EEPRS. BMI showed a significantly negative association with seizure quality in EEG in both models (▶ **Table 1**, supplementary data).

▶ **Table 3** Parameters of seizure quality.

	PSI	Control
Seizure quality (according to EEG phases) n (%)		
0	0	2 (1)
1	7 (4.7)	33 (15.7)
2	32 (23.9)	85 (40.5)
3	95 (70.9)	90 (42.9)
Seizure quality (EEPRS), n (%)		
Inadequate	1 (0.7)	24 (11.4)
Equivocal	89 (66.4)	141 (66.8)
Adequate	44 (32.9)	46 (21.8)
Seizure quality (meet TAIM criteria)		
Yes	43 (34.1)	39 (20.9)
No	83 (65.9)	148 (79.1)
Seizure concordance, mean (SD)	0.68 (0.18)	0.58 (0.20)
Central inhibition n (%)		
Adequate	67 (50)	71 (33.5)
Inadequate	67 (50)	141 (66.5)
Motor seizure time (s), mean (SD)	27.08 (10.23)	19.76 (10.72)
EEG seizure time (s), mean (SD)	41.13 (14.97)	35.28 (20.33)
ASEI (microV^2) mean (SD)	9296.2 (9241.48)	7617.44 (10749.16)
ASEI > 3500 microV^2, n (%)	84 (65.6)	62.33 (26.69)
Postictal suppression index (%), mean (SD)	68.3 (27.42)	62.33 (26.69)
Postictal suppression index > 70 % n, (%)	59 (50.4)	80 (50.6)
MSP (microV^2), mean (SD)	17848.03 (16679.65)	13763.72 (17079.06)
MSP > 6000 microV^2, n (%)	92 (70.2)	100 (55.2)
MSC (%), mean (SD)	90.57 (13.95)	82.63 (21.43)
MSC > 90 %, n (%)	98 (75.4)	97 (52.7)
TtoPP (s), mean (SD)	19.01 (16.72)	14.13 (8.26)
TtoPP < 20 s, n (%)	84 (64.1)	149 (81)
TtoPC (s), mean (SD)	32.26 (64.58)	17.44 (10.74)
TtoPC < 20 s, n (%)	61 (47.3)	126 (68.5)
Maximal HR (beats/min), mean (SD)	126.53 (21.86)	120.29 (25.06)
Maximal - pre-stimulus HR (beats/min), mean (SD)	37.66 (22.68)	29.3 (24.7)
HR > 140 beats/min n (%)	37 (30.3)	37 (21.4)

ASEI: Average seizure energy index; EEG: electroencephalogram; EEPRS: ECT–EEG Parameter Rating Scale; HR: heart rate; TtoPC: time to peak coherence; TtoPP: time to peak power; MSP: maximum sustained power; MSC: maximum sustained coherence; SD: standard deviation.

In the two models, the PSI was positively related to better seizure concordance, both motor seizure time and electroencephalographic time, MSC, and time to peak coherence (TtoPC) (▶ **Table 4**). In both models, the propofol dosage was also significantly and inversely related to motor seizure time and EEG seizure duration, while BMI only negatively correlated with seizure duration in the EEG. In the model with energy as the independent variable, energy showed a significant and inverse association with seizure concordance and with the automated parameters maximum sustained power (MSP) and Time to peak power (TtoPP) (▶ **Table 2**, Supplementary data).

The PSI was the only factor in both models that was positively and significantly associated with better seizure quality according to the EEG phases, greater seizure concordance, longer seizure time (both motor and electroencephalographic), and higher values on the MSC index (▶ **Table 4**). The PSI group obtained higher values than the control group in the average maximum post-stimulus heart rate, the pre-post difference, and the number of occasions where the value of 140 beats/min was exceeded. None of these variables reached significant differences between groups according to the linear models in autonomic activation (see ▶ **Table 3**, supplementary data).

Discussion

The main findings of the present study are the association between the use of the PSI and the improvement in seizure quality assessed through electroencephalographic recording and some of the parameters that are used as seizure indicators (duration of motor and electroencephalographic seizure, seizure concordance, MSC). In addition, our procedure required lower stimulation energy compared to the control group. These results align with those obtained in studies that measured anesthetic depth using other monitors [6, 9, 26].

Initially, one might think that the control group was at a disadvantage due to a deeper level of anesthesia when applying the stimulus at a Ramsay scale score of 6. However, this scale does not distinguish between levels of depth and those of sedation, and therefore, the score alone does not confirm that the patients in the control group had a higher level of narcosis than those in the PSI group [23]. The lack of PSI monitoring in the control group prevents confirmation of the extent to which anesthetic depth differed between the two groups when applying the electrical stimulus.

Unlike the study by Kranaster [6] using the bispectral index, its use has not been found to be associated with an improvement in the postictal suppression index, although it was associated with seizure concordance, which also reflects the inhibitory brain activity to end seizure [27]. The older age of the patients in our sample explains this difference since age inversely affects the postictal suppression index [26, 28].

The results of the present study indicate a relationship between anesthetic depth and the MSC parameter, as in the studies by Kranaster et al. [6] and Gasteiger et al. [9]. This measure refers to the synchronization of the seizure between both hemispheres, that is, one of the parameters that, together with the postictal suppression index, has been proposed as a possible predictor of the response to ECT [29], since the interhemispheric coherence measured during the seizure can be considered a reflection of its generalization [30]. A prolongation of TtoPC has been observed and related to worse quality [19]. Similar results have been found using theophylline as a seizure enhancer, yet the interpretation of these

▶ **Table 4** Results of the PSI and dependent variables to determine seizure quality according to linear models that include age or stimulus energy models.

	Model 1 (age)	Model 2 (energy)
	Odds Ratio (CI)	
Seizure quality (EEG)	6.91 (1.59, 35.28)**	8.11 (0,01, 0,8)**
Seizure quality (EEPRS)	2.2 (0.72, 6.92)	2.31 (0.01, 0.78)
Seizure quality (TAIM criteria)	2.84 (0.98, 8.91)	2.46 (0.01, 1.56)
HR > 140 beats/min	1.1 (0.22, 5.53)	1.08 (0.21, 5.58)
	Coefficient β (CI)	
Maximal HR	3.09 (−7.05, 13.22)	3.69 (−6.84, 14.23)
Maximal - pre-stimulus HR	7.35 (−1.48, 16.23)	7.8 (−1.29, 16.89)
Seizure concordance	0.1 (0.04, 0.16) **	0.09 (0.02, 0.15) *
Central inhibition	0.14 (−0.01, 0.29)	0.13 (−0.02–0.28)
Motor seizure time	8.3 (3.38, 13.22)**	8.28 (3.4, 13.16)**
EEG seizure time	8.01 (1.23, 14.85)*	8.02 (1.14, 14.87)*
ASEI	1218.32 (−2805.19, 5258.4)	946.37 (−3116.03, 4995.35)
Postictal Suppression Index	0.66 (−7.81, 9.3)	− 0.47 (−9.64, 8.71)
MSP	2833.84 (−3507.98, 9233.53)	1901.98 (−4242.33, 8021.26)
MSC	8.18 (1.88, 14.57)*	7.65 (1.24, 14.06)*
TtoPP	4.4 (0.25, 8.6)	3.46 (−0.53, 7.41)
TtoPC	14.08 (3.87, 24.88)*	14.67 (3.87, 26.08)*

(.) p = 0.05–0.1; (*) p = 0.01–0.05; (**) p = 0.001–0.01; PSI: patient state index; ASEI: Average seizure energy index; EEG: electroencephalogram; EEPRS: ECT–EEG Parameter Rating Scale; HR: heart rate; TtoPC: time to peak coherence; TtoPP: time to peak power; MSP: maximum sustained power; MSC: maximum sustained coherence; SD: standard deviation.

results is equivocal [29], although some authors have related them with presenting longer seizures [31].

These data raise the question of whether the strategy used to improve seizure quality has a specific effect only on some parameters that measure it, in the same way, that the modifications made to improve the seizure threshold often differ from those that prolong seizure duration [29, 31, 32], or for example, the observed influence of hyponatremia or the use of theophylline alone using the MSC parameter [18, 29].

Some authors, like Ingram et al. [33], have considered automated parameters to be less reliable than a review of the EEG tracing performed by an expert clinician due to the presence of artifacts in the electrical signals. In this sense, the use of the PSI also achieved a better seizure expression in the EEG.

Given that the EEG may have a limited capacity to determine seizure adequacy, a patient's heart rate may more accurately and significantly reflect the effectiveness of ECT as it shows the diffusion of the seizure and the activation of deep brain regions such as the diencephalon [34]. Thus, induced peak heart rate has also been considered in addition to the duration and power of the seizures, interhemispheric coherence, and postictal suppression [35, 36]. We did not find a positive association between the use of the PSI and this parameter. The attenuating effect of the sympathetic response caused by propofol might limit a maximum post-stimulus heart rate with higher values [37].

It is worth noting that the significant association of the use of the PSI precisely occurred with some parameters related to the neurophysiological aspects proposed for the antidepressant action of ECT (seizure concordance and interhemispheric coherence) [27]. Although benzodiazepines can affect seizure quality, it has been observed that the anticonvulsant effect of the anesthetic can have a greater impact than psychotropic medication [26]. We observed a significant negative association between the dose of propofol and the motor and electroencephalographic seizure time. Conversely, the dose of lorazepam did not reach statistical significance to be included in the correlation models. This finding differs from the results obtained by Minelli et al. [36], who found a negative effect of benzodiazepines because they affected synchrony between hemispheres and post-stimulus tachycardia, especially in the unilateral ECT modality. If this, in fact, happened, it would have disadvantaged the PSI group because they had a greater number of RUL sessions.

As there are no previous studies presenting the ideal PSI value in ECT, a range between 50 and 70 was used for stimulation based on the fact that the average values for loss of consciousness in the PSI would be between 30 and 45, influenced by the anesthetic protocol used and high interindividual variability [38]. The value of 50 was considered the threshold between consciousness and non-consciousness [39]. In comparison with other monitors, other authors have proposed a value > 65 in the bispectral index [6] and > 41 for Narcotrend™ [9] in ECT. Therefore, this is an aspect that should be assessed in further research.

The lack of differences in clinical response with the HDRS-17 between the two groups can be attributed to the fact that the score of this scale was used to determine when the patient completed the study, decreasing the likelihood of detecting differences in clinical response. Instead, other procedural variables of clinical relevance (e. g., number of sessions, restimulations, stimulus charge used) may differ between the two groups. Moreover, an adequate seizure does not ensure the optimal treatment outcome, as the predictive value of ictal EEG parameters regarding clinical outcomes is questioned [40], and clinical factors influencing the response to ECT are also known [41]. Other authors have demonstrated that delaying the application of the electrical stimulus relative to the administration of the anesthetic agent—without using anesthetic depth monitoring—can improve seizure quality, although there is no consensus on the optimal delay [42]. The use of anesthetic agents with less anticonvulsant effect than propofol could improve seizure expression but would reduce the utility of determining anesthetic depth.

Although this was a prospective and novel study addressing the use of the PSI during ECT, several limitations should be considered, such as: this was not a double-blind study; the values of the anesthetic depth indices are not yet standardized for psychiatric populations, which may exhibit anomalies in EEG recording with respect to the diagnosis or the use of psychotropic drugs that could interfere with the determination of the PSI, and whose presence was not discarded prior to inclusion in the study (a baseline EEG recording could resolve this issue); analysis of the evolution of HDRS-17

scores throughout treatment in each patient could show clinical differences between the two groups; although the MEC has been widely used, more sensitive neuropsychological tests could better detect differences in cognitive adverse effects between the two groups; the use of propofol may limit the extrapolation of these results to patients in whom another anesthetic agent is used.

Notwithstanding, the findings of the present study, such as a lower stimulus load, a longer motor and electroencephalographic seizure time, a higher quality in the EEG recording of the seizure, and higher MSC values, allowed us to conclude that the measurement of the anesthetic depth using the PSI improved seizure quality and is useful in determining the optimal time for applying the electrical stimulus compared to the usual ECT. Our findings also enable us to conclude that this procedure can maintain the efficacy of ECT, although it did not cause less cognitive impairment.

Conflict of Interest

The authors declare that they have no conflict of interest.

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