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Electroconvulsive therapy and autobiographical memory in patients with treatment-resistant depression

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Summary

Objectives. Electroconvulsive therapy (ECT) is the most effective treatment for drug-resistant depression. In most studies, cognitive functions including working and semantic memory showed only transient impairment after ECT. However, the deficits of episodic (autobiographical) memory were demonstrated to be long-lasting.

Methods. We investigated autobiographical memory in 20 patients (8 male, 12 female), aged 21–64 years, with drug-resistant depression, treated with ECT, using the Polish adaptation of the Autobiographical Memory Interview-Short Form (AMI-SF). The assessments were performed before, immediately after 10–12 ECT sessions, and 3 months thereafter.

Results. Before the ECT, the mean severity of depression was 30 ± 6 points on the 17-item Hamilton Depression Rating Scale and the treatment produced a significant clinical improvement in all patients. The indices of autobiographical memory, as assessed by the AMI-SF, were significantly lower immediately after ECT and 3 months thereafter. The impairment in autobiographical memory did not show correlation with clinical improvement and with any other clinical factors.

Conclusions. The results obtained in patients with drug-resistant depression confirm that ECT treatment produces a significant impairment of autobiographical memory persisting also three months after the procedure, suggesting that it may be the most important adverse cognitive effect of the ECT.

Key words: electroconvulsive therapy, drug-resistant depression, autobiographical memory

Introduction

The issue of drug-resistant depression has become increasingly important in recent years. This applies to both unipolar depression as well as to depression in the course of bipolar disorder. Electroconvulsive therapy (ECT) is the most effective treatment

for drug-resistant depression, according to recent recommendations [1]. The efficacy of ECT seems similar in both unipolar and bipolar depression [2, 3].

A significant concern about ECT is the possibility of its producing cognitive impairment. In their meta-analysis, Semkovska and McLoughlin [4] concluded that the ECT-related cognitive impairments are mainly limited to the first 3 days post-treatment and these deficits resolve during the subsequent 2 weeks. Fernie et al. [5] showed that the results of spatial recognition memory were poorer, compared to pre-ECT baseline, up to 3 months post-ECT, but significantly improved at 6 months. Kessler et al. [6] demonstrated no differences between general cognitive functions, before and after ECT, in treatment-resistant bipolar depression.

Previously, we investigated 63 patients (18 men, 45 women), aged 34–75 years. Cognitive assessments were performed before, immediately after 6–12 ECT sessions and 3 months thereafter, using *the Benton Visual Retention*, *Trail Making* (TMT), and *Rey-Osterrieth Complex Figure* (ROCF) tests, *the Digit Span* of *the Wechsler Adult Intelligence Scale*, and *the Rey Auditory Verbal Learning* (RAVLT), verbal fluency and Stroop tests. Immediately after ECT, a significant worsening was noted in some indices of memory and verbal functions. However, 3 months after ECT, the indices of both RAVLT and verbal fluency significantly improved compared to baseline, and those of the Benton and ROCF were significantly better than before ECT. *The Digit Span*, Stroop, and TMT were not affected by the treatment. The main weakness of our study was not measuring the autobiographical memory [7].

Apart from general cognitive functions, including working and semantic memory, the studies on the effect of ECT on episodic memory (autobiographical memory component) have consistently shown an adverse effect on this function, which may be long-lasting. In his review paper of 2008, Fraser et al. [8] presented the evidence of autobiographical memory (AM) impairment as a result of ECT. Objective measures found memory loss to be relatively short-term (< 6 months post-treatment), whereas subjective accounts reported amnesia to be more persistent (> 6 months post-ECT). They also indicated on some effect of the ECT technique on this memory. An impairment of AM after ECT has been also confirmed in more recent research of Kessler et al. [6].

In most studies, for the assessment of AM, *the Autobiographical Memory Interview* (AMI) or its short version (*Short Form* – SF), elaborated by the researchers from Columbia University, has been used. Recently, Semkovska et al. [9] raised some doubts as to the reliability of measuring AM with this scale. In response to this, Harold Sackeim, the founder of the tool, presented the results of many studies showing unequivocal evidence for ECT's adverse effect on AM, assessed using the AMI or AMI-SF, arguing for the usefulness of these scales [10].

Therefore, the aim of the present study was to assess the effect of ECT on autobiographical memory in a group of Polish patients with drug-resistant depression, using *the Autobiographical Memory Interview* with the measures being performed before, immediately after ECT sessions and at 3 months after completing ECT.

Method

Patients

The study included 20 patients (8 men, 12 women), aged 21–75 years (mean age 53 ± 12 years). The mean duration of illness was 12.8 ± 5.8 years, and the mean duration of the depressive episode was 4.5 ± 7.5 months. Unipolar depression was diagnosed in seven, and depression in the course of bipolar disorder (bipolar depression – BD) – in thirteen subjects, according to the ICD-10 diagnostic criteria [11]. The criterion for drug-resistant depression was a lack of improvement after at least two adequate courses of antidepressant and (or) mood stabilizing treatment (including augmentation) used in proper doses within the previous three months.

The most frequent drugs used before ECT were: quetiapine (19 patients), lithium (15 patients, including 4 UD, 11 BD), and venlafaxine (11 patients, 5 UD, 6 BD). During ECT, lithium and mood-stabilizing antiepileptic drugs were discontinued.

Qualification to ECT

Before ECT, each patient was examined by an anesthesiologist and a cardiologist and, if necessary, also by an endocrinologist to assess any contraindications for ECT. ECT was administered three times weekly, using a Thymatron System IV device. All the patients received 10–12 bilateral ECT sessions, with the two-sided arrangement of the electrodes in the frontotemporal area. As an anesthetic, patients received either propofol, in doses 2–3 mg/kg (9 patients), or ketamine, in doses 1–1.5mg/kg during second, fourth, sixth, eight and tenth session, alternatively with propofol (11 patients). As a muscle relaxant, succinylcholine, in doses 1–1.5 mg/kg, was used.

The applied electric charge varied between 100 and 300 mC and the parameters were chosen individually by the psychiatrist performing the procedure. The initial assessment was determined by adjusting to age and gender, and the dosage was determined at each session based on seizure activity, monitored by EEG recordings.

Assessment of depression severity

Depression severity was measured by the 17-item *Hamilton Depression Rating Scale* (HDRS). The inclusion criterion for the study was 18 points or higher on HDRS, and the mean severity of depression before the ECT in the whole group, as measured by the HDRS, was 30 ± 6 points. The HDRS measurement was performed after each ECT session. The criterion for response was a reduction of ≥ 50% of HDRS score compared with baseline. The remission was assumed when the HDRS score was 7 or less. The physicians assessing depression severity by the HDRS had previous training in its use.

Measurement of autobiographical memory

Autobiographical memory was assessed using the Columbia University *Autobiographical Memory Interview-Short Form* (AMI-SF) [12] translated into Polish by two of the authors (A.B. and J.R.) and adapted to Polish conditions. The AMI-SF consists of 30 questions about 6 autobiographical events. The main adaptation to Polish conditions was changing 'birthday' event to 'name-day' one, which is the more celebrated event in Poland. The patients were assessed using the AMI-SF before ECT, immediately after ECT sessions and 3 months after completing ECT.

The study was approved by the Bioethics Committee of Poznan University of Medical Sciences and all patients gave their informed consent after the nature of the procedures had been fully explained to them.

Statistical methods

The results of the subtests of autobiographical memory were presented as means ± *SD*. Comparisons were made between the results at baseline and immediately after ECT and 3 months after ECT completion. The Shapiro-Wilk test was applied to check for a normal distribution. Since data did not follow the normal distribution, non-parametric tests were used. The comparison of parameters between three time points was performed by the use of ANOVA, Friedman test, with *post-hoc* analysis. Comparisons with the baseline for results obtained immediately after ECT and 3 months after ECT completion were done by means of the Mann-Whitney and Wilcoxon tests. The Spearman's *r* test was used to determine a correlation between variables. The calculations were performed using the Statistica (StatSoft) version 10 statistical package. The level of statistical significance was determined at alpha < 0.05.

Results

Before the ECT, the mean severity of depression in the whole group was 30 ± 6 points (mean ± *SD*), in patients with UD 32 ± 7 points and in patients with BD 29 ± 5 points on *the Hamilton Depression Rating Scale* (HDRS). After the ECT, the mean severity of depression was 5 ± 6 points, in patients with UD 9 ± 7 points and in patients with BD 3 ± 5 points. Higher severity of depression after ECT in UD compared with BD group attained statistical trend ($p = 0.08$, Mann-Whitney test). In 18 patients (6 with UD and 12 with BD), a significant clinical improvement (≥ 50% reduction of HDRS score compared to baseline) was shown. In 15 patients (4 with UD and 11 with BD), the remission (7 or fewer points on HDRS) was obtained. The HDRS score after 3 months was 7 ± 7, and 10 patients (3 with UD and 7 with BD) remained in remission.

The results of the autobiographical tests at baseline, immediately after ECT and 3 months after ECT completion are shown in Table 1.

Table 1. **The effect of ECT on autobiographical memory – a study using the Polish adaptation of the Autobiographical Memory Interview-Short Form in 20 patients with treatment-resistant depression (the values are given as mean ± SD)**

Components of autobiographical memory	Baseline	Immediately after ECT	3 months after ECT	Friedman ANOVA
Family member	7.3 ± 2.8	6.3 ± 3.0*	7.5 ± 2.6	p = 0.008
Travel	7.7 ± 2.8	6.0 ± 3.2**	6.2 ± 3.0**	p = 0.002
New Year's Eve	9.0 ± 1.4	6.7 ± 3.1**	7.4 ± 1.7**	p = 0.002
Name-day	7.0 ± 3.1	5.0 ± 3.5*	5.9 ± 3.1**	p < 0.001
Employment	7.4 ± 2.5	6.1 ± 2.5**	6.9 ± 2.7	p = 0.005
Physical illness	5.1 ± 3.2	2.5 ± 2.5**	3.5 ± 2.3**	p < 0.001
Total	43 ± 10	31 ± 12***	27 ± 19***	p < 0.001

Significant difference vs. baseline (Wilcoxon test): * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

The indices of autobiographical memory, both total and in all domains of the AMI-SF, were significantly lower immediately after ECT and at 3 months thereafter, except for the scores on family member and employment, which, at 3 months, were similar to the pre-treatment values. Amnesia score showing the percentage of retrieved information immediately after ECT was 72%, and three months thereafter – 60%, however, these values were not significantly different.

Baseline results of the indices of AM did not correlate with age, duration of the depressive episode and initial HDRS score. The results of part III of the test (New Year's Eve) showed a negative correlation with duration of the illness both before and immediately after ECT completion. Amnesia scores both immediately and after 3 months following the procedure did not show correlation with age, gender, diagnosis, duration of illness, duration of the depressive episode, the percentage of improvement, and using propofol or propofol alternatively with ketamine for anesthesia.

Discussion

In this paper, the dynamics of autobiographical memory was assessed in the time-frame of ECT treatment, using the Polish adaptation of the AMI-SF, in patients with treatment-resistant depression. The main finding of the study confirms that the retrograde amnesia for autobiographical information makes an adverse effect of ECT. The indices of autobiographical memory, both total and in all domains of the AMI-SF, were significantly lower immediately after ECT and at 3 months thereafter, except for the scores on family member and employment, which, at 3 months, were similar to the pre-treatment values. This may confirm the results of recent meta-analyses and research of this topic [5, 6, 10].

In our study, the only obtained correlation was that between duration of the illness and one subdomain of the AMI-SF (New Years' Eve). Apart from this, the impairment of AM did not correlate with age, gender, diagnosis, duration of illness, duration of the

depressive episode, the percentage of improvement, and using propofol or propofol alternatively with ketamine for anesthesia. Therefore, the AM impairment in treatment-resistant depressed patients in the course of ECT treatment may be independent of clinical factors.

Analyzing the effect of ECT on autobiographical memory, several variables should be taken into account such as (1) time of the measurement; (2) a tool used for the assessment (self-descriptive or objective); (3) specificity of the procedure (number of sessions, electric charge, type of anesthesia, placement of the electrodes); (4) individual patients' features such as depression severity and cognitive functioning before ECT.

Sackeim et al. [13] showed that AM index at 2 months after ECT (after the previous worsening) remains at the same level as before ECT. They measured autobiographical memory by means of *the Autobiographialc Memory Interview* (AMI) in its full version as well as *the Subjective Self-assessment Memory Questionnaire* (SSMQ). The AMI was used in its basic form regarding childhood, early adulthood and present life. Also, Calev et al. [14] demonstrated that AM index, after the previous worsening, at 1 month after ECT achieves the baseline levels and after 6 months it achieves a higher level than before ECT. For the assessment of AM, they used the SSMQ and *the Personal Memory Questionnaire* (PMQ), from which the AMI was adapted. Some studies [15] show that an impairment of AM after ECT affects the events closer to ECT, which we included in our study using the AMI-SF, therefore the AMI index in our study can be lower compared with quoted studies. *The Autobiographical Memory Interview*, as an objective tool, seems less susceptible to worsening of AM during depressive episode than self-description tests (e.g., SSMQ) [16], however, in its basic form, having a high number of items and focusing on earlier periods may to less extent reflect an impairment due to ECT.

The results of our study confirm worsening of AM with bilateral placement of the electrodes [17], with their frontal location [18] and a high electric current [19]. Adjusting electric current to seizure activity did not have a significant effect in our study. In a research of Mayur et al. [20], it was found that AM was less affected when in ECT procedure 0.3-millisecond ultra-brief pulses were used compared with 1-millisecond brief-pulses.

An important limitation of our study is a lack of a control group of depressed patients, not having ECT, in which serial assessment of autobiographical memory was performed. In studies using the AMI-SF tool, a decrease in AM has been also found in depressed patients who have never received ECT [21, 22]. On the other hand, in his recent paper, Jelovac et al. [23] showed a reduction of episodic autobiographical memory in depressed patients both before ECT as well as at the end of treatment course and at 3-month follow-up, using *the Kopelman Autobiographical Memory Interview* [24].

The study has many other limitations such as, e.g., a small number of assessed patients and the follow-up assessment performed only at 3 months following the procedure. Furthermore, the baseline cognitive functioning was not assessed, and therefore individual factors affecting cognitive reserve, which could influence AM, were not included.

It should be borne in mind that a measured phenomenon of AM could have been altered by the illness itself. Contemporary research on AM in depression show that dysfunctions of this memory can be a precursor of depression and also a consequence of depressive symptoms. These dysfunctions have the form of less detailed and specific autobiographical memories, characterized by excessive generalization referred to as 'over-general autobiographical memory' [26, 27]. It is conceivable that such abnormality has also been present in our patients with treatment-resistant depression.

Bearing all these limitations in mind, we believe that our results confirm an adverse effect of ECT on autobiographical memory, as assessed by the AMI-SF. Therefore, this cognitive function seems to be the most vulnerable to this procedure and may be an important adverse cognitive effect of ECT.

Conclusions

1. In the studied patients with drug-resistant depression, ECT caused a significant deterioration of autobiographical memory assessed using the Polish version of the AMI-SF.
2. Deterioration of autobiographical memory also persisted three months after ECT.
3. Deterioration of autobiographical memory may be the most important cognitive adverse effect of ECT.

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