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Does electroconvulsive therapy (ECT) affect cognitive components of auditory evoked P300?

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Short communication

Abstract. Electroconvulsive therapy (ECT), as a treatment tool for psychiatric disorders, is believed to be safe and effective. Nevertheless, it has a negative impact on cognitive functioning, especially on memory, causing both retrograde and anterograde amnesia. However, ECT effects on more subtle stages of information processing are not studied enough. Event-related potentials, and especially P300, are thought to reflect physiology of cognition. Thus, we aimed to evaluate the effects of ECT treatment on parameters of endogenous components (N2, P3) of the P300 potential. Seventeen patients suffering from schizophrenia, schizoaffective disorder and recurrent depressive disorder participated at the study. After the course of ECT, significant increase of N2 amplitude in parietal midline region and prolongation of P3 latency in frontal midline region, of which the magnitude positively correlated with the number of ECT procedures, have been obtained.

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Electroconvulsive therapy (ECT) has been used in psychiatric practice since its first application by Cerletti and Bini in 1938 (Fink 2001). Nowadays, it is a safe and effective (effectiveness rate 30–80%) treatment tool for medication therapy resistant forms of depression, mania, schizoaffective disorder and schizophrenia (Fink 2001, Griskova et al. 2004). The method of ECT is based on the passing of an electrical current through the brain, while the patient is under general anesthesia and muscle relaxation, to cause synchronous depolarization of the neurons and subsequent induction of generalized seizure (Swartz and Abrams 1994). It has been shown that induced seizures may produce therapeutic effects through changes in neurotransmission and neuronal architecture. Nevertheless, these changes also are considered to be the cause of the cognitive adverse effects of ECT that are the main reason for restricted use of the method. The cognitive effects most frequently reported by patients as being adversely affected by the treatment are the effects of ECT on memory. These effects have been extensively studied and reviewed (Abrams 1997, Coleman et al. 1996, Lisanby et al. 2000, Sackeim et al. 1994, Weiner 2000). It is well established that ECT affects processes engaged in memory and learning, causing both generally short-lasting retrograde and anterograde amnesia. However, ECT effects on more subtle processes underlying attention, information perception, storage and retrieval remain unclear.

It is accepted that event-related potentials (ERPs) can indicate cognitive processing stages and reflect physiology of cognition. The most widely used ERP is P300, especially of auditory modality. Generally, it is elicited by a typical oddball task, when a series of two different tone stimuli is presented with the rare tone occurring less frequently than the standard, and the subject is required to note the occurrence of this target and to not respond to the standard (Hruby and Marsalek 2003, Picton 1992, Polich and Kok 1995). P300 can be considered as a manifestation of CNS activity involved in the processing of new information when attention is engaged to update memory representation (Hruby and Marsalek 2003, Muller-Gass and Campbell 2002, Polich and Kok 1995, Vandoolaeghe et al. 1998), and its underlying cellular mechanisms probably are those of cortical inhibition (Michalski 2001). It consists of early components (P1, N1, P2), which are considered to reflect the sensation and discrimination of a stimulus, i.e., input-related processes, and late components (N2, P3), which are related to the perception, cognition and activation of the processes engaged in working memory. N2 wave may reflect stimulus categorization and be closely related to stimulus evaluation. P3 wave is related to task completion and decision-making (Frodl et al. 1998, 1999, Vandoolaeghe et al. 1998) and it is the most commonly analysed component of the P300 potential, appearing as a positive wave approximately 300 ms after the subject makes a conscious detection of the target stimulus. The main parameters for evaluation of P300 components are the amplitude and latency. The amplitude is linked to the amount of attentional resources engaged in task completion. The latency is thought to reflect the time needed for cognitive processing (Frodl et al. 1998, 1999, Hruby and Marsalek 2003, Picton 1992). It has been stated that the P300 potential is affected in several psychiatric disorders, such as schizophrenia and depression, which are linked to changes in levels of various neurotransmitters and cerebral architecture (Frodl et al. 1999, Hruby and Marsalek 2003). P300 studies are widely used to evaluate the effects of medication therapy on cognitive functions of psychiatric patients. Nevertheless, the effects of ECT treatment on P300 have not been investigated enough. Thus, we aimed to evaluate the effects of ECT treatment in psychiatric patients on parameters of the endogenous components (N2, P3 waves) of the P300 potential.

Seventeen inpatients (nine males, eight females) referred for ECT formed the sample for this study. The exclusion criteria were cardiovascular and neurological illnesses. Informed consent for the study was obtained from all the participants. Mean age of the patients was 41.2 ± 12.5 years (range 24–62 years). Diagnoses were made by clinicians according to ICD–10: eight patients had paranoid schizophrenia, four schizoaffective disorder, depressive type and five depressive episode without psychotic symptoms. For the patients with diagnoses of schizophrenia and schizoaffective disorder clinical symptoms were evaluated using Positive and Negative Syndrome Scale (PANSS). The severity of depressive symptoms in the cases of depression and schizoaffective disorders was evaluated with the 17-item Hamilton Depression Rating Scale (HDRS). All the patients were taking medication before and during the course of ECT. Patients with the diagnoses of schizophrenia and schizoaffective disorder were taking antipsychotics: haloperidol (4–20 mg/d), quetiapine (0.3–0.6 mg/d) or olanzapine (0.01 mg/d). Patients with the diagnosis of depression were taking the antidepressant mirtazapine (0.03–0.06 mg/d).

A comparison group for P300 parameters (without ECT) comprised healthy volunteers (nine males, six females; mean age 40.9 ± 13.1 years, range 21–63 years) that had no known neurological or psychiatric problems.

In this study the auditory oddball paradigm was applied. The subjects were comfortably sitting with their eyes closed. The auditory stimuli were presented binaurally through the earphones. Frequent tone as a pitch with a frequency of 1 000 Hz occurred with the probability of 80%; the rare tone as a pitch of 2 000 Hz occurred randomly with the probability of 20%. The intensity of both the non-target and target stimuli was 60 dB and the duration was 50 ms. Inter-stimulus interval was 1 500 ms. There were two trials for each subject with 30 tones presented during each trial. The subjects were asked to count 2000 Hz tones. Recordings were made from 3 sites (Fz, Cz, Pz electrodes placed according to the international 10/20 electrode placement system) referenced to linked ears. The signals were filtered with a band-pass filter (0.01–30 Hz). Single trial epoch was 1 000 ms duration. Epochs that contained voltage exceeding ± 100 μV at Fz were rejected.

In the responses to the rare tone, cognitive P300 complex consisting of N2 and P3 and representing the endogenous response was identified. Two main parameters were measured: peak latency and amplitude. Latencies were defined as the time of most negative (for N2) or most positive (for P3) point of the curve between 200–500 ms. Amplitudes were measured as peak-to-peak voltages for P2-N2 and N2-P3. P300 potential recordings for the control subjects were made once. For the patients, P300 potential was recorded twice: before the first ECT procedure and a day after the last ECT procedure (mean number of ECT procedures was 8.6 ± 2.1, range 6–12).

ECT was administered twice weekly. Only bilateral ECT using bitemporal electrode placement was given. The ECT stimulus was delivered using a brief pulse, constant current ECT device (Thymatron DGx). This machine has the following stimulation parameters: peak current 0.9 A; pulse frequency 70 Hz; pulse width 1 ms. The total stimulus dose (in mC) was adjusted by setting the stimulus train length (3–5 s).

Data on the latency and amplitude of N2 and P3 were examined statistically. Since none of the data distributed normally, non-parametric statistical tests were applied: Mann-Whitney U test for independent samples, Wilcoxon test for dependent samples and Spearman's R correlation test. The level of significance was set at $P \leq 0.05$.

Analysis of the data included the following: PANSS and HDRS scores of the patients were calculated before and after ECT and compared. The values of N2, P3 latency and amplitude recorded with Fz, Cz, Pz electrodes were measured for control group, patient group before ECT and patient group after ECT. The data of the patients before ECT were compared to that after ECT. Both the data before and after ECT were compared to that of healthy subjects. The changes of values of P300 parameters with regard to the baseline were expressed in percent and the correlation with the number of ECT procedures was checked.

The following results were obtained: A significant (P=0.01 for all the scales) improvement of the clinical symptoms after the ECT course has been shown: HDRS mean before ECT 31.5 ± 7.55 vs. 10.23 ± 7.42 after ECT; PANSS mean 116.18 ± 32.87 vs. 64.73 ± 22.15. There were no significant differences in N2 latency between controls and patient group before ECT. However, Frodl and coauthors (1999) and Lebedeva and coauthors (2002) have shown that N2 latency may be delayed in both schizophrenic and depressed subjects. N2 amplitude of the patients before ECT was higher compared to healthy subjects, especially in frontal midline area (7.10 ± 4.31 μV vs. 4.09 ± 2.80 μV, P=0.04) (Fig. 1). This finding is of particular interest because it is inconsistent with the results reported by Frodl and coauthors (1998), Lebedeva and coauthors (2000, 2002) and presented in Alfimova and coauthors (1999). These authors have observed reduction of N2 amplitude in schizophrenic as well as depressed patients. We could specu-

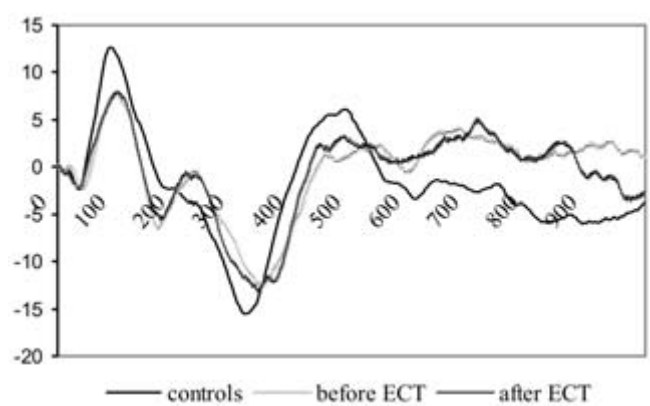

Fig. 1. Grand average curve of P300 recorded from Fz (frontal midline region) for controls, patients before ECT, and patients after ECT

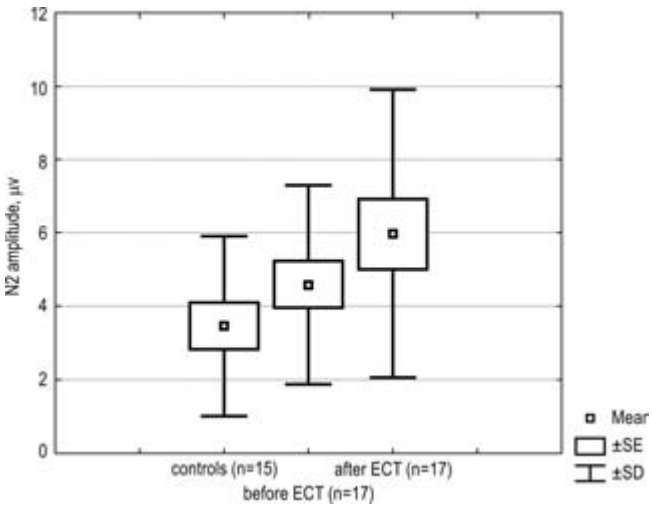

Fig. 2. N2 amplitude (parietal midline region) for controls, patients before ECT, and patients after ECT

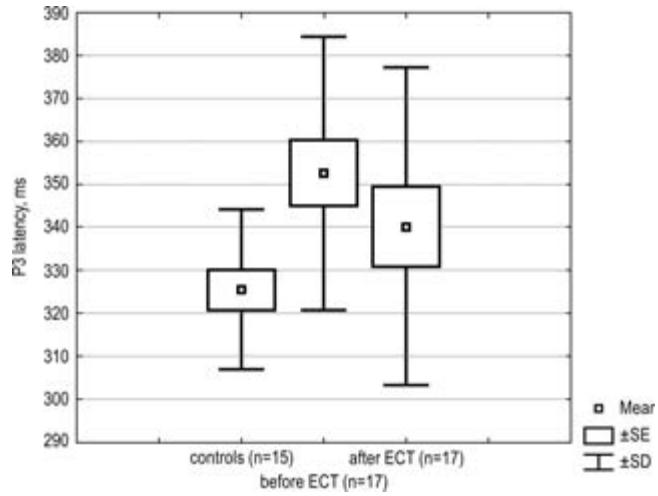

Fig. 3. P3 latency (frontal midline region) for controls, patients before ECT, and patients after ECT

late that this discrepancy could be due to the use of a different method for amplitude measuring (herein peak-to-peak amplitude was measured, thus P2 amplitude changes could affect the results). After the ECT course, N2 amplitude became significantly larger compared to healthy subjects in parietal midline region (5.99 ± 3.93 μV vs. 3.77 ± 2.46 μV, P=0.04) (Fig. 2). We suppose that the processes of stimulus classification and categorization in patients referred for ECT require more neuronal resources. A significantly longer P3 latency of patients before ECT course was obtained in frontal (352.59 ± 31.77 ms vs. 325.47 ± 18.49 ms, P=0.007), central (349.53 ± 32.68 ms vs. 328.8 ± 17.50 ms, P=0.03) and parietal (349.41 ± 32.22 ms vs. 332.53 ± 18.74 ms, P=0.05) midline regions in comparison with control subjects. These results are in agreement with those of Alfimova and coauthors (1999), Frodl and coauthors (1998), Karaaslan and coauthors (2003), Lebedeva and coauthors (2000, 2002) and Vandoolaeghe and coauthors (1998), who have showed that prolongation of P3 latency can be observed both in schizophrenia and depression. After the ECT treatment P3 latency remained increased only in frontal midline region when compared to control group (340 ± 37.03 ms vs. 325.47 ± 18.49 ms, P=0.049) (Fig. 1). Still, in comparison to that of patients before ECT, a slight reduction of P3 latency was observed, although the difference did not reach a statistically significant level (340 ± 37.03 ms vs. 352.59 ± 31.77 ms) (Fig. 3). Taking into account the significance of frontal regions for cognitive functioning, it could be speculated that ECT may affect the speed of cognitive processing. P3 amplitude differences between the control group, patients before ECT and patients after ECT were non-significant. However, P3 amplitude before ECT was slightly diminished in the patient group. The impairment of P3 amplitude in schizophrenic and depressed subjects has also been reported by Karaaslan and coauthors (2003) and Lebedeva and coauthors (2000, 2002). Moreover, it is suggested that P3 amplitude reduction is a trait marker of schizophrenic patients (Manthalon et al. 2000). Significant positive correlation (r=0.53, P=0.03) was found only for percentage expression of P3 latency difference and number of ECT procedures in frontal midline region. In other words, the larger the number of administered ECT procedures, the more different is P3 latency after ECT compared to that before ECT.

CONCLUSION

Electroconvulsive therapy has no negative impact on the parameters of endogenous components (N2, P3) of auditory evoked P300 potential. The differences obtained in this study were that in comparison to healthy volunteers, however, amplitudes and latencies of N2 wave and of P3 wave did not change significantly after the course of ECT compared to that before ECT.

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