Seizure threshold variations in ECT-treated chronic patients with schizophrenia: a brief report

La variazione della soglia convulsiva nei pazienti con schizofrenia cronica trattati con TEC: un breve report

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SUMMARY. Seizure threshold (ST) is a parameter that differs in each person and can be modified both spontaneously and because of drug intake and/or other exogenous factors. A rise in ST during a course of electroconvulsive therapy (ECT) has been demonstrated in patients with depression and mania, but little information has been available as to whether the same result occurs in schizophrenia (SCZ). 11 male patients underwent estimation of the seizure threshold over a bilateral ECT course. Mean ST changed not significantly. No correlations were found between baseline ST and Positive and Negative Syndrome Scale (PANSS) scores. A significant positive correlation emerged between baseline ST and the variation of Hamilton Depression Rating Scale (HDRS) total and cognitive scores. The results suggest that ST in SCZ patients is not related to baseline psychopathological features, it is not related to clinical improvements of negative or positive SCZ symptoms and it does not change during the ECT course but it appears predictive of the improvement of affective and cognitive symptmos.

KEY WORDS: electroconvulsive therapy, schizophrenia, seizure threshold.

RIASSUNTO. La soglia convulsiva (SC) è un parametro funzionale diverso in ogni individuo che può variare sia spontaneamente sia a causa di fattori esogeni. L'obiettivo del presente studio è di investigare se, similmente a quanto avviene nei disturbi affettivi, la SC di pazienti affetti da schizofrenia cambia nel corso della terapia elettroconvulsivante (TEC). 11 pazienti sono stati coinvolti nello studio; dopo essere stati inquadrati sul piano psicopatologico tramite la Positive and Negative Syndrome Scale (PANSS) e la Hamilton Depression Rating Scale (HDRS), i pazienti sono stati sottoposti a sessioni di TEC bilaterale. Le variazioni medie della SC si sono rivelate non significative; non è emersa nessuna correlazione tra la SC di partenza e i punteggi della scala PANSS; è emersa una correlazione lineare positiva tra la SC di partenza e la variazione dei punteggi totali della scala HDRS e della sottoscala relativa al funzionamento cognitivo. Tali risultati suggeriscono che la SC nei pazienti affetti da schizofrenia non è legata alle condizioni psicopatologiche di partenza, non è legata a miglioramenti clinici della sintomatologia positiva o negativa della schizofrenia, non varia nel corso della terapia con TEC, ma risulta predittiva dei possibili miglioramenti sul piano cognitivo.

PAROLE CHIAVE: terapia elettroconvulsivante, schizofrenia, soglia convulsiva.

INTRODUCTION

Brain-modulating techniques treatments are nowadays considered additional options for the treatment of several pharmacoresistant psychiatric disorders[1-5]; electroconvulsive therapy (ECT) is one of the oldest forms of brain stimulation and has shown efficacy in a range of psychiatric disorders including depression, bipolar disorder and schizophrenia (SCZ)[6-8]. In ECT the seizure threshold (ST) is defined as the minimum stimulus intensity required to produce a generalized and adequate seizure; ST is a dynamic parameter that differs in each person and can be modified both spontaneously and because of drug intake or other exogenous factor[9,10].

Several studies have investigated the variations of the ST in manic and depressed patients. ST proved to be higher in men and proportional to age in depressed patients; during

the ECT treatment, the ST of depressed patients usually shows a gradual rise that is a predictive index of favourable treatment outcome[11-13]. Studies carried out on manic patients showed a lower ST than in depressed people[14]. The antimanic effect of ECT seems to be associated with significant ST elevation during bilateral ECT treatment. Differently from depressed, low baseline ST appears to be associated with poor treatment response[9]. Based on these evidences, ECT had previously been used even to treat seizure disorders and their associated behavioural problems[15,16].

SCZ is a psychotic disorder marked by severely impaired thinking, emotions, and behaviors[17-23]. Antypsychotic medications are the firs-line intervention to treat the disorder[24-27], but ECT still represents a potential therapeutic intervention[28]. Despite recent renewals of interest in the use of ECT in SCZ[29,30], data on ST in this disorder are presently less consistent in comparison with affective disorder. Only one study of Chanpattana et al.[31] in 2001 analyzed this issue.

Given to above, the aim of the present study was firstly to investigate whether ST in SCZ patients undergoes modifications during an ECT course similarly to what happens in mood disorders and secondly to ascertain any correlation between ST and treatment outcome.

MATERIAL AND METHODS

Subjects

11 male pharmacoresistant (resistant to 2 adequate for duration and dosage trials with different antipsychotics) inpatients (mean age: 28.45 ± 5.92; duration of illness: 8.72 ± 5.49 years) meeting DSM-IV-TR criteria for SCZ and without any psychiatric comorbidity were enrolled in the study. They were considered for ECT treatment if they were not in acute phases of the disease.

Patients underwent ECT at the Psychiatric unit of Policlinico Umberto I University Hospital, Sapienza University of Rome, between January 1999 and January 2001. ECT was administrated as an add-on treatment to patients who were stabilized on standard pharmacological maintenance therapies, that remained unchanged. All patients were on stable pharmacological treatment from at least two months. No patients received ECT in the past. All patients gave written informed consent and their relatives were also informed on the treatment and gave consent.

Clinical assessment

Patients' clinical status was assessed through the Positive and Negative Syndrome Scale (PANSS) and the Hamilton Depression Rating Scale (HDRS) at baseline and after the 8th ECT session. PANSS subscales (positive, negative, general psychopathology) and factor scores (anergy, thought disorder, activation, paranoid, depression) were calculated. HDRS total score and HDRS factor scores (anxiety, loss of weight, diurnal variation, cognitive disturbance, retardation, sleep disturbance) were calculated.

Anaesthesia

Anaesthesia comprised 0.5 mg intravenous (i.v.) atropine, 0.5 mg/kg i.v. succinylcholine, and 1 mg/kg propofol in rapid infusion. All patients were subjected to assisted ventilation with 100% O_2, administered through a mask and carried on until complete patient awakening.

ECT procedure

A MECTA apparatus, model SR-1, was used to induce seizures. Patients were subjected to bifrontal ECT. They were anaesthetized under electroencephalografic (EEG), electrocardiographic and clinical monitoring throughout the entire treatment session. As soon as eyelid reflexes and EEG alpha-resynchronisation became apparent again following the deepest stage of anaesthesia, the electrical stimulus was delivered. The protocol provided a complete course of 10 sessions of bilateral ECT (research of baseline and final ST and 8 therapeutic sessions), at a rate of 3 sessions per week.

Titration method

The determination of ST was carried out according to the MECTA manual. Current dosage was measured in joules. The initial dosage was 5.6 J for all patients; in case of a poor response (i.e, absence of seizure or seizure duration less than 25 sec), current administration was repeated after 10 minutes, in concomitance with a second propofol administration; the time interval was such to avoid that a possible subclinical first discharge could influence the seizures threshold in the following one. Within the same session, no more than 2 discharges were allowed, postponing the use of a higher current energy stimulus to the day after. Only in one case, four sessions were necessary to establish initial ST; in all other cases, an adequate seizure (at least 25 seconds of EEG duration) was obtained within the first or second session. Once ST was determined, ECT was carried out with the electrical current dosages recommended by the MECTA Manual. In case of stimulus ineffectiveness (absent or inadequate seizure) during the course of the treatment due to threshold elevation, the dosage was increased according to the same recommendations. The research of ST was repeated after the 8th therapeutic session.

Statistical methods

The variations of ST and clinical scales after the ECT course were analysed through wilcoxon-Mann-Whitney test. Spearman's Correlation Coefficient was used to evaluate the correlations between baseline ST and baseline psychopathological components. Significance threshold was arbitrarily chosen at 0.05.

RESULTS

The whole group showed significant clinical improvement in all symptomatological components (Table 1). Mean PANSS total score moved from 108.1±16.6 to 76.6±17.0 ($p<.001$), with a mean percent improvement of 29.3±10.3%. Mean HDRS total score moved from 22.6±5.6 to 13.7±4.1 ($p<.001$), with a mean percent improvement of 37.2±18.6%.

ST modifications during the ECT treatment were non-significant (ST baseline: 12.23±6.18; ST final: 12.91±6.7). No correlations were found between baseline ST and baseline PANSS scores. Significant positive correlations emerged between base-

Table 1. PANSS and HDRS variations

	Baseline	Final	P	Percent improvement (final score vs baseline)
PANSS Total	108.1±16.6	76.6±17.0	<.001**	29.3±10.3
S. positive	23.6±9.7	13.8±5.6	.003**	37.8±17.3
S. negative	28.9±10.8	22.4±8.0	.001**	19.5±17.4
S. general psychopathology	55.5±8.9	40.4±8.8	<.001**	27.4±9.5
C. anergy	13.5±5.3	11.2±3.0	.028*	6.7±38.4
C. thought disorder	14.4±5.2	9.0±3.5	.004**	34.6±18.8
C. activation	9.1±2.4	7.4±2.6	.003**	15.1±30.2
C. paranoid	9.3±2.2	5.3±2.4	<.001**	40.4±28.8
C. depression	13.9±4.2	7.3±1.8	<.001**	45.2±15.4
HRDS Total	22.6±5.6	13.7±4.1	<.001**	37.2±18.6
S. anxiety	6.3±2.5	4.2±1.8	.011*	30.1±24.0
S. loss of weight	0.0±0.0	0.0±0.0	-	-
S. diurnal variation	0.0±0.0	0.0±0.0	-	-
S. cognitive disturbance	6.4±1.9	3.6±1.6	.002**	38.9±29.2
S. retardation	7.3±2.8	5.0±1.8	.007**	28.0±18.5
S. sleep disturbance	2.4±1.4	0.9±0.7	<.001**	52.2±40.1

* p<.05; ** p<.01

line ST and the variation of HDRS total scores (r=.731, p=.011) and HDRS cognitive cluster scores (r=.747, p=.008) (Table 2).

DISCUSSION

Although a progressive rise in threshold had been demonstrated during ECT in patients with depression and mania, only one prior investigation had described whether the same result occurs in patients with SCZ[31]. The objective of the study was firstly to investigate whether ST in SCZ patients undergoes modifications during a course of ECT similarly to what happens in patients with mood disorders and secondly to ascertain any correlation between ST and treatment outcome.

The whole sample showed a significant clinical response in terms of symptom reduction. This response was homogeneous and confirmed both the validity of ECT in SCZ patients and its safety[28-32].

No significant modifications of ST were observed during the ECT course, differently from what was found in the previous study of Chanpattana et al.[31]. The absence of ST modifications in relation to clinical outcomes differs from what is reported in depressed and manic patients, where an increase of ST during the ECT course is predictive of favourable clinical outcome[9].

Significant reductions in PANSS and HDRS scores were obtained. No relationship was found between baseline ST and PANSS psychopathological items. The only correlations were found between baseline ST and the degree of improvement of depressive and cognitive symptoms. This result suggests that, even if ST variation is not predictive of therapeutic response, in SCZ patients high ST at baseline can be predictive of improvement in affective and cognitive symptoms. Moreover, the improvement of cognitive cluster scores of HDRS empirically contrasts with the general idea that ECT induces cognitive impairments[33].

The meaning of the correlation between baseline ST and change in HDRS cognitive factor is unclear. It could be expected that high dosage of energy may induce a greater cognitive impairment, but the results show an opposite tendency. By a clinical point of view, it could be hypothesized that cognitive symptoms may be considered as part of the psychopathological profile of both SCZ and depression and that a higher electrical dosage treatment could thus exert a therapeutic effect on them.

In conclusion, the results of the present study suggest that ST in SCZ patients it is not related to baseline psychopathological features, it is not related to clinical improvements of negative or positive SCZ symptoms, and it does not change during the ECT course but it appears predictive of the improvement of affective and cognitive symptoms.

Since this study was carried out on a small sample of patients and it showed results different from those of the unique previous study, further investigations are needed on the topic. Elucidating the meaning of ST could contribute to shed some light on the mechanism of action and on the prediction of clinical response to ECT in SCZ patients.

Conflict of interest

All authors of this paper have no relevant affiliations or financial involvement with any organization or entity with a financial interest in, or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, hono-

Table 2. Correlations between Baseline ST and the variations of PANSS and HDRS

			Baseline ST
Variation (final score – basal score) of PANSS	Total	r	.431
		Sig. (2-tailed)	.186
	S. positive	r	.358
		Sig. (2-tailed)	.280
	S. negative	r	.117
		Sig. (2-tailed)	.732
	S. general psychopathology	r	.349
		Sig. (2-tailed)	.293
	C. anergy	r	-.307
		Sig. (2-tailed)	.359
	C. thought disorder	r	.404
		Sig. (2-tailed)	.218
	C. activation	r	.472
		Sig. (2-tailed)	.143
	C. paranoid	r	.134
		Sig. (2-tailed)	.695
	C. depression	r	-.146
		Sig. (2-tailed)	.668
Variation (final score – basal score) of HDRS	HDRS Total	r	.731*
		Sig. (2-tailed)	.011
	S. anxiety	r	.542
		Sig. (2-tailed)	.085
	S. loss of weight	r	-
		Sig. (2-tailed)	-
	S. diurnal variation	r	-
		Sig. (2-tailed)	-
	S. cognitive disturbance	r	.747**
		Sig. (2-tailed)	.008
	S. retardation	r	.244
		Sig. (2-tailed)	.469
	S. sleep disturbance	r	.154
		Sig. (2-tailed)	.650

* p<.05; ** p<.01

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