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ORIGINAL ARTICLE

Randomized Clinical Trial

Effect of quantitative consciousness index on seizure parameters during electroconvulsive therapy in patients with major depressive disorder

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Abstract

BACKGROUND

Electroconvulsive therapy (ECT) is both an effective treatment for patients with major depressive disorder (MDD) and a noxious stimulus. Although some studies have explored the effect of sedation depth on seizure parameters in ECT, there is little research on the noxious stimulation response to ECT. In this study, we used two electroencephalography (EEG)-derived indices, the quantitative consciousness (qCON) index and quantitative nociceptive (qNOX) index, to monitor sedation, hypnosis, and noxious stimulation response in patients with MDD undergoing acute ECT.

AIM

To evaluate the effect of anesthesia depth based on the qCON and qNOX indices on seizure parameters.

METHODS

Patients with MDD (n = 24) underwent acute bilateral temporal ECT under propofol anesthesia. Before ECT, the patients were randomly divided into three groups according to qCON scores (qCON60-70, qCON50-60, and qCON40-50). Continuous qCON monitoring was performed 3 minutes before and during ECT, and the qCON, qNOX, vital signs, EEG seizure parameters, and complications during the recovery period were recorded. The 24-item Hamilton Rating Scale for Depression, Zung's Self-rating Depression Scale, and Montreal Cognitive Assessment scores were evaluated before the first ECT session, after the fourth ECT session, and after the full course of ECT.

RESULTS

A total of 193 ECT sessions were performed on 24 participants. The qCON index significantly affected the EEG seizure duration, peak mid-ictal amplitude, and maximum heart rate during ECT ($P < 0.05$). The qNOX index significantly affected the post-ictal suppression index ($P < 0.05$). Age, number of ECT sessions, and anesthetic-ECT time intervals also had a significant effect on EEG seizure parameters ($P < 0.05$). However, there were no significant differences in complications, 24-item Hamilton Rating Scale for Depression scores, Zung's Self-rating Depression Scale scores, or Montreal Cognitive Assessment scores among the three groups ($P > 0.05$).

CONCLUSION

Electrical stimulation at a qCON index of 60-70 resulted in better EEG seizure parameters without increasing complications in patients with MDD undergoing bilateral temporal ECT under propofol anesthesia.

Key Words: Electroconvulsive therapy; Propofol; Nociception; Depression; Electroencephalogram

Core Tip: Anesthesia depth based on quantitative consciousness index and quantitative nociceptive index affects electroconvulsive therapy (ECT) seizure parameters during acute ECT in patients with major depressive disorder. Electrical stimulation at a quantitative consciousness index of 60-70 will improve electroencephalography seizure parameters while not increasing complications. The quantitative nociceptive index had a significant effect on post-ictal suppression index, and patients with higher post-ictal suppression index may suffer from greater noxious stimulation during ECT. We should not only consider the effect of sedation depth on the quality of seizure but also the degree of noxious stimulation brought by the treatment technology itself during ECT.

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INTRODUCTION

Depression is a common clinical mental illness characterized by high incidence, recurrence rate, suicide rate, and disability rate[1-3]. As a first-line treatment for treatment-resistant depression with a high risk of suicide and obvious psychiatric symptoms, electroconvulsive therapy (ECT) has been shown to have a definite therapeutic effect on depression[4-7]. Whether the mechanism of action for ECT on mental diseases can be contributed to the effect of seizures, electric currents on the brain alone, or their combined effects is not yet known[8,9]. Nonetheless, extensive epileptic discharge into the cerebral cortex is necessary to ensure ECT[10-13].

The quality of seizures can be continuously evaluated using electroencephalography (EEG) parameters such as EEG seizure duration, peak mid-ictal amplitude, post-ictal suppression index (PSI), coherence, and maximum heart rate during ECT[14,15]. There are differences in seizure thresholds among patients. The quality of seizures in ECT is affected by patient factors, treatment techniques, and anesthesia, including age, sex, previous ECT history, benzodiazepine medication, electrode position, pulse width, electrical dose, ECT treatment sessions, anesthetic drugs, and anesthesia depth[16-18]. Most anesthetics, such as barbiturates or propofol, have anticonvulsant properties, which have a negative impact on the quality of seizures and may affect the antidepressant effect[19-21]. Modifying the parameters of ECT, such as stimulus intensity, can improve the quality of seizures, but may also lead to higher cognitive side effects[13,22]. The depth of anesthesia also affects seizure quality in ECT, and seizure quality is higher under light anesthesia[23]. However, if anesthetic drugs are reduced to improve the quality of seizures, patients may be at risk of awareness, especially during the positioning of unilateral non-dominant electrodes[24].

To determine the appropriate anesthesia depth for ECT, anesthesiologists use anesthesia depth monitoring equipment [such as bispectral index (BIS) and Narcotrend] to guide anesthesia for ECT[25-29]. However, the EEG indices contained in the BIS and Narcotrend can only evaluate the sedative and hypnotic effects of anesthesia rather than the nociceptive stimulus response during general anesthesia[30-33], and all of them are affected by age and body temperature[34-36]. Currently, the observation of nociceptive stimulus responses is mainly based on heart rate variability (HRV), skin conductance (SC), a combination of HRV and SC parameters, changes in pupil size, or other parameters of HRV-derived parasympathetic nerve activity[37-43]. However, brain signal analysis methods based on EEG are usually empirical, because there is no clear consensus on the characteristics of EEG changes in the process of nociceptive stimulus response. Monitoring the quantitative consciousness (qCON) index (also known as the index of consciousness, IoC1) and the quantitative nociceptive (qNOX) index (also known as the pain index, IoC2) is a relatively new method based on dynamic EEG to monitor anesthesia depth. It uses an adaptive neuro-fuzzy inference system and non-linear analysis to calculate a value between 0 and 99, independent of the autonomic nerve activity. The qCON index is similar to the BIS and Narcotrend indices, which mainly reflect the depths of sedation and hypnosis. A qCON of 80-99 represents wakefulness, 60-79 represents sedation or light anesthesia, 40-60 represents appropriate anesthesia depth, and < 40 represents deep anesthesia[44]. The qNOX index reflects the degree of nociceptive stimulus response; the higher the qNOX index, the higher the nociceptive stimulus response. The qCON index combined with the qNOX index has been widely used to monitor anesthesia depth under general anesthesia, and they are considered to be well correlated with the BIS index for monitoring of sedative hypnosis depth[32-33,44-47], while their usefulness for monitoring nociceptive stimulus response has limited confirmation[48-50]. As ECT is both a therapeutic method and noxious stimulus for patients[51,52], it seems that a combination of the qCON and qNOX indices is appropriate for monitoring the depth of anesthesia during ECT. However, to the best of our knowledge, no such study has been conducted.

Therefore, in this study, the qCON and qNOX indices were combined to monitor the anesthesia depth during ECT, and the primary aim was to evaluate the effect of different anesthesia depths on EEG seizure parameters in patients with major depressive disorder (MDD) undergoing ECT. We hypothesized that light anesthesia would achieve better EEG seizure parameters. As a secondary objective, we evaluated the relationship between the qNOX index and EEG seizure parameters. We also evaluated adverse events during the recovery period and the clinical effects on patients with MDD after ECT under different anesthesia depths.

MATERIALS AND METHODS

Sample and study design

Participants were recruited from among psychiatric inpatients at the First Affiliated Hospital of Chongqing Medical University from June 12, 2023 to December 15, 2023. Although the view that EEG seizure duration is the main determinant of the treatment effect is changing, an EEG seizure duration < 25 seconds is still considered insufficient in the treatment of depression[53], and a motor duration < 15 seconds can lead to insufficient treatment[54]. Therefore, the sample size calculation in this study considers EEG seizure duration as the main goal. According to Kranaster *et al*[55], the correlation coefficient between anesthesia depth and EEG seizure duration was 0.26, assuming that qCON and BIS monitoring can also reflect anesthesia depth, and assuming the test is a bilateral test with an α of 0.05 and assurance (1-β) of 0.8. In one course of ECT, there are an average of eight sessions. The correlation coefficient for this group was 0.5. The participants were randomly divided into three groups before ECT: Group 1, with a qCON of 60-70, group 2, with a qCON of 50-60, and group 3, with a qCON of 40-50. A sample size of sufficient power was estimated to be 21 patients, and the required sample size for enrollment was estimated to be 24 patients, considering a 10% loss before the completion of the study.

Inclusion criteria: (1) Inpatients who met the diagnostic criteria for MDD in the 11th edition of the International Classification of Diseases; (2) Age 18-60 years; (3) Primary school education or above; (4) A 24-item Hamilton Depression Rating Scale (HAM-D) scores of ≥ 35 points; (5) Indications for ECT; (6) Normal hearing and vision (including color discrimination ability); and (7) Voluntary agreement to participate in this study and sign informed consent forms, while their guardians signed informed consent forms simultaneously. Exclusion criteria: (1) Presence of comorbid physical diseases, organic brain diseases, other mental diseases, or a history of alcohol or psychoactive substance abuse; (2) Primary insomnia; and (3) Pregnant and lactating women.

Randomisation and masking

In this study, a computer randomization method was used. First, the participants were numbered in sequence, and random numbers were generated using SPSS 26 software (IBM, Armonk, NY, United States). The random numbers were ranked and sorted. According to the order, the participants were randomly divided into three groups: qCON 60-70, qCON 50-60, and qCON 40-50. The participants' groupings were placed in 24 envelopes and maintained by a nurse anesthetist who was not involved with the treatment. Because anesthesiologists must decide the timing of electrical stimulation according to the qCON index in this study, a single-blind method was adopted. The participants and data collectors were blinded to the grouping situation.

Anesthesia and ECT procedures

A Thymatron System IV (Somatics LLC, Venice, FL) device was used as the ECT device. All the participants were placed with a traditional bilateral temporal stimulation electrode (short pulse: 0.5 ms; stimulation mode: DGX). The stimulus intensity was based on age; that is, the power was set to 50% of age. The dose was adjusted according to EEG seizure parameters and clinical reactions of the patients, which were determined by psychiatrists. A two-channel EEG with electrodes at the Fp1 and Fp2 sites was used to determine the length and characteristics of the EEG seizures. None of the participants stopped using antidepressants before ECT. All participants had fasted for 8 hours and been deprived of water for 2 hours. Continuous qCON monitoring (Apollo-9000A, Chongqing Xider Medical Instrument Co., Chongqing, China) was performed 3 minutes before and during ECT. Blood pressure, heart rate, and pulse oxygen saturation were monitored simultaneously, and oxygen was administered for 3 minutes in advance. qCON monitoring uses three electrodes to collect the original EEG signals from the forehead. Monitoring included qCON, qNOX, burst suppression, and signal quality index. All participants were anesthetized by the intravenous administration of propofol (1.5 mg/kg; AstraZeneca, Oxford, United Kingdom; concentration: 10 mg/mL) for 30 seconds. After propofol injection, the anesthesiologist continuously referred to the patient's name. When the patient was confirmed to have no response and the eyelash reflex disappeared, the patient was injected with succinylcholine (1 mg/kg; Shanghai Xudong Haipu Pharmaceutical Co., Shanghai, China, concentration: 2 mL/0.1 g) for muscle relaxation and was given mask ventilation. After propofol injection, the qCON index first rapidly decreased and then slowly rebounded. According to the grouping of participants, electrical stimulation was performed when the qCON index rose to the corresponding range. If the patient still had consciousness or eyelash reflex after receiving 1.5 mg/kg of propofol, anesthesiologists increased the dose of propofol. After the seizure, mask ventilation was continued until the patient recovered from the anesthesia.

During the treatment period, blood pressure, heart rate, pulse oxygen saturation, time intervals (the interval between anesthesia induction and electrical stimulation), dose of anesthetic drugs, qCON index, qNOX index, burst suppression, signal quality index, EEG seizure parameters, recovery time (from the end of the seizure to eye opening), and complications during the recovery period were recorded. The 24-item HAM-D, Zung's Self-rating Depression Scale (SDS), and Montreal Cognitive Assessment (MoCA) scores of each subject were evaluated 24 hours before the first ECT, 24 hours after the fourth ECT, and 24 hours after the full course of ECT. The 24-item HAM-D and MoCA scores were evaluated by psychiatrists, and SDS scores were scored by the participants themselves.

Statistical analysis

All statistical analyses were performed using SPSS 26 software (IBM). All measurement data were subjected to Shapiro-Wilk normality tests and represented by mean ± SD, if normally distributed or median and interquartile range if not. The demographic data (age, height, and weight), respiratory and circulatory indexes (blood pressure, heart rate, and pulse oxygen saturation) at baseline before ECT, and 24-item HAM-D, SDS, and MoCA scores at the time of the treatment session were analyzed by one-way analysis of variance (ANOVA). Multiple comparisons were used for comparisons between groups, and the Kruskal-Wallis test was used for non-normally distributed data. A generalized linear mixed-effect model was used to analyze the effects of patient, treatment, and anesthesia factors on EEG seizure parameters. The repeated measurements were the treatment sessions of ECT, the covariance structure was a first-order autoregressive structure (AR1), and the fixed effect included a random intercept. Based on the qCON index, the anesthesia depth was divided into three levels. With anesthesia depth as an independent variable and the same covariance structure, the effect of anesthesia depth on EEG seizure parameters was analyzed using a single generalized mixed-effect model. The clinical effect of ECT (24-item HAM-D scores, SDS scores, and MoCA scores) was evaluated using repeated-measures ANOVA. Adverse events during the recovery period were analyzed using Fisher's exact test. The statistical significance test was a double-tailed test; significance was set at $P < 0.05$, and the Bonferroni correction was used for multiple comparisons between groups.

RESULTS

Characteristics of patients

A total of 193 ECT sessions performed on 24 participants were available for analysis. In the 193 ECT treatment sessions, no patients received additional doses of propofol, and the dose of propofol was 1.5 mg/kg in all patients. The baseline demographic and clinical characteristics of the enrolled patients did not differ among the three groups (Table 1).

Clinical factors on EEG seizure parameters

The qCON index significantly affected the EEG seizure duration, peak mid-ictal amplitude, and maximum heart rate during ECT ($P < 0.05$). The higher the qCON index during electrical stimulation, the longer the EEG seizure duration, the larger the median amplitude, and the higher the maximum heart rate during ECT. qNOX index had a more significant effect on PSI ($P < 0.05$); the higher the qNOX index, the higher the PSI. Age significantly affected the EEG seizure duration and recovery time of patients ($P < 0.05$). The older the age, the shorter the EEG seizure duration and the longer the recovery time. The number of ECT had significant effects on the EEG seizure duration, average seizure energy index (ASEI), and PSI ($P < 0.05$). The longer the treatment sessions, the shorter the EEG seizure duration, the lower the ASEI, and the lower the PSI. The anesthetic-ECT time intervals also had a significant effect on the EEG seizure duration and PSI ($P < 0.05$); the longer the anesthetic-ECT time intervals, the longer the EEG seizure duration, and the higher the PSI, while the charge dose had no significant effect on the seizure parameters (Table 2).

Anesthesia depth on EEG seizure parameters

The effect of anesthesia depth on EEG seizure parameters was analyzed using a generalized mixed-effects model alone. The results showed that anesthesia depth significantly affected the maximum heart rate, EEG seizure duration, PSI, peak mid-ictal amplitude and coherence during ECT ($P < 0.05$); the lighter the anesthesia, the higher the maximum heart rate, the longer the EEG seizure duration, the larger the median amplitude, the higher the PSI, and the higher the coherence. However, this had no significant effect on ASEI or recovery time (Table 3).

Clinical effects and adverse events

There were no significant differences in the 24-item HAM-D, SDS, and MoCA scores (Figure 1) before and after ECT or in complications during the recovery period among the three groups (Table 4).

Table 1 Demographic data, Hamilton Depression Rating Scale score, Zung's Self-rating Depression Scale score, Montreal Cognitive Assessment score, and cardiorespiratory findings of three groups of patients

Characteristics	Group 1: qCON 60-70	Group 2: qCON 50-60	Group 3: qCON40-50
Age, years	32.3 ± 14.2	33.9 ± 15.0	31.9 ± 13.6
Male	2/8	1/8	1/8
Weight, kg	55.6 ± 7.0	55.9 ± 13.6	57.8 ± 15.5
Height, cm	162.3 ± 9.1	162.1 ± 9.9	164.9 ± 5.9
Propofol dose, mg (IQR)	85.5 (72.0, 88.5)	87.0 (70.5, 100.5)	85.5 (66.0, 105.0)
Succinylcholine dose, mg (IQR)	57.0 (48.0, 59.0)	58.0 (47.0, 67.0)	57.0 (44.0, 70.0)
Interventions, median (IQR)	8 (7, 9)	8 (6.5, 10)	8 (7.5, 8)
Baseline HAMD-24 score	42.8 ± 4.4	41.3 ± 4.4	42.3 ± 4.0
HAMD-24 score after fourth ECT	21.0 ± 4.4	22.4 ± 5.9	27.9 ± 7.7
HAMD-24 score after full ECT course	12.3 ± 4.7	13.3 ± 5.1	17.0 ± 6.0
Baseline SDS score	69.2 ± 7.4	65.8 ± 6.7	67.8 ± 6.0
SDS score after fourth ECT	57.7 ± 7.9	56.1 ± 11.6	60.3 ± 5.3
SDS score after full ECT course	49.7 ± 3.9	49.7 ± 5.7	54.4 ± 5.4
Baseline MoCA score	24.8 ± 2.6	25.1 ± 2.9	24.9 ± 2.9
MoCA score after fourth ECT	22.6 ± 2.1	23.5 ± 3.3	22.6 ± 3.1
MoCA score after full ECT course	23.4 ± 1.7	24.4 ± 2.9	24.1 ± 2.5
Cardiorespiratory data			
Baseline heart rate, bpm	89.0 ± 9.8	87.0 ± 16.8	84.3 ± 19.3
Baseline systolic blood pressure, mmHg	118.9 ± 14.1	113.5 ± 14.0	112.1 ± 11.3
Baseline diastolic blood pressure, mmHg	74.4 ± 8.8	74.3 ± 11.3	70.0 ± 7.1
Baseline peripheral oxygen saturation, %	96.8 ± 1.4	97.3 ± 1.2	97.3 ± 1.2

ECT: Electroconvulsive therapy; HAM-D: Hamilton Depression Rating Scale; SDS: Zung's Self-rating Depression Scale; MoCA: Montreal Cognitive Assessment; qCON: Quantitative consciousness.

DISCUSSION

In this study, the qCON and qNOX indices were combined to monitor the anesthesia depth of acute ECT in patients with MDD. The qCON index significantly affected the EEG seizure duration, peak mid-ictal amplitude, and maximum heart rate during bilateral temporal ECT under propofol anesthesia. The qNOX index has a significant effect on PSI, which has not been previously reported. This study also found that age, ECT treatment sessions, and anesthetic-ECT time intervals had significant effects on EEG seizure parameters, which is consistent with previous studies[12,19,29,56-58].

The qCON index is similar to the BIS and Narcotrend indices, which mainly reflect the depths of sedation and hypnosis. In this study, the participants were divided into three groups according to the range of the qCON index during electrical stimulation. Participants in the three groups were subjected to electrical stimulation at different depths of anesthesia. The results showed that anesthesia depth significantly affected the EEG seizure duration, PSI, peak mid-ictal amplitude, EEG coherence, and maximum heart rate during ECT. The lighter the anesthesia, the better the EEG seizure parameters and the higher the maximum heart rate during ECT, which was consistent with previous studies on the effect of anesthesia depth monitored by BIS or Narcotrend on EEG seizure parameters during ECT[28,29,59-61].

None of the patients in the three groups were aware during their ECT treatments. The main reasons are as follows. First, after the injection of propofol, the anesthesiologist continuously called the patient's name. When they ensured that the patient had no response and the eyelash reflex had disappeared, succinylcholine was injected for muscle relaxation. Second, the timing of electrical stimulation should be when the qCON index increases to the corresponding range, rather than immediately after propofol injection. After propofol injection, the qCON index decreased rapidly and then increased slowly, indicating that the blood concentration of propofol in the brain reached its peak and was then redistributed, and the ECT in this study adopted a bilateral temporal position. When patients are treated with bilateral temporal ECT, which tends to obliterate the memory of the ECT procedure[24]. Therefore, even if patients are conscious during ECT, they are unlikely to remember their consciousness after treatment.

Table 2 Generalized linear mixed model examining effect of treatment, patient, and anesthesia factors on electroencephalography seizure parameters

Covariate/dependent	EEG endpoint (s)			ASEI (μV²)			PSI (%)			Mid-ictal amplitude (μV)			Coherence (%)			Maximum heart rate, (bpm)			Recovery time (min)		
	Est	SE	*P* value	Est	SE	*P* value	Est	SE	*P* value	Est	SE	*P* value	Est	SE	*P* value	Est	SE	*P* value	Est	SE	*P* value
qCON	0.339	0.160	0.036[a]	34.150	140.526	0.808	0.057	0.095	0.553	0.531	0.232	0.023[a]	0.096	0.062	0.125	0.331	0.140	0.019[a]	-0.017	0.039	0.664
qNOX	-0.011	0.116	0.922	-2.927	116.196	0.980	0.162	0.079	0.042[a]	0.216	0.191	0.259	0.001	0.051	0.988	0.061	0.114	0.593	0.022	0.029	0.457
Age (years)	-0.597	0.213	0.006[a]	142.879	94.214	0.131	-0.079	0.063	0.211	-0.064	0.162	0.693	0.034	0.046	0.456	0.091	0.104	0.384	0.096	0.046	0.039[a]
ECT number	-	-	0.000[a]	-	-	0.000[a]	-	-	0.024[a]	-	-	0.418	-	-	0.158	-	-	0.128	-	-	0.266
Charge, mC	0.068	0.667	0.307	-32.539	30.452	0.287	0.014	0.020	0.491	0.032	0.052	0.545	-0.007	0.015	0.647	-0.024	0.034	0.483	0.002	0.015	0.888
Anesthetic-ECT time, interval (min)	0.157	0.048	0.001[a]	-17.207	43.983	0.696	0.072	0.030	0.018[a]	0.041	0.073	0.575	0.007	0.020	0.724	0.074	0.044	0.093	-0.001	0.012	0.922

[a]$P < 0.05$.

Est: Estimate; SE: Standard error; EEG endpoint: Electroencephalograph seizure duration; ASEI: Average seizure energy index; PSI: Post-ictal suppression index; qCON: Quantitative consciousness; qNOX: Quantitative nociceptive; ECT: Electroconvulsive therapy.

An unexpected finding of this study was that the qNOX index significantly affected the PSI. The standard β coefficient was 0.162, which indicated that the higher the qNOX index, the higher the PSI. PSI refers to EEG suppression after a seizure and is considered to be an indication of good seizure quality if the PSI is greater than 80%[15,55]. The qNOX index reflects the degree of nociceptive stimulus response. The results of this study showed that the degree of noxious stimulation in patients after ECT was positively correlated with the PSI. Therefore, the higher the PSI score, the greater the noxious stimulation of patients. However, the influence of noxious stimulation on the clinical effects (such as antidepressant effects and cognitive impairment) of ECT in patients with depression remains unclear, and further large-scale clinical research is needed. This also suggests that higher PSI is not always advantageous, because excessive PSI may represent greater noxious stimulation of ECT in patients.

This study also examined the recovery time and complications of ECT in patients with MDD with different qCON indices. It was found that the recovery time was only related to the age of patients. The older the patient, the longer the recovery time. However, there was no significant relationship with the qCON index. White *et al*[61] showed that depth of anesthesia (BIS index) was positively correlated with recovery time, while Gombar *et al*[60] found that depth of anesthesia (BIS index) was negatively correlated with recovery time. The reasons for the inconsistent results among studies may be related to the different ages of the people included in these studies, the different electrode positions used in ECT, and the different anesthetic drugs used. Common complications during the recovery period included headache, dizziness, muscle soreness, nausea, and vomiting; there were no significant differences among the three groups. This indicates that the depth of anesthesia did not significantly affect complications during the recovery period when propofol anesthesia was used for bilateral temporal ECT.

This study also compared the clinical effects of ECT at different anesthesia depths in patients with MDD. Although light anesthesia can yield better EEG seizure parameters, there were no significant differences in the 24-item HAM-D, SDS, or MoCA scores among the three groups. The main reason for this may be that we used an age-based method

Table 3 The effect of anesthesia depth on electroencephalography seizure parameters: Findings of generalized linear mixed model analyses

Characteristics (dependent variable)	*F* value	*P* value
Maximum heart rate	3.460	0.034[a]
EEG endpoint	3.326	0.038[a]
ASEI	0.236	0.790
PSI	7.041	0.001[a]
Mid-ictal amplitude	5.717	0.004[a]
Coherence	3.364	0.037[a]
Maximum systolic blood pressure	1.490	0.228
Maximum diastolic blood pressure	0.375	0.688
Recovery time after treatment	0.095	0.909

[a]$P < 0.05$.
EEG endpoint: Electroencephalograph seizure duration; ASEI: Average seizure energy index; PSI: Post-ictal suppression index.

Table 4 Adverse events reported by participants during anesthesia recovery period: Findings of Fisher's precision probability test, *n* (%)

Adverse event	Group 1[1]	Group 2[2]	Group 3[3]	χ^2	*P* value
Headache	5 (7.9)	7 (10.8)	4 (6.2)	0.926	0.629
Dizziness	3 (4.8)	6 (9.2)	3 (4.6)	1.404	0.603
Nausea/vomiting	3 (4.8)	6 (9.2)	4 (6.2)	1.041	0.677
Muscle soreness	6 (9.5)	5 (7.7)	4 (6.2)	0.508	0.776
Delirium	0 (0)	0 (0)	0 (0)	-	-
Total	11 (17.5)	12 (18.5)	10 (15.4)	7.292	0.274

[1]Quantitative consciousness index 60-70.
[2]Quantitative consciousness index 50-60.
[3]Quantitative consciousness index 40-50.

instead of titration to set the initial stimulus dose. The age-based method does not require titration of the seizure threshold for the participants. Although there may be some patients with higher seizure thresholds, the initial stimulus dose based on one-half the patient's age is often higher than the seizure threshold determined by titration[62,63]. The effect of anesthesia depth on seizure threshold may be masked by a higher stimulation charge. However, the implementation of ECT was mainly carried out by psychiatrists who chose to set the initial stimulus dose, which not only simplifies the operation and avoids multiple titrations, but can also quickly exert antidepressant effects in patients with MDD. Another reason may be that the sample size of this study was small and the same dosage of anesthetic propofol was used, so the comparison of clinical effects is only exploratory.

This study had several limitations. First, the participants in this study were all patients with MDD, and antidepressants and their enhancers had not been removed or reduced during ECT. Hence, the effects of antidepressants and enhancers (such as benzodiazepines, lithium, and antiepileptic drugs) on seizures cannot be excluded in this study[19-21,64]. Second, this study used an age-based method instead of titration to set the initial stimulus dose; although this approach can quickly exert antidepressant effects in patients with MDD, it may mask the effect of anesthesia depth on seizure threshold and may result in excessively high suprathreshold stimulation for some patients. Thirdly, end-tidal partial pressure of CO_2 was not monitored in this study. Some studies have suggested that excessive ventilation can improve the quality of seizures, although some controversies remain[60,65]. Finally, this was a single-center, randomized, single-blind study with a small sample size. The secondary result of the study is exploratory, and thus needs to be further confirmed by a multicenter large-sample study.

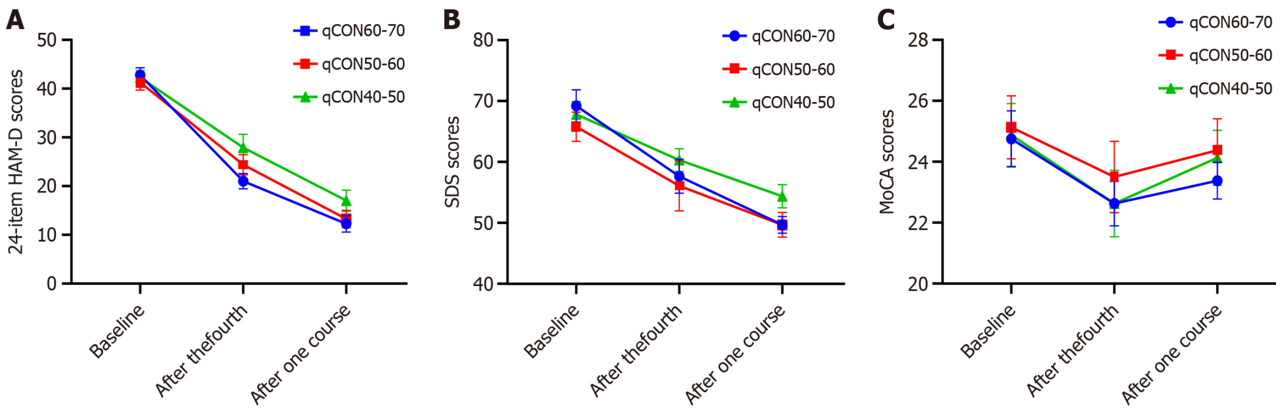

Figure 1 Comparison of clinical effects of electroconvulsive therapy among three groups of patients (*n* = 24). A: Comparison of 24-item Hamilton Depression Rating Scale score changes before and after electroconvulsive therapy (ECT) among three groups of patients (P = 0.188); B: Comparison of Zung's Self-rating Depression Scale score changes before and after ECT among three groups of patients (P = 0.214); C: Comparison of Montreal Cognitive Assessment score changes before and after ECT among three groups of patients (P = 0.920). ECT: Electroconvulsive therapy; HAM-D: Hamilton Depression Rating Scale; SDS: Zung's Self-rating Depression Scale; MoCA: Montreal Cognitive Assessment.

CONCLUSION

This study confirmed that the qCON index can be used to monitor the sedation depth of ECT in patients with MDD and to guide the appropriate time of electrical stimulation during ECT. Electrical stimulation at a qCON index of 60-70 resulted in improved EEG seizure parameters. The qNOX index reflects the degree of noxious stimulation caused by ECT and is positively correlated with PSI. The higher the PSI, the greater the noxious stimulation experienced by patients. In ECT, we should consider both the influence of sedation depth on the quality of seizures and the degree of noxious stimulation caused by the treatment technology itself.

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FOOTNOTES

Author contributions: Zhao BS prepared the manuscript for publication and contributed to the study design, data collection, and analysis; Deng B and Yang Y contributed to the statistical analysis and preparation of the tables and figures; Li X contributed to the electroshock therapy, psychiatric assessment, and electroencephalography analysis; Chen QB administered anesthesia in clinical practice; Min S contributed to the study design and analysis. All authors revised and approved the final version of the manuscript.

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