

## Two-Year Follow-Up of Cognitive Functions in Schizophrenia Spectrum Disorders of Adolescent Patients Treated with Electroconvulsive Therapy

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### Abstract

**Objective:** The aim of the current study was to investigate the long-term cognitive effects of electroconvulsive therapy (ECT) in a sample of adolescent patients in whom schizophrenia spectrum disorders were diagnosed.

**Methods:** The sample was composed of nine adolescent subjects in whom schizophrenia or schizoaffective disorder was diagnosed according to DSM-IV-TR criteria on whom ECT was conducted (ECT group) and nine adolescent subjects matched by age, socioeconomic status, and diagnostic and Positive and Negative Syndrome Scale (PANSS) total score at baseline on whom ECT was not conducted (NECT group). Clinical and neuropsychological assessments were carried out at baseline before ECT treatment and at 2-year follow-up.

**Results:** Significant differences were found between groups in the number of unsuccessful medication trials. No statistically significant differences were found between the ECT group and the NECT group in either severity as assessed by the PANSS, or in any cognitive variables at baseline. At follow-up, both groups showed significant improvement in clinical variables (subscales of positive, general, and total scores of PANSS and Clinical Global Impressions–Improvement). In the cognitive assessment at follow-up, significant improvement was found in both groups in the semantic category of verbal fluency task and digits forward. However, no significant differences were found between groups in any clinical or cognitive variable at follow-up. Repeated measures analysis found no significant interaction of time  $\times$  group in any clinical or neuropsychological measures.

**Conclusions:** The current study showed no significant differences in change over time in clinical or neuropsychological variables between the ECT group and the NECT group at 2-year follow-up. Thus, ECT did not show any negative influence on long-term neuropsychological variables in our sample.

### Introduction

ELECTROCONVULSIVE THERAPY (ECT) HAS been demonstrated to be a safe and effective procedure in adult patients. There is also evidence that ECT is useful in children and adolescents with certain severe psychiatric disorders who fail to respond to pharmacotherapy or require a quick response due to life-threatening symptoms (Ghaziuddin et al. 1996; Moise and Petrides 1996; Baeza et al. 2010). Variable rates of improvement or remission of symptoms by the end of the course of ECT have been observed:

63% for patients with depression, 80% in patients with mania, and 42% for those with schizophrenia (Rey and Walter 1997). A relatively low incidence of relevant adverse events in adolescents has also been described (Taieb et al. 2002; Bloch et al. 2008).

In adults, short-term follow-up studies have shown memory impairments in patients treated with ECT (for a review, see Rami-Gonzalez et al. 2001; Ingram et al. 2008). Specifically, studies with patients with different mood disorders have found difficulties encoding new information and in long delay verbal recall after ECT treatment (Steif et al. 1986; Rami-Gonzalez et al. 2003b) as well as

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retrograde amnesia for remote events (Squire 1977; Lisanby et al. 2000; Ingram et al. 2008). Moreover, electrode position, energy, and type of current have been related with the degree of cognitive impairments. Specifically, some of them (Weeks et al. 1980; Squire and Chace 1996; Sackeim et al. 2008) have found that unilateral right positions have less severe cognitive effects than bilateral positions, which support previous review studies (Squire 1977; Calev et al. 1995; Squire and Chace 1996). Sackeim et al. (2008) in a double-blind study investigate the effects of different electrode placement (bilateral vs. right unilateral) and pulse width (0.3 vs. 1.5 ms) and found that the ultrabrief right unilateral group had less cognitive side effects than the other groups. Regarding electrical dosage, Sackeim et al. (2000) compared different electrode position (bilateral vs. right unilateral) and electric dosage (50% vs. 150% and 500% above the seizure threshold) and found that a high dosage result in a greater cognitive impairment. Most of these studies have also shown that both learning and retaining were totally recovered between a few weeks and 7 months after the ECT series (Weeks et al. 1980; Frith et al. 1983; Calev et al. 1991; Squire and Chace 1996). Moreover, Zervas et al. (1993) associated patient age in adults to the risk of short-term memory deficits in patients treated with ECT. Thus, the authors found more severe deficits in older patients for verbal and visuospatial anterograde and retrograde memory, thereby concluding that older patients were more vulnerable to cognitive effects of ECT.

A few studies have investigated other cognitive functions, most finding no differences between ECT and no-ECT groups of patients (Vothknecht et al. 2003; Rami et al. 2004). However, two case-control studies analyzing the effects of maintenance ECT found some impairments in verbal fluency (Rami-Gonzalez et al. 2003a) and speed of information processing (Tsourtos et al. 2007).

In adolescents, Ghaziuddin et al. (2000) reported a sample of 16 adolescents with mood disorder and administered a cognitive battery before the ECT treatment, 1 week after the last ECT session, and ~8 months after the last session. Results showed significant impairments in attention, verbal and visual delayed recall, and verbal fluency between the pretreatment evaluation and 1 week post-treatment assessment, which had disappeared at the second post-treatment assessment 8 months later.

Regarding long-term studies with a follow-up longer than 1 year, there are to our knowledge only three studies that have analyzed the cognitive effects of ECT in adult samples (Russell et al. 2003; Johanson et al. 2005; MacQueen et al. 2007). Johanson et al. (2005) analyzed the cognitive effects of ECT in 55 patients with depression who were followed up 20–24 years after the ECT treatment. Patients showed a slight impairment of working memory and verbal memory, but there was no control group against which to make a comparison. MacQueen et al. (2007) studied subjective and objective memory impairments in three samples of subjects matched for age and sex but not for clinical severity: A group of 20 patients with bipolar disorder treated with ECT, a group of 20 patients with bipolar disorder with no ECT treatment, and 20 healthy controls were followed up during 45 months. The authors concluded that the patients who received ECT had significantly lower scores in memory and verbal learning tests. Nevertheless, Russell et al. (2003) carried out a retrospective study of 43 patients with different diagnoses (depression, bipolar disorder, and schizoaffective disorder) who had received at least 1 year of maintenance ECT and found no significant differences in cognitive domains assessed with the Mini-Mental State Exam between baseline and follow-up evaluations.

Only one study has analyzed cognitive effects of ECT in a sample of adolescents with a long-term follow-up (Cohen et al.

2000). A sample of 10 adolescents in whom mood disorder was diagnosed were followed up until 3.5 years after the last ECT session and compared with 10 psychiatric comparison subjects. The authors found that adolescents treated with ECT did not show cognitive impairment at long-term follow-up in objective measures of cognitive function; nevertheless, they found a subjective memory impairment measured with the Squire's Subjective Memory Questionnaire in two subjects.

No follow-up studies have been carried out in relation to cognition in adolescents with schizophrenia spectrum disorder treated with ECT.

Thus, taking into account this lack of information from previous long-term studies in children and adolescents with schizophrenia spectrum disorder, the aim of the current study was to investigate the long-term cognitive effects of ECT in a sample of adolescent patients with these disorders. We hypothesized that no significant differences would be found in cognitive measures after 2-year follow-up between an ECT group and a no-ECT group.

## Methods

### Subjects

We included nine adolescent subjects aged between 13 and 18 (22% men), and in whom schizophrenia ( $n=7$ ) or schizoaffective disorder ( $n=2$ ) was diagnosed according to DSM-IV-TR criteria on whom ECT was conducted following the American Psychiatric Association (2001) and the American Academy of Child and Adolescent Psychiatry (AACAP) recommendation criteria (ECT group) (Ghaziuddin et al. 2004). All subjects were admitted between January 2005 and December 2009 into the inpatient ward of the Child and Adolescent Psychiatry and Psychology Department of Hospital Clinic of Barcelona. Of the 137 patients with schizophrenia spectrum disorder (schizophrenia or schizoaffective disorder, DSM-IV criteria) hospitalized in our center during this period, 13 of them (9.49%) were treated with ECT. Our ECT Committee approved the indication for each of the patients, and written informed consent for ECT was provided by the patients' parents or legal guardians. Lack of response to at least two adequate pharmacotherapeutic trials and/or intolerance to medication side effects were the most common reason for indication of ECT ( $n=7$ ; 77.8%). ECT was considered earlier in other cases when subjects presented with catatonia ( $n=2$ ; 22.2%). Statistical analysis was performed with a sample of nine subjects who had completed all clinical and neuropsychological assessments. All subjects received additional pharmacotherapy (including antipsychotics, mood stabilizers, antidepressants, and benzodiazepines) during the acute ECT phase. No negativism, no mutism, and no staring were observed in any of the patients with catatonia when neuropsychological tests were assessed.

Subjects treated with ECT were compared with nine subjects selected from the same 137 treated during this period (44% men). Schizophrenia ( $n=7$ ) or schizoaffective disorder ( $n=2$ ) was diagnosed in these controls, and they were treated with psychiatric drugs but without ECT (NECT group). They were matched for age, socioeconomic status, and PANSS at baseline. Socioeconomic status of the sample was estimated with the Hollingshead Redlich scale (Hollingshead and Redlich 1958).

Exclusion criteria for both groups included (1) presence of another concomitant Axis I disorder at the time of assessment that might account for the psychotic symptoms, including substance-induced psychotic disorder, post-traumatic stress disorder, or acute stress disorder; (2) Intelligence Quotient (IQ) below 70 with impaired functioning; (3) pervasive developmental disorder; and (4)

neurological disorders, including history of head trauma with loss of consciousness.

All patients were retrospectively assessed at baseline and at 2-year follow-up; and the study was approved by the Ethics Committee of the institution.

### *Psychopathological assessment*

All subjects were evaluated with the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impressions–Improvement (CGI-I) Scale just before beginning the ECT course and at the 2-year follow-up assessment.

PANSS: This is a 30-item rating scale that aims at assessing the symptom severity of subjects with psychosis. It is subdivided into three subscales—positive, negative, and general psychopathology—and a total score (Kay et al. 1987; Peralta and Cuesta 1994). Each subscale and the total score are all evaluated from 1 to 7 according to the severity of the symptoms. It was always administered by the same psychiatrist (I.B.).

CGI-I scale: This is a clinical scale scored from 1 to 7 that assesses the severity of symptoms. A better level is indicated by lower scores (Guy 1976).

The Neurological Examination Scale (NES) (Buchanan and Heinrichs 1989): This scale assesses neurological soft signs. It comprises 26 items clustered into four subscales: Sensory integration, motor coordination, sequencing of complex motor tasks, and other neurological soft signs. In this study, it was used to assess motor and coordination problems that could affect subjects' performance in neuropsychological tests.

### *Therapeutic intervention*

All subjects received ECT thrice per week with a constant-current, brief-pulse device. Using a systematic protocol, all treatment stimuli were delivered with bifrontotemporal electrode placement administered using a MECTA-SR2 ECT device. Seizure threshold was titrated at the first session, with Stimulus dosing at subsequent treatments of 1.5 times the seizure threshold. Table 1 shows the ECT parameters.

Electroencephalographic and motor seizure manifestations were monitored to ensure adequate duration. Succinylcholine (30–120 mg), atropine (0–1 mg), and sodium tiopental (75–450 mg) or propofol (120–170 mg) were used for anesthesia. The acute ECT course was continued until the acute symptoms remitted or no further improvement was shown over the course of three consecutive sessions.

### *Neuropsychological assessment*

Cognitive assessment was performed between 4 and 8 weeks after admission when subjects had reached a low in acute psychotic

symptoms, before the ECT treatment and at 2-year follow-up, by means of a comprehensive neuropsychological battery designed to assess the following cognitive domains: IQ, working memory, attention, verbal learning and memory, and executive functioning.

To rule out mental retardation, IQ was estimated using the Block Design and Vocabulary subtests of the Wechsler Adult Intelligence Scale-III Revised (WAIS III) (Wechsler 2001) or the Wechsler Intelligence Scale for Children-Revised (Wechsler 1974), depending on the subject's age. Raw scores for each subscale were converted into standard scores with a mean of 10 and a standard deviation of 3.

Working memory was evaluated using the scores obtained on Digits backward and Letter-Number Sequencing of the WAIS III (Wechsler 2001). The first task requires the subject to say in reverse order the digits that have been read by the examiner. In the letter-number sequencing task, the examiner reads a list of letters and numbers and asks the subject first to say the numbers, from lowest to highest, and then the letters, in alphabetical order.

Attention was assessed by means of the Trail Making Test part A (TMT-A) (Reitan and Wolfson 1985) and Digits forward of the WAIS III (Wechsler 2001). In the first task, the subject is instructed to join with lines the numbers from 1 to 25 on a sheet of paper in the shortest time possible. The time of response was taken into account. In Digits forward, the subject should repeat a series of numbers in the same order as has been read by the examiner.

Verbal memory and learning were evaluated by the Verbal Learning Test-Complutense Spain, the Spanish adaptation of the California Verbal Learning Test, which provides a learning curve and an immediate and delayed memory score (Benedet and Alexandre 1998).

Finally, executive functions were assessed by number of categories, number of mistakes, number of perseverative errors, and number of perseverations on the Wisconsin Card Sorting Test (WCST) (Heaton et al. 1997), the interference part of the Stroop test (Golden 1978), the TMT part B (TMT-B) (Reitan and Wolfson 1985), and the verbal fluency task (FAS) (Lezak 1995). The WCST is a measure of executive function that requires planning strategies and cognitive flexibility to change the use of learned strategies. The interference part of the Stroop test measures the subject's ability to inhibit an automatic predominant response. The FAS is a test of verbal fluency that requires the subjects to generate as many words as possible beginning with a given letter in 60 seconds. In the TMT-B, subjects have to join with lines, alternatively, numbers (in increasing order) and letters (in alphabetical order) in the shortest possible time. We used the time to complete the task as a measure of executive function.

### *Statistical analysis*

To test the normality of the sample distribution, the Kolmogorov-Smirnov test was applied, with the Levene test to assess the

TABLE 1. ELECTROCONVULSIVE THERAPY PARAMETERS

	<i>Mean</i>	<i>Maximum</i>	<i>Minimum</i>	<i>Median</i>	<i>Standard deviation</i>	<i>Valid N sessions</i>
Pulse width (ms)	1	2	1	1	0	120
Frequency (hertz)	65	80	60	60	8	120
Stimulus duration (s)	0.89	1.50	0.75	1.00	0.15	120
Current (amps)	0.63	0.80	0.60	0.60	0.07	120
Number ECT sessions	13	20	7	12	4	

ECT = electroconvulsive therapy.

equality of variances. These two conditions were achieved for both clinical and neuropsychological variables. Categorical socio-demographic variables were compared between the two groups using the chi-square test or *t*-test as appropriate. Between-group comparisons were conducted at first assessment and at 2-year follow-up via multivariate analysis of variance (MANOVA) with variables that differed between groups as covariates. Bonferroni correction for multiple comparisons was applied to avoid the presence of false positives. To assess the change between the first and the second assessment in clinical and neuropsychological variables, a repeated-measures analysis for the General Linear Model was conducted. In neuropsychological assessment, both analyses were conducted according to distinct cognitive domains (Table 2 shows cognitive domains and the associated neuropsychological variables). All analyses were performed using the statistical package SPSS 15.0.

## Results

### *Socio-demographic characteristics of the sample*

Table 2 shows the gender, age, and socio-economic status of ECT and NECT groups. No significant differences in age, sex, or socio-economic status were found between these two groups.

### *Treatment characteristics of the sample*

All subjects were receiving pharmacological treatment at first assessment (Table 3). Significant differences were found between groups in the number of unsuccessful medication trials ( $t = -2.357$ ,  $p = 0.034$ ) and dose ( $t = 2.089$ ,  $p = 0.048$ ), both being higher in the ECT group than in the NECT group. Taking into account that the number of failed treatments is interpreted as a severity index, statistical analysis was performed with this variable as a covariate. The mean number of ECT sessions per patient was  $12.67 \pm 3.4$  during the acute phase. The mean duration of EEG seizure was  $45.8 \pm 17.2$  (minimum = 21 s; maximum = 93 s). No subjects presented prolonged seizures.

With regard to adverse events with ECT, only mild and transient side effects were reported during and after ECT sessions, such as headache (5.9%) and agitation (0.5%). There were no cases of tardive seizures.

At second assessment, two subjects in the ECT group and one patient in the NECT group were not taking medication. All of them reported that they did not want to be on pharmacological treatment.

### *Comparison between ECT group and no-ECT group at first assessment*

No statistically significant differences were found between the ECT group and NECT group in global severity of symptomatology at baseline (PANSS:  $F = 0.368$ ,  $df = 4.13$ ,  $p = 0.826$ ; CGI:  $F = 1.276$ ,  $df = 1$ ,  $p = 0.279$ ), nor were significant differences observed in any subscale of NES at baseline (sensory integration:  $F = 0.170$ ,  $p = 0.691$ ; motor coordination:  $F = 0.040$ ,  $p = 0.847$ ; sequencing of complex motor tasks:  $F = 0.061$ ,  $p = 0.812$ ; other neurological soft signs:  $F = 1.200$ ,  $p = 0.305$ ). Table 2 shows the results obtained by each group on PANSS and CGI.

Regarding the cognitive variables, no significant differences were found between the groups at first assessment (Working Memory:  $F = 1.507$ ,  $df = 2.15$ ,  $p = 0.261$ ; Attention:  $F = 1.506$ ,  $df = 2.15$ ,  $p = 0.261$ ; Verbal Memory:  $F = 1.424$ ,  $df = 3.14$ ,  $p = 0.288$ ; Executive Functions:  $F = 1.948$ ,  $df = 8.6$ ,  $p = 0.316$ ). Table 2 shows the cognitive variables in both groups.

### *Comparison between ECT group and no-ECT group regarding changes at 2-year follow-up*

Regarding changes between the first and the second assessment, both groups showed significant improvement in clinical variables, specifically in the subscales of positive, general, and total score of PANSS ( $F = 25.504$ ,  $df = 4.13$ ,  $p < 0.001$ ) and CGI ( $F = 110.278$ ,  $df = 1$ ,  $p < 0.001$ ). Moreover, repeated-measures analysis found no significant interaction of time  $\times$  group in either PANSS ( $F = 1.185$ ,  $df = 4.13$ ,  $p = 0.363$ ) or CGI ( $F = 0.405$ ,  $df = 1$ ,  $p = 0.533$ ), which indicates that changes in clinical variables did not differ between the groups (Table 4).

Overall, the analysis of cognitive variables showed higher scores in some attentional ( $F = 12.753$ ,  $df = 2.15$ ,  $p = 0.001$ ) and executive function variables ( $F = 4.239$ ,  $df = 8.6$ ,  $p = 0.048$ ). Specifically, in our sample, there was an improvement in digits forward at second assessment in both ECT and NECT groups and in the semantic category of FAS. No significant changes were found in other cognitive measures between the first and the second assessment either in the ECT or in the NECT group (Working Memory:  $F = 1.138$ ,  $df = 2.15$ ,  $p = 0.347$ ; Verbal Memory:  $F = 1.531$ ,  $df = 4.12$ ,  $p = 0.255$ ). Table 4 shows changes in PANSS, CGI, and neuropsychological variables in both groups. As in the case of clinical variables, the repeated-measures analysis did not reveal significant differences in the interaction time  $\times$  group (Working Memory:  $F = 0.063$ ,  $df = 2.15$ ,  $p = 0.939$ ; Attention:  $F = 1.124$ ,  $df = 2.15$ ,  $p = 0.351$ ; Verbal Memory:  $F = 0.90$ ,  $df = 4.12$ ,  $p = 0.984$ ; Executive Functions:  $F = 2.216$ ,  $df = 8.6$ ,  $p = 0.174$ ), which means that there were no significant differences between the groups in terms of changes in neuropsychological measures.

### *Comparison between ECT group and no-ECT group at 2-year follow-up assessment*

At 2-year follow-up, there were no significant differences between groups in any clinical variable (PANSS:  $F = 2.152$ ,  $df = 3.14$ ,  $p = 0.152$ ; CGI:  $F = 2.048$ ,  $df = 1$ ,  $p = 0.176$ ), and no significant differences were observed between the groups in any NES subscale (sensory integration:  $F = 0.736$ ,  $p = 0.416$ ; motor coordination:  $F = 0.143$ ,  $p = 0.715$ ; sequencing of complex motor tasks:  $F = 0.581$ ,  $p = 0.468$ ; other neurological soft signs:  $F = 3.540$ ,  $p = 0.097$ ).

The comparison of cognitive variables showed no significant differences between ECT and NECT groups in any neuropsychological measure after Bonferroni adjustment (Working Memory:  $F = 1.653$ ,  $df = 2.15$ ,  $p = 0.232$ ; Attention:  $F = 2.107$ ,  $df = 2.15$ ,  $p = 0.164$ ; Verbal Memory:  $F = 0.202$ ,  $df = 3.13$ ,  $p = 0.892$ ; Executive Functions:  $F = 2.355$ ,  $df = 8.9$ ,  $p = 0.156$ ).

Table 2 shows clinical and neuropsychological results of both groups at follow-up assessment.

## Discussion

The main finding of the current study was that, as hypothesized, after 2 years, neuropsychological changes in subjects treated with ECT were similar to those found in subjects not treated with ECT. We found no significant differences in any changes in clinical or neuropsychological variables between the groups during follow-up or at second assessment after 2 years.

Specifically, in our study, both the ECT and NECT groups were matched by age and total PANSS score; therefore, subjects had similar severity of clinical variables at baseline. As was expected, the ECT and NECT groups differed in the number of unsuccessful medication trials, this is due to the fact that the lack of response to at



TABLE 2. SOCIO-DEMOGRAPHIC, CLINICAL, AND NEUROPSYCHOLOGICAL VARIABLES AT BASELINE AND AT 2-YEAR FOLLOW-UP  
IN ELECTROCONVULSIVE THERAPY AND NO ELECTROCONVULSIVE THERAPY GROUPS

<i>Socio-demographic variables</i>	<i>ECT (n = 9) (mean ± SD)</i>	<i>NECT (n = 9) (mean ± SD)</i>	$\chi^2$	<i>p-Value</i>	<i>ECT-2 (mean ± SD)</i>	<i>NECT-2 (mean ± SD)</i>	<i>F<sup>a</sup></i>	<i>p-Value</i>
Gender: male	2 (22.2%)	4 (44.400%)	1.000	0.317				
Age	15.78 ± 1.30	15.78 ± 1.48	0.000	1.000				
Socio-economic status	2.22 ± 0.97	3.11 ± 1.26	4.000	0.406				
<i>Clinical variables</i>								
PANSS positive	23.11 ± 6.25	23.11 ± 7.49	0.718	0.412	11.56 ± 4.80	8.67 ± 2.17	7.409	0.139
PANSS negative	14.44 ± 8.96	12.67 ± 3.04	0.005	0.946	14.88 ± 7.07	16.00 ± 4.18	0.507	0.489
PANSS general	35.33 ± 9.31	36.56 ± 7.79	0.071	0.794	23.11 ± 4.34	19.88 ± 3.14	3.514	0.083
PANSS total	72.89 ± 15.91	71.22 ± 14.09	0.112	0.743	49.55 ± 12.62	44.55 ± 7.05	4.644	0.204
CGI	7.0 ± 0	6.33 ± 1	1.276	0.279	3.11 ± 1.83	2.88 ± 0.92	2.048	0.176
<i>Cognitive variables</i>								
Estimated IQ	78.44 ± 14.47	75.44 ± 12.08	3.017	0.106				
Working memory								
WAIS III digits backward	4.22 ± 1.31	3.67 ± 1.12	0.925	0.354	4.33 ± 1.00	3.77 ± 0.66	0.512	0.487
WAIS III letters and numbers	7.00 ± 2.95	6.78 ± 2.11	0.284	0.603	8.11 ± 3.05	7.44 ± 1.13	3.422	0.087
Attention								
WAIS III digits forward	5.33 ± 1.32	5.11 ± 0.78	1.886	0.193	6.44 ± 1.13	5.66 ± 1.11	3.112	0.101
Time to complete TMT-A	41.11 ± 10.97	46.22 ± 16.33	0.932	0.352	32.00 ± 10.71	40.33 ± 17.42	0.363	0.557
Verbal memory								
TAVEC total learning	37.89 ± 8.47	37.89 ± 10.12	0.477	0.502	42.12 ± 13.23	41.77 ± 9.44	0.359	0.560
TAVEC short-term free recall	8.56 ± 3.35	6.89 ± 2.57	0.711	0.415	8.22 ± 3.27	8.22 ± 3.45	0.012	0.915
TAVEC long-term free recall	8.67 ± 3.57	6.67 ± 2.74	0.813	0.384	8.87 ± 3.13	7.77 ± 3.52	0.038	0.848
Executive functions								
Number of errors from TMT-B	92.11 ± 28.53	97.67 ± 39.41	0.948	0.353	101.77 ± 53.52	122.22 ± 59.43	0.982	0.340
Number of words on the FAS	31.12 ± 10.41	26.77 ± 12.02	0.068	0.799	33.44 ± 13.41	31.00 ± 7.50	0.126	0.728
Number of words on the semantic category of FAS	16.33 ± 5.85	13.33 ± 3.32	2.013	0.186	19.66 ± 4.12	15.88 ± 3.01	4.342	0.057
Stroop interference score	1.78 ± 6.14	-2.35 ± 5.16	3.022	0.113	2.44 ± 6.44	-2.22 ± 9.35	2.039	0.177
WCST number of errors	36.87 ± 17.31	28.12 ± 13.40	0.992	0.343	40.11 ± 17.62	23.55 ± 17.01	0.969	0.343
WCST number of perseverative errors	24.00 ± 19.39	15.37 ± 8.73	0.129	0.727	20.44 ± 11.76	9.77 ± 6.6	1.992	0.182
WCST number of correct responses	76.88 ± 9.22	75.88 ± 6.72	0.120	0.736	75.55 ± 9.28	73.44 ± 9.07	0.639	0.438
WCST number of categories	5.25 ± 1.16	5.75 ± 0.71	0.150	0.707	5.00 ± 1.41	5.33 ± 1.65	0.147	0.708

<sup>a</sup>MANOVA.

ECT-1 = electroconvulsive therapy group at baseline; NECT-1 = no electroconvulsive therapy group at baseline; ECT-2 = electroconvulsive therapy group at 2-year follow-up; NECT-2 = no electroconvulsive therapy group at 2-year follow-up; PANSS = Positive and Negative Syndrome Scale; CGI = Clinical Global Impressions-Improvement Scale; WAIS-III = Wechsler Adult Intelligence Scale Third Edition; TMT-A = Trail Making Test part A; TAVEC = Complutense Verbal Learning Test; TMT-B = Trail Making Test part B; FAS = verbal fluency task; Stroop = Stroop color-word test; WCST = Wisconsin Card Sorting Test; IQ = Intelligence Quotient.

TABLE 3. PHARMACOLOGICAL TREATMENT  
IN ELECTROCONVULSIVE THERAPY (ECT)  
AND NO ELECTROCONVULSIVE THERAPY GROUPS

<i>Patients</i>	<i>First assessment</i>	<i>Second assessment</i>
ECT1	Clozapine 400 mg/day Risperidone 3 mg/day Lorazepam 3 mg/day	Clozapine 275 mg/day
ECT2	Clozapine 600 mg/day Risperidone 2 mg/day	Clozapine 275 mg/day Ziprasidone 240 mg/day
ECT3	Trifluoperazine 25 mg/day	Long acting Risperidone 50 mg/14 days
ECT4	Aripiprazole 15 mg/day Lorazepam 3 mg/day	Without treatment
ECT5	Risperidone 4 mg/day Clonazepam 2.5 mg/day	Without treatment
ECT6	Risperidone 2 mg/day Quetiapine 1,200 mg/day	Clozapine 500 mg/day
ECT7	Oxcarbazepine 600 mg/day Lithium carbonate 1,600 mg/day Quetiapine 1,100 mg/day	Clozapine 425 mg/day Risperidone 1 mg/day Lithium Carbonate 100 mg/day Valproic Acid 1,000 mg/day Diazepam 5 mg/day
ECT8	Lithium Carbonate 1,000 mg/day Olanzapine 20 mg/day	Clozapine 300 mg/day Lithium Carbonate 1,200 mg/day
ECT9	Quetiapine 100 mg/day	Quetiapine 500 mg/day Valproic Acid 800 mg/day
No-ECT1	Risperidone 6 mg/day	Risperidone 4 mg/day Propranolol 30 mg/day
No-ECT2	Risperidone 3 mg/day Diazepam 5 mg/day Biperiden 4 mg/day	Risperidone 1 mg/day Diazepam 10 mg/day
No-ECT3	Risperidone 3 mg/day Propranolol 30 mg/day Lorazepam 1 mg/day Sertraline 150 mg/day	Quetiapine 300 mg/day Valproic Acid 1,000 mg/day
No-ECT4	Quetiapine 400 mg/day Sertraline 100 mg/day	Quetiapine 1,000 mg/day Sertraline 100 mg/day
No-ECT5	Risperidone 4 mg/day Sertraline 100 mg/day	Long Acting Risperidone 37.5 mg/14 days Risperidone 3 mg/day
No-ECT6	Risperidone 4 mg/day	Risperidone 3 mg/day
No-ECT7	Risperidone 5 mg/day Biperiden 1 mg/day	Risperidone 4 mg/day
No-ECT8	Risperidone 2 mg/day Lorazepam 2 mg/day	Without treatment
No-ECT9	Risperidone 6 mg/day	Olanzapine 20 mg/day

least two antipsychotics is a recommendation criteria of ECT in the AACAP (Ghaziuddin et al. 2004). Regarding the cognitive variables, our study supports other investigations that have assessed the influence of ECT on cognition and have reported no differences in memory and learning after a few weeks to 7 months of treatment (Weeks et al. 1980; Frith et al. 1983; Smith et al. 2010). Most of these studies do not have a control group against which to compare the baseline results (Calev et al. 1991; Squire and Chace 1996; Smith et al. 2010), and none of them have matched both groups while taking into account the psychopathology that has a clear influence on neuropsychological performance (Basso et al. 1998; Bilder et al. 2000; Fitzgerald et al. 2004; Good et al. 2004). Matching by total PANSS score, our results did not reveal any difference in cognitive variables at first assessment.

At follow-up, our study showed a significant improvement in positive, general, and total score of PANSS in both groups. Previous studies carried out with adolescent samples treated with antipsychotics had showed an improvement in clinical severity of symptoms assessed with the PANSS (Sikich et al. 2008; Arango et al. 2009; Haas et al. 2009; Robb et al. 2010). With ECT and in adolescent patients, Baeza et al. (2010) analyzed a sample of 13 adolescents with schizophrenia syndrome disorder followed-up during 6 months and observed a significant improvement in positive and general PANSS subscales scores. Moreover, Rey and Walter (1997) reviewed studies published about the use of ECT in persons 18 years of age or younger, concluding that the rate of improvement across the studies was 42% for schizophrenia immediately after the ECT treatment and 10% 6 months after ECT.

Interestingly, in our study, the repeated-measures analysis found no significant interaction of time  $\times$  group; thus, changes in clinical variables seemed to be similar in both groups and were independent of the ECT treatment.

Regarding the cognitive assessment, an improvement in digits forward and the semantic category of FAS was found in both groups 2 years after the ECT treatment. Very few studies have analyzed these cognitive functions. Rami-Gonzalez et al. (2003a) found impairment in verbal fluency. However, the sample of that study was composed of patients with different diagnoses (schizophrenia, depression and bipolar disorder), and the assessment was performed during maintenance ECT. No long-term studies of verbal fluency are found in the literature, and other studies conducted with adolescent samples with severe mood disorders have found no significant differences in attention at long term follow-up (Cohen et al. 2000; Russell et al. 2003).

No significant changes were detected in other neuropsychological variables at 2-year follow-up. These results support other long-term studies that have found no cognitive differences at follow-up (Cohen et al. 2000; Russell et al. 2003). When we analyzed the results with a repeated-measures method, no significant interaction time  $\times$  group was found. Thus, the treatment with ECT in our sample had no influence on changes in neuropsychological variables. To our knowledge, no studies in the literature have aimed at analyzing differences in neuropsychological change in adolescent samples with schizophrenia treated with ECT.

Finally, the comparison between the ECT and the NECT groups at 2-year follow-up showed no significant differences between groups in any clinical or neuropsychological variable. Kutcher and Robertson (1995) studied a sample of 22 young patients, aged between 13 and 19, in whom a bipolar disorder was diagnosed and divided them into two groups: 16 who accepted ECT and 6 who refused it and continued with pharmacological treatment. A significant improvement of clinical symptoms was observed in the ECT group. No long-term follow-up studies in children or adolescents in whom schizophrenia was diagnosed and who were treated with ECT have been conducted using the PANSS to assess clinical outcome.

Regarding the cognitive assessment, there are few studies that assess neuropsychological functions in adolescent samples with which to compare our results. Nevertheless, our study supports the research of Cohen et al. (2000) with affective patients. Theirs was the only long-term follow-up study conducted with a sample of adolescent patients treated with ECT, and they found no differences in neuropsychological variables between the ECT group and a psychiatric comparison group.

One of the main limitations of our study is the small sample size, but this is due to the fact that ECT is not a first-choice treatment and is only administrated in specific cases (following the AACAP guidelines). As a result, the study is not powered enough to show rare

TABLE 4. CHANGES IN CLINICAL AND NEUROPSYCHOLOGICAL VARIABLES BETWEEN FIRST AND SECOND ASSESSMENT IN ELECTROCONVULSIVE THERAPY AND NO ELECTROCONVULSIVE THERAPY GROUPS

	<i>Time</i>		<i>Time × group</i>	
	F <sup>a</sup>	p-Value	F <sup>a</sup>	p-Value
<i>Clinical variables</i>				
PANSS positive	<b>80.791</b>	< <b>0.001</b>	0.997	0.333
PANSS negative	0.711	0.412	0.415	0.528
PANSS general	<b>30.263</b>	< <b>0.001</b>	0.716	0.410
PANSS total	<b>24.671</b>	< <b>0.001</b>	0.110	0.745
CGI	<b>110.278</b>	< <b>0.001</b>	0.405	0.533
<i>Cognitive variables</i>				
<i>Working memory</i>				
WAIS III digits backward	0.180	0.677	0.000	1.000
WAIS III letter and number	2.129	0.164	0.133	0.720
<i>Attention</i>				
WAIS III digits forward	<b>11.688</b>	<b>0.004</b>	1.299	0.271
Time to complete TMT-A	3.996	0.063	0.184	0.673
<i>Verbal memory</i>				
TAVEC total learning	4.068	0.062	0.008	0.930
TAVEC short-term free recall	2.301	0.150	0.017	0.899
TAVEC long-term free recall	1.369	0.260	0.004	0.952
<i>Executive functions</i>				
Number of errors from TMT-B	3.004	0.107	0.651	0.434
Number of words on the FAS	2.938	0.110	0.180	0.679
Number of words on the semantic category of FAS	<b>9.229</b>	<b>0.010</b>	0.012	0.914
Stroop interference score	2.365	0.148	0.776	0.394
WCST number of errors	1.267	0.281	1.742	0.210
WCST number of perseverative errors	4.659	0.050 <sup>b</sup>	4.659	0.050 <sup>b</sup>
WCST number of correct responses	0.70	0.796	0.129	0.726
WCST number of categories	0.059	0.812	0.059	0.812

Significant values marked in bold.

<sup>a</sup>MANOVA.

<sup>b</sup>Repeated measures analysis.

ECT-1=electroconvulsive therapy group at baseline; NECT-1=no electroconvulsive therapy group at baseline; ECT-2=electroconvulsive therapy group at 2-year follow-up; NECT-2=no electroconvulsive therapy group at 2-year follow-up; PANSS=Positive and Negative Syndrome Scale; CGI=Clinical Global Impressions-Improvement Scale; WAIS-III=Wechsler Adult Intelligence Scale Third Edition; TMT-A=Trail Making Test part A; TAVEC=Complutense Verbal Learning Test; TMT-B=Trail Making Test part B; FAS=verbal fluency task; Stroop=Stroop color-word test; WCST=Wisconsin Card Sorting Test; IQ=Intelligence Quotient.

incidence events such as those due to secondary effects. Another limitation was that the cognitive assessment was not conducted in a blind fashion, and biographic memory had not been assessed.

Among the strengths of the study, it should be noted that this research has been conducted with two homogeneous samples of adolescents in whom schizophrenia has been diagnosed and matched by age, socio-economic status, and PANSS total score to avoid the influence of severity of clinical symptoms on the neuropsychological assessment. Moreover, all subjects included in the analysis had a long-term follow-up of clinical and cognitive variables that allowed us to assess the long-term influence of ECT on cognitive functions. Indeed, this is the first study to investigate the long-term influence of ECT treatment in a sample of children and adolescents with schizophrenia.

Future research is needed to investigate the long-term cognitive effects of ECT in adolescent patients in whom schizophrenia spectrum disorders have been diagnosed.

### Clinical Significance

The current study shows no significant differences in changes over time in any clinical or neuropsychological variable between an ECT group and a no-ECT group at follow-up. ECT did not seem to have

any negative influence on clinical or neuropsychological variables in our sample at 2-year follow-up. Thus, ECT treatment should be taken into serious consideration as a possible treatment in adolescents in whom schizophrenia spectrum disorder is diagnosed, where patients have not responded to at least two adequate pharmacotherapeutic trials. More research is needed to increase knowledge about the long-term effects of ECT on cognition in adolescent subjects.

### Disclosures

Elena de la Serna, Itziar Flamarique, Alexandre Pons, Olga Puig, Susana Andrés-Perpiña, Luisa Lázaro, Juan Miguel Garrido, and Inmaculada Baeza affirm that they have no conflicts of interest.

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## References

- American Psychiatric Association: The Practice of ECT: Recommendations for Treatment, Training, and Privileging. A Task Force Report, 2nd ed. Washington, DC; 2001.
- Arango C, Robles O, Parellada M, Fraguas D, Ruiz-Sancho A, Medina O, Zabala A, Bombin I, Moreno D: Olanzapine compared to quetiapine in adolescents with a first psychotic episode. *Eur Child Adolesc Psychiatry* 18:418–428, 2009.
- Baeza I, Flamarique I, Garrido JM, Horga G, Pons A, Bernardo M, Morer A, Lázaro ML, Castro-Fornieles J: Clinical experience on ECT in adolescents with schizophrenia spectrum disorders. *J Child Adol Psychopharmacol* 20:205–209, 2010.
- Basso MR, Nasrallah HA, Olson SC, Bornstein RA: Neuropsychological correlates of negative, disorganized and psychotic symptoms in schizophrenia. *Schizophr Res* 31:99–111, 1998.
- Benedet MJ, Alejandre MA: TAVEC, Test de aprendizaje Verbal España-Complutense. Madrid: TEA Ediciones, 1998.
- Bilder RM, Goldman RS, Robinson D, Reiter G, Bell L, Bates JA, Pappadopoulos E, Willson DF, Alvir JM, Woerner MG, Geisler S, Kane JM, Lieberman JA: Neuropsychology of first-episode schizophrenia: Initial characterization and clinical correlates. *Am J Psychiatry* 157:549–559, 2000.
- Bloch Y, Sobol D, Levkovitz Y, Kron S, Ratzoni G: Reasons for referral for electroconvulsive therapy: A comparison between adolescents and adults. *Australas Psychiatry* 16:191–194, 2008.
- Buchanan RW, Heinrichs DW: The Neurological Evaluation Scale (NES): A structured instrument for the assessment of neurological signs in schizophrenia. *Psychiatry Res* 27:335–350, 1989.
- Calev A, Nigal D, Shapira B, Tubi N, Chazan S, Ben Yehuda Y, Kugelmass S, Lerer B: Early and long-term effects of electroconvulsive therapy and depression on memory and other cognitive functions. *J Nerv Ment Dis* 179:526–533, 1991.
- Calev A, Gaudino EA, Squires NK, Zervas IM, Fink M: ECT and non-memory cognition: a review. *Br J Clin Psychol* 34:505–15, 1995.
- Cohen D, Taieb O, Flament M, Benoit N, Chevrete S, Corcos M, Fossati P, Jeammet P, Allilaire JF, Basquin M: Absence of cognitive impairment at long-term follow-up in adolescents treated with ECT for severe mood disorder. *Am J Psychiatry* 157:460–462, 2000.
- Fitzgerald D, Lucas S, Redoblado MA, Winter V, Brennan J, Anderson J, Harris A: Cognitive functioning in young people with first episode psychosis: relationship to diagnosis and clinical characteristics. *Aust N Z J Psychiatry* 38:501–510, 2004.
- Frith CD, Stevens M, Johnstone EC, Deakin JF, Lawler P, Crow TJ: Effects of ECT and depression on various aspects of memory. *Br J Psychiatry* 142:610–617, 1983.
- Ghaziuddin M, Kutcher S, Knapp P, The Work Group on Quality Issues: Practice parameter for use of electroconvulsive therapy with adolescents. *J Am Acad Child Adolesc Psychiatry* 43:1521–1539, 2004.
- Ghaziuddin N, King CA, Naylor MW, Ghaziuddin M, Chaudhary N, Giordani B, Dequardo JR, Tandon R, Greden J: Electroconvulsive treatment in adolescents with pharmacotherapy-refractory depression. *J Child Adolesc Psychopharmacol* 6:259–271, 1996.
- Ghaziuddin N, Laughrin D, Giordani B: Cognitive side effects of electroconvulsive therapy in adolescents. *J Child Adolesc Psychopharmacol* 10:269–276, 2000.
- Golden CJ: Stroop Color and Word Test. Wood Dale, IL: Stoelting Co., 1978.
- Good KP, Rabinowitz J, Whitehorn D, Harvey PD, DeSmedt G, Kopala LC: The relationship of neuropsychological test performance with the PANSS in antipsychotic naive, first-episode psychosis patients. *Schizophr Res* 68:11–19, 2004.
- Guy W: Clinical Global Impression. ECDEU Assessment Manual for Psychopharmacology, Revised National Institute of Mental Health. Rockville, MD., 1976.
- Haas M, Unis AS, Armenteros J, Copenhaver MD, Quiroz JA, Kushner SF: A 6-week, randomized, double-blind, placebo-controlled study of the efficacy and safety of risperidone in adolescents with schizophrenia. *J Child Adolesc Psychopharmacol* 19:611–621, 2009.
- Heaton RK, Chelune GJ, Talley JL, Kay G, Curtiss G: Wisconsin Card Sorting Test (WCST). Madrid: TEA Ediciones; 1997.
- Hollingshead, A. B and Redlich F.C. Social Class and Mental Illness. Wiley, New York. 1958.
- Ingram A, Saling MM, Schweitzer I: Cognitive side effects of brief pulse electroconvulsive therapy: A review. *J ECT* 24:3–9, 2008.
- Johanson A, Gustafson L, Risberg J, Rosen I, Sjöbeck M, Silfverkiöld P: Long-term follow-up in depressed patients treated with electroconvulsive therapy. *J ECT* 21:214–220, 2005.
- Kay SR, Fiszbein A, Opler LA: The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 13:261–276, 1987.
- Kutcher S, Robertson HA: Electroconvulsive therapy in treatment-resistant bipolar youth. *J Child Adolesc Psychopharmacol* 5:167–175, 1995.
- Lezak MD: Neuropsychological Assessment, 3rd ed. New York: Oxford University Press, 1995, pp. 333–686.
- Lisanby SH, Maddox JH, Prudic J, Devanand DP, Sackeim HA: The effects of electroconvulsive therapy on memory of autobiographical and public events. *Arch Gen Psychiatry* 57:581–590, 2000.
- MacQueen G, Parkin C, Marriott M, Begin H, Hasey G: The long-term impact of treatment with electroconvulsive therapy on discrete memory systems in patients with bipolar disorder. *J Psychiatry Neurosci* 32:241–249, 2007.
- Moise FN, Petrides G: Case study: Electroconvulsive therapy in adolescents. *J Am Acad Child Adolesc Psychiatry* 35:312–318, 1996.
- Peralta V, Cuesta MJ: Psychometric properties of the positive and negative syndrome scale (PANSS) in schizophrenia. *Psychiatry Res* 53:31–40, 1994.
- Rami L, Bernardo M, Boget T, Ferrer J, Portella MJ, Gil-Verona JA, Salamero M: Cognitive status of psychiatric patients under maintenance electroconvulsive therapy: a one-year longitudinal study. *J Neuropsychiatry Clin Neurosci* 16:465–471, 2004.
- Rami-Gonzalez L, Bernardo M, Boget T, Salamero M, Gil-Verona JA, Junque C: Subtypes of memory dysfunction associated with ECT: Characteristics and neurobiological bases. *J ECT* 17:129–135, 2001.
- Rami-Gonzalez L, Salamero M, Boget T, Catalan R, Ferrer J, Bernardo M: Pattern of cognitive dysfunction in depressive patients during maintenance electroconvulsive therapy. *Psychol Med* 33:345–350, 2003a.
- Rami-Gonzalez L, Bernardo M, Portella MJ, Goti J, Gil-Verona JA, Salamero M: Assessment of frontal functions in psychiatric patients during maintenance electroconvulsive therapy. *Actas Esp Psiquiatr* 31:69–72, 2003b.
- Reitan RM, Wolfson D: The Halstead-Reitan Neuropsychological Test Battery. Tucson AZ: Neuropsychology Press, 1985.
- Rey JM, Walter G: Half a century of ECT use in young people. *Am J Psychiatry* 154:595–602, 1997.
- Robb AS, Carson WH, Nyilas M, Ali M, Forbes RA, Iwamoto T, Assuncao-Talbott S, Whitehead R, Pikalov A: Changes in positive and negative syndrome scale-derived hostility factor in adolescents with schizophrenia treated with aripiprazole: *post hoc* analysis of randomized clinical trial data. *J Child Adolesc Psychopharmacol* 20:33–38, 2010.
- Russell JC, Rasmussen KG, O'Connor MK, Copeman CA, Ryan DA, Rummans TA: Long-term maintenance ECT: A retrospective review of efficacy and cognitive outcome. *J ECT* 19:4–9, 2003.



- Sackeim HA, Prudic J, Devanand DP, Nobler MS, Lisanby SH, Peyser S, Fitzsimons L, Moody BJ, Clark J: A prospective, randomized, double-blind comparison of bilateral and right unilateral electroconvulsive therapy at different stimulus intensities. *Arch Gen Psychiatry* 57:425–34, 2000.
- Sackeim HA, Prudic J, Nobler MS, Fitzsimons L, Lisanby SH, Payne N, Berman RM, Brakemeier EL, Perera T, Devanand DP: Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *Brain Stimul* 1:71–83, 2008.
- Sikich L, Frazier JA, McClellan J, Findling RL, Vitiello B, Ritz L, Ambler D, Puglia M, Maloney AE, Michael E, De Jong S, Slifka K, Noyes N, Hlatala S, Pierson L, McNamara NK, Delporto-Bedoya D, Anderson R, Hamer RM, Lieberman JA: Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: Findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study. *Am J Psychiatry* 165:1420–1431, 2008.
- Smith GE, Rasmussen KG, Cullum CM, Felmler-Devine MD, Petrides G, Rummans TA, Husain MM, Mueller M, Bernstein HJ, Knapp RG, O'Connor MK, Fink M, Sampson S, Bailine SH, Kellner CH: A randomized controlled trial comparing the memory effects of continuation electroconvulsive therapy versus continuation pharmacotherapy: Results from the Consortium for Research in ECT (CORE) study. *J Clin Psychiatry* 71:185–193, 2010.
- Squire LR: ECT and memory loss. *Am J Psychiatry* 134:997–1001, 1977.
- Squire LR, Chace PM: Memory functions six to nine months after electroconvulsive therapy. 1975. *Convuls Ther* 12:239–256, 1996.
- Steif BL, Sackeim HA, Portnoy S, Decina P, Malitz S: Effects of depression and ECT on anterograde memory. *Biol Psychiatry* 21:921–930, 1986.
- Taieb O, Flament MF, Chevret S, Jeammet P, Allilaire JF, Mazet P, Cohen D: Clinical relevance of electroconvulsive therapy (ECT) in adolescents with severe mood disorder: Evidence from a follow-up study. *Eur Psychiatry* 17:206–212, 2002.
- Tsourtos G, Spong J, Stough C: The effects of electro-convulsive therapy on the speed of information processing in major depression. *J Affect Disord* 103:263–266, 2007.
- Vothknecht S, Kho KH, van Schaick HW, Zwinderman AH, Middelkoop H, Blansjaar BA: Effects of maintenance electroconvulsive therapy on cognitive functions. *J ECT* 19:151–157, 2003.
- Wechsler D: WAIS-III Wechsler Intelligence Scale for Adults. Madrid: TEA Ediciones, 2001.
- Wechsler D: Wechsler Intelligence Scale for Children-Revised (WISC-R). Madrid: TEA Ediciones, 1974.
- Weeks D, Freeman CP, Kendell RE: ECT: III: Enduring cognitive deficits? *Br J Psychiatry* 137:26–37, 1980.
- Zervas IM, Calev A, Jandorf L, Schwartz J, Gaudino E, Tubi N, Lerer B, Shapira B: Age-dependent effects of electroconvulsive therapy on memory. *Convuls Ther* 9:39–42, 1993.

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