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ARTÍCULO ORIGINAL

Cognitive functions and electroconvulsive therapy in affective psychiatric patients

Funciones cognitivas y terapia electroconvulsiva en pacientes psiquiátricos con enfermedad afectiva / Funções cognitivas e terapia eletroconvulsiva em pacientes psiquiátricos com doenças afetiva

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ABSTRACT

Objective: Electroconvulsive therapy (ECT) has been considered a safe and effective treatment for depression, manic episodes, and other serious psychiatric conditions. Its main reported side effect has been cognitive impairment. This study describes the cognitive effects of ECT in psychiatric patients referred for treatment at a private clinic.

Methodology: Descriptive case series study. A baseline assessment conducted before starting ECT, and another two (at one week and at six months) after completing the treatment cycle were used to describe the effects of frontotemporal bilateral ECT on neurocognitive function in terms of the change from the baseline to the final assessment in the domains of memory, psychomotor speed, reaction time, complex attention, and cognitive flexibility, as well as global cognitive function, as well as to determine ECT's safety by reporting adverse events. Cognitive assessment was conducted with a neuropsychological test battery and severity of psychiatric illness with the Clinical Global Impression-Severity scale (CGI-S). Six patients referred for treatment during six months were included.

Results: No statistically significant differences were observed between the medians of the evaluations of CGI-S scale, global cognitive function or any of the domains evaluated.

Conclusions: ECT did not produce changes in the cognitive functions assessed in the six studied patients.

Keywords: electroconvulsive therapy; cognitive functions; adverse events; neuropsychological evaluation.

RESUMEN

Objetivo: la terapia electroconvulsiva (TEC) se ha considerado un tratamiento seguro y eficaz para episodios de depresión mayor, para episodios maníacos y otros trastornos psiquiátricos serios. El estudio describe los efectos cognitivos de la TEC en pacientes referidos para tratamiento a una clínica privada.

Metodología: estudio descriptivo del tipo de serie de casos. En cada participante se realizó una evaluación basal antes del inicio de la TEC y otras dos (una a la semana y otra a los seis meses) después de terminado el ciclo de tratamientos, para describir el efecto de la TEC frontotemporal bilateral en la función neurocognitiva mediante el cambio, desde el estado basal hasta la evaluación final en los dominios de memoria, velocidad psicomotora, tiempo de reacción, atención compleja y flexibilidad cognoscitiva, así como en la función cognoscitiva global; y determinar su seguridad por el reporte de eventos adversos. La evaluación cognitiva se realizó con una batería de pruebas neuropsicológicas y la severidad de la enfermedad psiquiátrica se evaluó con la escala

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Clinical Global Impression Severity (CGI-S). Se incluyeron seis pacientes remitidos para tratamiento durante el periodo de seis meses.
Resultados: no se observaron diferencias estadísticamente significativas entre las medianas de las evaluaciones de CGI-S, ni de la función cognitiva global, así como de ninguno de los dominios evaluados.
Conclusiones: la TEC no produjo cambios en las funciones cognitivas analizadas en los seis pacientes estudiados.
Palabras clave: terapia electroconvulsiva; funciones cognitivas; eventos adversos; evaluación neuropsicológica.

RESUMO
Objetivo: a terapia eletroconvulsiva (TEC) se há considerado um tratamento seguro e eficaz para episódios de depressão maior, para episódios maníacos e outros transtornos psiquiátricos sérios. O estudo descreve os efeitos cognitivos da TEC em pacientes referidos para tratamento a uma clínica privada.
Metodologia: estudo descritivo do tipo de série de casos. Em cada participante se realizou uma avaliação basal antes do início da TEC e outras dois (uma em uma semana e outra aos seis meses) depois de terminado o ciclo de tratamentos, para descrever o efeito da TEC frontotemporal bilateral na função neurocognitiva mediante a mudança, desde o estado basal até a avaliação final nos domínios de memória, velocidade psicomotora, tempo de reação, atenção complexa e flexibilidade cognoscitiva, assim como na função cognoscitiva global; e determinar sua segurança pelo reporte de eventos adversos. A avaliação cognitiva se realizou com uma bateria de provas neuropsicológicas e a severidade da doença psiquiátrica se avaliou com a escala Clinical Global Impression Severity (CGI-S). Se incluíram seis pacientes remitidos para tratamento durante o período de seis meses.
Resultados: não se observaram diferencias estatisticamente significativas entre as média das avaliações de CGI-S, nem da função cognitiva global, assim como de nenhum dos domínios avaliados.
Conclusões: a TEC não produziu mudanças nas funções cognitivas analisadas nos seis pacientes estudados.
Palavras chave: terapia eletroconvulsiva; funções cognitivas; eventos adversos; avaliação neuropsicológica.

INTRODUCTION

Electroconvulsive therapy (ECT) is a safe and effective treatment used to treat some psychiatric disorders. There are historical records of the induction of seizures to treat mentally ill patients dating from the sixteenth century. However, it could be stated that ECT as such emerged in 1935 when Professor Ugo Cerletti, his assistant Luigi Bini undertook the study of the effects of seizures on brain structure and in 1939 when the first therapeutic use on psychotic patients was reported[1].

Currently, its application is widespread, and organizations such as the American Psychiatric Association, the Royal College of Psychiatrists, and their counterparts in Austria, Canada, Australia, Denmark, Holland, Germany, and India have developed guidelines for its use[2-4].

The main indications for ECT are either unipolar or bipolar depressive episodes, especially when they are severe and accompanied by food negativism, high suicide risk, marked psychomotor retardation or psychotic symptoms; in acute mania with severe psychomotor agitation or when it is resistant to pharmacological treatment or is rapid cycling; in schizophrenia, when antipsychotics are ineffective or not tolerated; in catatonia, when lorazepam has been ineffective; in neuroleptic malignant syndrome; in refractory schizoaffective disorder; and in Parkinson's disease, when the "on-

off" syndrome is present[2,5]. Its efficacy and safety are well documented, and its use is based on its speed of action and specificity. Between 5% and 10% of unipolar depression cases are considered resistant, refractory, or intractable, but these are likely to have favorable response rates of up to 78% with ECT[6]. In bipolar patients with severe refractory depression and delusional symptoms, ECT produces excellent response[7], and as many as 80% of patients with acute mania or those medication-resistant manic patients respond well to ECT[8].

The side effects of ECT can be anticipated by obtaining a good clinical history of preexisting cardiac, pulmonary and neurological conditions. Arrhythmias are mostly brief and do not require pharmacological intervention and the rate of ECT-related mortality is estimated at one per 10 000 patients or one per 80 000 treatments[2,5]. Some other side effects are prolonged seizure and status epilepticus, whose rate of occurrence is low and most likely not different from population base rates; mild or moderate frontal headache of unknown etiology occurs in up to 45% of patients, nausea occurs in 1% to 23%, and a few patients experience a post-ictal state of delirium or agitation that may require pharmacological treatment [2].

Cognitive disturbances are perhaps the main side effect attributed to ECT. There is no conclusive evidence that ECT affects executive functions, abstract reasoning, creativity, semantic memory, implicit memory, or skill acquisition or retention[2]: and the cognitive disturbances clearly established as an adverse effect are: a transient post-ictal confusional state (disorientation and impaired alteration, praxis, and memory) and a prolonged period of impairment of memory expressed as retrograde (for pretreatment events) and anterograde (for events subsequent to treatment) amnesia[2,5]. Recovery of anterograde memory occurs more quickly than retrograde amnesia and does not persist for longer than a few weeks after completing the ECT course[2]. Abrams[5] asserts that there is no evidence of persistent memory loss or any loss that is maintained long-term that is attributable to ECT and points out that retrograde amnesia for personal events is resolved more quickly than evocation of impersonal events and when they are assessed two months after ECT treatment, there were not significantly difference from pre-ECT baseline performance. Meeter *et al.*[9], in a comparative study, found that after three months of follow-up, memory for events before treatment had returned to its pre-ECT level. Factors associated with treatment, such as number and frequency, bilateral or unilateral application, stimulus parameters used and the doses of anesthetics administered, each have been independently associated with the presence and severity of cognitive effects[2,5]. Likewise, individual factors, such as pre-existing neurological conditions, cognitive impairment in depressed patients, prolonged confusional state after ECT, or the concurrent administration of lithium carbonate or anticholinergics in elderly patients, may be relevant to memory alterations[2,5].

Most of the published literature on cognitive impairments in ECT are the results on patients with unipolar or bipolar depression[2,5,10]; and the research that studies effects of ECT on the cognition of manic patients are scare and results inconsistent[11,12].

Therefore, the purpose of this study was to describe the cognitive side effects of ECT in a group of depressed and manic patients treated at a private university clinic in the city of Medellin (Colombia) with affective psychiatric diagnoses according to criteria from the DSM-IV-TR[13], and followed during six months after the last ECT administration. As a secondary objective, other presented adverse effects were evaluated.

METODOLOGY

Participants

This is a descriptive case series study. Six patients referred to a private university clinic and scheduled to start ECT treatment were included upon meeting the inclusion criteria, such as having an affective psychiatric diagnosis consistent with the DSM-IV-TR, having signed an informed consent for the study, and having sufficient comprehension to understand the nature of the investigation, to communicate intelligibly and to use a computer.

Exclusion criteria included the following: severe, uncorrected visual disturbances, a history or diagnosis of dementia, ADHD, learning disorders, mental retardation, or substance/alcohol abuse or dependence; neurological or medically severe, unstable, or uncontrolled diseases; a history of non-response to ECT or having received ECT in the past four months; and the need for continued treatment with anticholinergics.

Patients were referred by psychiatrists or health institutions for ECT application at the private university clinic during the months of July to December 2009.

Assessment

Before starting the study, the investigators standardized the procedures for data collection, for DSM-IV-TR diagnostic criteria confirmation, and for the application of the Clinical Global Impression-Severity (CGI-S) scale[14] and of the CNS Vital Signs (CNSVS) (CNS Vital Signs LLC Morrisville, NC,USA) battery of neuropsychological tests[15].

Three assessments were performed per patient. The selection interview or baseline evaluation was completed prior to applying the first ECT procedure wherein personal information on the patient's background, history of disease, and treatments was obtained; the patient was reviewed for meeting all inclusion criteria and no exclusion criteria. The CGI-S scale and CNSVS battery were administered. For the second evaluation, the patient was assessed one week after completing the ECT series. The CGI-S scale and CNSVS battery were administered, the subjective complaints of the patient and drug treatment were recorded, and information from each of the ECT sessions was recorded with respect to the parameters of application of the procedure, its duration, seizure characteristics, doses of anesthetics, muscle relaxants, and other drugs, and adverse effects during the ECT course. The third evaluation was scheduled six months after the last ECT administration when the CGI-S scale and CNSVS battery were administered and information on subjective complaints, drug treatments received, and adherence to treatment were recorded. There was no lost to follow-up and the six patients completed the three scheduled evaluations.

All six patients were administered the CGI-S scale to assess the severity of disease and its changes during the study and the cognitive assessment was performed with the CNSVS, a computerized battery of neuropsychological instruments designed to be self-administered and developed to assess the domains of memory, psychomotor speed, reaction time, complex attention, and cognitive flexibility. It allows the evaluation of changes across time and provides a neurocognition index (NCI) corresponding to the average of the values of the five domains—i.e. an assessment of global cognitive function of the patient—and it is recorded as a normative value compared by age group with healthy subjects in a database according to five range options: "superior" (high function and high capacity), "average" (normal function and normal capacity), "below average" (mild deficits and mild impairment), "low" (moderate deficit and possible impairment), and "very low" (probable deficit and impairment)[15,16]. Its application was administered without the patient having received medication for agitation, anxiety, or insomnia in the previous 12 hours. This battery has been used on depressive and bipolar patients in clinical trials and after ECT treatments[17,18].

ECT was applied with a Thymatron System IV with a "flexdial" regulator (Somatics Inc., Lake Bluff, IL, USA) that provided electrical stimuli as brief bidirectional pulses with an amplitude of 0.25 to 1.5 milliseconds in increments of 0.25 ms, a frequency of 10 to 70 Hz and a fixed current of 0.9 A. The stimulus duration could be adjusted in times ranging from 0.14 to 7.99 seconds for determining seizure threshold and providing ECT treatment. Its other stimulus parameters were set by the manufacturer and remained constant throughout all treatments.

One of the researchers with extensive experience in the application of ECT was assigned to administer the procedure. All treatments were given after hyperoxygenation for at least one minute with 100% oxygen. Sodium thiopental was administered as an anesthetic, and succinylcholine was administered as a muscle relaxant. The application of the electrodes followed a standard frontotemporal bilateral placement, commonly referred to as "bilateral"[2]. The seizure threshold was obtained using the upward titration method in the first ECT, and from the second session, a stimulus equivalent to 1.5 times the threshold was applied to ensure its efficacy. The minimum duration of the seizure considered to be adequate was 20 seconds[2], and it was documented by the observation of motor expression in the right foot using the muscle relaxant-blocking cuff technique[2,5]. A maximum of three re-stimulations were allowed when the first stimulus failed. ECT was administered three times per week. When ECT required analgesic medication, dipyrone was administered, and if any other drug was received, it was considered concomitant medication and was documented.

Given the characteristics of the patients, it was not possible to keep them free from psychiatric medication during ECT. In agreement with the referring psychiatrist, it was attempted to suspend or reduce medication to a minimum before the first ECT session, and one of the patients received 2 mg doses of clonazepam during the entire course of ECT. Table 1 outlines the psychopharmacological treatment received by the group of patients before, during, and after ECT.

The study was approved by the clinic and the Pontifical Bolivarian University Human Health Research Ethics Committee.

Statistics

For the analysis of the data, the minimum, maximum, median, and interquartile ranges were used to describe the study variables. Medians were compared for the intrasubject evaluations of the CGI-S, of the global cognitive function and for each of the domains of CNSVS, and it was checked if there was a relationship between the time of evaluation and the scoring of the instruments using the Friedman test, a nonparametric test for repeated measures.

Table 1. Psychotropic drugs received by patients before, during, and after ECT.

Patient	Medicaments		
	Before	During	After
1	Venlafaxine Levomepromazine Clonazepam Zolpidem	Venlafaxine Levomepromazine Clonazepam	Fluoxetine Clozapine Clonazepam Imipramine Lithium carbonate Thyroid hormone
2	Venlafaxine Zolpidem Trazodone	Venlafaxine Sertraline Trazodone	Venlafaxine Olanzapine Trazodone
3	Sulpiride Escitalopram	Sulpiride Escitalopram	Sulpiride Escitalopram
4	Fluoxetine Duloxetine Trazodone Aripiprazole Diazepam Carbamazepine	Fluoxetine Reboxetine Trazodone Aripiprazole	Fluoxetine Duloxetine Trazodone Zolpidem Alprazolam Carbamazepine
5	Valproic acid Clozapine Risperidone	Valproic acid Clozapine	Valproic acid Clozapine
6	Duloxetine	Duloxetine	Venlafaxine

RESULTS

All 10 patients referred to start ECT from July to December 2009 were evaluated. Six of them were included in the study, and four did not join. Of the patients admitted, four had recurrent refractory major depressive disorder (MDD) (three females and one male); one female patient had bipolar disorder type I (BPD I) in a depressive phase with psychotic symptoms and a poor response to mood stabilizers and antidepressants; and another female patient had BPD I in a manic phase (rapid cycling). Reasons for non-admission to the study included severe medically uncontrolled disease (one patient), total functional limitation of an upper limb (one patient), withdrawal of informed consent (one patient) and change of the institution for applying ECT (one patient).

The median age was 38.5 years; five were female and one was male; all were right-handed; and a median of 15 years of schooling was reported. Chronicity, considered as the time course of the disease since inception, had a median of 19 years. The medians for the number of ECT procedures, doses of stimulus, and seizure duration were 12, 157.2 millicoulombs (mC), and 31.3 seconds, respectively. The median doses of thiopental and succinylcholine were 204.8 mg and 100.0 mg, respectively; four of the cases received on some occasion 50 mg of propofol as an adjunct anesthetic. The median numbers of days until the second and third evaluations that corresponded to valuations following ECT were 12 and 185 days, respectively (Table 2).

Table 3 shows the descriptive statistics of the neuropsychological tests used according to the time of evaluation. Differences between the medians of CGI-S, NCI and CNSVS domains for each patient were checked, showing they were not significant.

Thus, it was observed that ECT did not cause changes in the aspects analyzed in this series of six patients.

The patient 1, with mild clinical improvement, maintained a marked cognitive deficit during the three assessments, without persistent changes in range (Table 4); patient 2, who had a very good clinical improvement, showed no significant changes between the baseline and final assessments; patient 3 had a good clinical response,

Table 2. General and clinical characteristics of the six patients treated with ECT.

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Age in years	35	49	40	31	53	37
Sex	M	F	F	F	F	F
Schooling in years	16	14	18	13	5	20
Right dominance	Yes	Yes	Yes	Yes	Yes	Yes
Diagnosis:						
MDD* recurrent, refractory	Yes	Yes	Yes	No	No	Yes
BPD I† (Psychotic depressive episode)	No	No	No	Yes	No	No
BPD I† (Manic episode, rapid cycling)	No	No	No	No	Yes	No
Chronicity in years	18	25	8	11	30	20
Number of ECTs	18	15	5	12	12	10
Average stimulus dose (mC)‡	403.2	74.33	141.12	220.50	229.81	146.16
Average duration of the seizure (seconds)	18.695	32.6	32.8	29.916	23.9	40.8
Medication received during the procedure:						
Dose of thiopental (mg¶)	240.27	195	155	214.583	183.3	227.5
Dose of succinylcholine (mg¶)	102.22	99.33	100	100	100	77.5
Received additional anesthetic: Propofol 50 mg¶	Yes	Yes	Yes	Yes	No	No
Second and third evaluation (days post-ECT):						
Second; median (Interquartile range)	14	7	10	19	15	7
Third, median (Interquartile range)	203	186	199	184	181	184

*MDD= major depressive disorder, † BPD I= bipolar disorder type I, ‡mC= millicoulombs. ¶mg=milligrams

maintaining cognitive values within the same ranges in the three assessments, except for memory, which improved at six months; patient 4, with mild clinical improvement, showed marked deficits during the three evaluations, without changes in range; patient 5 exhibited a very good initial clinical response and symptomatic recurrence at six months, with improvement in the domain of memory and cognitive flexibility at the last evaluation; and patient 6 responded moderately well in the clinic but showed inconsistent results for the assessments of the cognitive domains. It should be noted that the NCIs of all patients remained in the same respective ranges throughout the study except for patient 2, who improved upon the second evaluation and showed a regression of range upon the third evaluation.

Regarding adverse effects, three patients had transient headaches, in one case intense, and they resolved upon the administration of analgesics. One participant had a superficial lesion on the lip and tongue that did not require any intervention; in another case, with concomitant medication (valproic acid and clozapine), there was self-limited asystole lasting a few seconds. Four patients with MDD and one with BPD I depression made subjective complaints of impairment in memory, and the only patient who did not report this had a diagnosis of BPD I mania.

DISCUSSION

Our results showed no significant changes in the NCI or the evaluated domains of memory, psychomotor speed, reaction time, complex attention and cognitive flexibility. When compared with baseline evaluations, there was no deterioration in variables assessed one week or six months after ECT with respect to status prior to application; thus, they conform to the statement that ECT is safe and does not produce persistent cognitive impairment[5].

Table 3. Descriptive statistics of the tests used, according to the time of evaluation.

	Minimum	Maximum	Median	Quartile 1	Quartile 3
CGI-S*					
Baseline	5.0	7.0	6.0	5.0	6.3
Second evaluation	1.0	4.0	2.0	1.0	4.0
Third evaluation	1.0	5.0	3.0	1.0	4.0
CNSVS†					
Neurocognition Index (NCI)					
Baseline	-15.0	99.0	72.0	9.0	97.5
Second evaluation	-3.0	100.0	73.5	30.0	100.0
Third evaluation	38.0	105.0	67.5	38.0	105.0
Memory domain					
Baseline	50.0	95.0	90.0	68.8	95.0
Second evaluation	62.0	94.0	83.5	70.2	91.8
Third evaluation	71.0	105.0	88.5	81.5	102.8
Psychomotor speed domain					
Baseline	34.0	163.0	111.0	77.5	156.3
Second evaluation	48.0	163.0	118.0	81.0	155.5
Third evaluation	64.0	168.0	93.0	66.2	156.8
Reaction time domain					
Baseline	506.0	1 227.0	619.0	555.5	999.8
Second evaluation	523.0	1 152.0	813.5	582.2	1 146.7
Third evaluation	558.0	1 082.0	733.5	594.7	1 041.5
Complex attention domain					
Baseline	7.0	101.0	14.5	7.0	53.0
Second evaluation	4.0	73.0	8.5	5.5	33.2
Third evaluation	6.0	31.0	15.5	6.0	25.0
Cognitive flexibility domain					
Baseline	-12.0	51.0	25.5	-10.5	48.0
Second evaluation	-2.0	62.0	31.5	16.0	50.7
Third evaluation	-3.0	58.0	32.0	3.7	53.5

*CGI-S =Clinical Global Impression-Severity scale, † CNSVS =CNS Vital Signs.

Studies such as those from Malloy *et al.*and Ng *et al.*[20] showed no permanent impairments on measures of global intellectual functioning; Devanand *et al.*[21] found no measurable long-term cognitive impairment in eight patients who each received greater than 100 ECT sessions; and in a preliminary study, Sienaert *et al.*[22] reported absences of impairment in global cognitive function, verbal memory, attention, executive function, autobiographical memory or subjective cognitive functions one and six weeks after ECT.

Our sample of six right-handed patients, 86% female and only one (16.7%) male, with a mean age of 38.5 years, diagnosed with refractory recurrent MDD (66.6%) (Patients 1, 2, 3, and 6) and BPD I (33.4%) (patient 4 with psychotic depression poorly responding to drug treatment and patient 5, a rapid cycler in manic episode), showed a therapeutic response with a 66.66% decrease in the CGI-S for the first week after ECT and a 50% reduction upon the final evaluation. However, the NCI, with medians of 72.0, 73.5 and 67.5 for each

Table 4. CGI-S* and individual cognitive results obtained from each patient.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
CGI-S*						
Baseline	6	6	5	6	7	5
Second evaluation	4	2	1	4	1	2
Third evaluation	5	1	1	4	3	3
CNSVS†						
Neurocognition Index (NCI)						
Baseline	55▼	89■	99►	17▼	-15▼	97►
Second evaluation	56▼	91►	100►	41▼	-3▼	100►
Third evaluation	38▼	86■	105►	38▼	49▼	100►
Memory domain						
Baseline	89■	91■	95►	75▼	50▼	95►
Second evaluation	82▼	85◄	94►	75▼	62▼	91■
Third evaluation	89■	88■	105▲	71▼	85◄	102►
Psychomotor speed domain						
Baseline	93▼	129▼	154■	92▼	34▼	163►
Second evaluation	93▼	143◄	153■	92▼	48▼	163►
Third evaluation	64▼	102▼	9 15■	84▼	67▼	168►
Reaction time domain						
Baseline	924▼	611►	572▲	1 227▼	627►	506▲
Second evaluation	1 024▼	603►	523▲	1 145▼	1 152▼	602►
Third evaluation	858▼	607►	558▲	1 028▼	1 082▼	609►
Complex attention domain						
Baseline	18▼	7►	7►	37▼	101▼	11■
Second evaluation	10■	6►	7►	20▼	73▼	4►
Third evaluation	31▼	6►	6►	21▼	23▼	10■
Cognitive flexibility domain						
Baseline	17▼	34■	47►	-10▼	-12▼	51►
Second evaluation	23▼	40►	47►	22▼	-2▼	62▲
Third evaluation	-3▼	41►	52►	6▼	23◄	58▲

*CGI-S= Clinical Global Impression-Severity scale, †CNSVS= CNS Vital Signs.
Conventions: ▲: upper range (high function and high capacity) ►: average range (normal function and normal capacity) ■: below average range (mild deficit and mild deterioration) ◄: low range (moderate deficit and possible deterioration) ▼: very low range (most likely deficit and deterioration)

of the assessments (baseline-first, second, and third, respectively), remained within the "very low" range in the assessments of patients 1, 4, and 5, within the "average" range for the three assessments of patients 3 and 6, and in the "below average"-"average"-"below average" ranges for patient 2 in each domain. The inconsistency between these two parameters leads us to consider other factors that could have affected NCI.

For reasons underlying their disease, patients in our sample were susceptible to cognitive impairment of different types. In unipolar depression, impairment when present affected attention and concentration, learning, and in some cases, executive function[23]. These symptoms may be transient and dependent on the depressive state; they may be fluctuating and sometimes totally absent despite severe depression[24]. Gualtiere *et al.*[25] found that pharmacologically treated unipolar depressive patients cognitively function 3% below healthy people and that untreated unipolar depressives are functioning with a 7% detriment. Paykel[26], on the basis of the Hamilton Rating

Scale for Depression, observed residual symptoms in 32% of patients with MDD in remission. Regarding BPD, although not all patients show evidence of cognitive impairment, bipolar euthymic individuals as a group tend to manifest lower-than-average performances in different neurocognitive measures[24], and changes are reported on tests of authobiographical memory and problem-solving ability[27]. Attentional impairments in BPD patients often persist into euthymia[28]. Therefore, residuality is neither ruled out nor shown to be susceptible to underestimation in our sample.

The standardized bilateral ECT application used in this study corresponds to the most frequently used technique but is considered the greater producer of memory impairments[29]. The entire group had a median stimulus dose of 157.2 mC, a median duration of seizure of 31.3 seconds and a median of 12 sessions per patient; and received thiopental as an anesthetic (median 204.8 miligrams) during ECT. Four patients further required propofol (50 mg) in some sessions. It is known that hight dosage of barbiturate anesthetic used may intensify amnesia following the seizure[2], but studies on the cognitive effects of thiopental and propofol during ECT are inconclusive. Ingram *et al.*[30] reported favorability of the former over the latter in a one-month follow-up study, whereas Geretsegger *et al.*, in a study with a two-month follow-up, suggested that propofol may be associated with some cognitive improvement in ECT compared with other anesthetics[31].

The entire group continued receiving psychopharmacological treatment during ECT application and after termination thereof. Concomitant use of psychotropic drugs during or after therapy is a common practice[2], and it is considered that treatment may also have the additional benefit of preventing early relapse in depressed patients[32]. Our patients received antidepressants, mood stabilizers, antipsychotics, benzodiazepines, and hypnotics that could affect cognitive function. Antidepressants can affect cognitive function depending mainly on their sedative and anticholinergic effects[2,5], and it has been reported that venlafaxine can worsen retrograde amnesia when associated with ECT[32]. With respect to lithium, patients have often complained of "cognitive dulling" and in individuals with bipolar disorder, it can have negative effects on memory and speed of information processing[33]; however, its use in ECT is considered quite safe for most patients, although with high or even therapeutic serum levels, there may be a risk of prolonged seizures and increased incidence of delirium[2,5]. Regarding anticonvulsants, in a comparative study, Gualtieri *et al.*[34] identified relative neuropsychological effects of five of them and in lithium for bipolar patients, categorizing lamotrigine and oxcarbazepine as having a minor effect on neurocognition, lithium as having intermediate-grade effects, and topiramate, valproic acid, and carbamazepine, as having the greatest effects. The literature suggests that predominantly GABAergic anticonvulsants, such as valproic acid, benzodiazepines, and barbiturates, are relatively sedating and are associated with feelings of fatigue and cognitive blunting[34]. Furthermore, benzodiazepines have an amnesic effect[2]. With antipsychotics, the effect is given by their sedative and anticholinergic action. Eschweiler *et al.*[35], in a comparative study over three weeks period, found no evidence that the combination of ECT with lithium, any types of antidepressant, or any atypical antipsychotic, such as olanzapine increases cognitive impairment in patients with resistant major depression. Antipsychotics can cause the loss of memory for personal events[36], and those with anticholinergic action have a marked amnesic effect[37]. Concomitant use of medications has implications that cognitively affect patients.

The subjective complaints of memory impairment in the five patients with depression presently indicate a controversial aspect, given the difficulty in corroborating this perception with objective neuropsychological tests for memory[2]. Discrepancy between objective testing results and subjective memory capability is attributed to different factors, such as awareness of the normal transient amnesia that accompanies ECT, partial therapeutic response to treatment, presence of residual or recurring symptoms, concomitant medication, or neurobiologically idiosyncratic effects among others[38]. Most ECT studies using questionnaires to assess subjective memory find that a subjective feeling of improved memory significantly correlates with improvement in depression[5], however, Prudic *et al.*[39] reported a negative association between subjective memory complaints and the mood state, and Squire and Chace[40] found no relationship between the clinical response to treatment and the subjective estimates of memory functions. In our study, no instruments to assess subjective memory were administered.

The presence of other adverse effects, such as headache in half of the patients, asystole, and oral soft tissue injuries, are within the events reported in patients receiving ECT[2,38].

Our study has limitations, and its results should be viewed with caution. The lack of objective information on the characteristics of premorbid cognitive functions, the partial response to treatment or presence of residual symptoms, the use of psychotropic drugs during the study, the group heterogeneity and the small sample size do not support statistical analyses for detecting if the changes observed between assessments were significant nor determine the extent of such changes; they are factors that may have influenced the results.

In conclusion, ECT under standard conditions produced no impairment in evaluated neurocognitive functions in the six participating patients.

STATEMENT OF CONFLICT OF INTERESTS

The authors have no conflicts of interest or financial disclosures to report.

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