

## Multiple EEG examinations in patients with recurrent, refractory major depression and bipolar depression after course of UECT

Robert Teodor Hese<sup>1</sup>, Barbara Jędrzejewska<sup>2</sup>

<sup>1</sup> From the Psychiatric Department at the Mining Hospital in Bytom  
Head: R.T. Hese, M.D., Ph. D.

<sup>2</sup> From the EEG Laboratory at the Mining Hospital in Bytom  
Head: B. Jędrzejewska, M. D.

*In 37 patients with the diagnosis of recurrent, refractory, major depression and bipolar depression after completing a course of unilateral ECT, multiple EEG examinations were performed over a one-year period of observation.*

*Key words:* refractory depression, ECT, EEG

### Introduction

The present paper extends studies into one of the problems dealt with in an earlier report [8] regarding changes in the brain bioelectric function after treatment with some chosen antidepressants or after electroconvulsive therapy (ECT). The literature on electroencephalographic (EEG) investigations performed in patients a few hours, or a few days or weeks after termination of a course of ECT is pretty voluminous [2, 11, 14, 23]. On the other hand, however, there are only few papers on late EEG tracings observed several months after ECT<sub>s</sub>. These kinds of investigations are quite laborious, and close cooperation with patients is required [11, 23, 29].

These studies are very important as the persistence of changes in EEG recordings could provide support for brain damage – the outcome of past therapy.

Some disparity of results of EEG investigations after a completed course of ECT was found to be due, amongst others, to individual differences of the studied patients, the applied ECT method, as well as the assessment techniques (visual, automatic or others) of EEG recordings [7, 17, 27, 28, 29].

Slowing of the basic rhythm, the presence of regular and generalized theta and delta waves, or seizures activity predominantly in the frontal or frontotemporal regions were found to be the most characteristic features of EEG after a course of ECT. Only few reports on spike and slow waves activity have been published [23, 29]. Most authors

underline reversibility of the above mentioned changes [7, 13, 24, 29], however, there are not many papers on persistent abnormalities of EEG recordings caused by ECT application. According to these authors the discussed changes might be the outcome of encephalopathy following application of that mode of treatment [12, 13].

### **The aim of the paper**

The aim of the paper was to assess frequency, form and persistence of changes in EEG recordings in patients with diagnosed Refractory, Recurrent, Major Depression (unipolar) and Bipolar Depression after a course of unilateral ECT over a one-year observation period.

### **Patients and Method**

180 patients of the Psychiatric Department at the Mining Hospital in Bytom with diagnosed Recurrent, Refractory Major Depression and Bipolar Depression were divided at random in to three groups of 60 people each, each group being treated in the years 1980- 1992 with one of the following methods- amitriptyline, mianserine and unilateral electroconvulsive therapy (UECT). The random choice of patients for the UECT group was disturbed by the lack of agreement to this treatment at the part of 150 patients from 210 proposed. Informed consent to participate in the study was obtained from each patient, however, those who were found to have EEG changes prior to unilateral ECT<sub>s</sub> (21 patients) and 2 others, who did not cooperate, were not enrolled in the study. In that way the final number of patients participating in the study fell to 37. The investigated group comprised 27 women and 10 men, their mean age was  $49.8 \pm 10.3$  years. Affective Unipolar Disorder (UD), was found in 21 patients, and Bipolar Disorder in the remaining 16 cases. The diagnosis was established upon the criteria of DSM-III. The mean time duration of illness in patients with UD was 6,6 years and in BP – 15.6 years. The mean number of episodes (in the past), was in the UD group – 4.1 and in BP patients – 7.0. The mean duration of the present depressive episode (before starting treatment), was 3.9 months in UD patients and 2.7 months in the BP group. Depression intensity and therapeutic efficacy were assessed according to the 24-item Hamilton Rating Scale for Depression (HRSD) and the Clinical Global Impression Scale (CGI). Pretreatment scores of the depression intensity in the studied group were as follows: moderate ( $x=21-29$  pts) – in 25 patients, severe ( $x \geq 30$  HRSD pts) – in 12 patients.

The current study considers only patients who throughout the recurrence period of the disease, received at least two ineffective one-month courses of treatment with different tricyclic antidepressants (TCA<sub>s</sub>) – doxepin, imipramine or amitriptyline at a mean daily dose of  $166.2 \text{ mg} \pm 28.3 \text{ mg}$ , or those who after TCA<sub>s</sub> application received combined treatment with TCA<sub>s</sub> + lithium carbonate or with TCA<sub>s</sub> + carbamazepine. All investigated patients underwent a general physical examination, and routine laboratory and accessory tests were made. Laboratory tests and if necessary, specialist consultations, were repeated concurrently with EEG examinations in order to exclude

metabolic, endocrinological and hydroelectrolytic disorders which could affect EEG tracings. Unilateral ECT<sub>s</sub>, under general anaesthesia, muscle relaxation and electrode placement according to Lancaster [7, 8, 9] over the non-dominant hemisphere, were applied twice weekly. ECT<sub>s</sub> were induced with the English Electron Doupulse MK-4 device which facilitated application of unidirectional electric stimuli of the following parameters: pulse width – 6 ms, duration of total amount of stimulation – 0.5 s, and the passage of electrical current – 18.8 J. Mean number of unilateral ECT<sub>s</sub> per one course was  $8.5 \pm 2.8$ . A detailed description of the ECT method applied at the Psychiatric Department in Bytom is given elsewhere [8,9]. After termination of unilateral ECT<sub>s</sub> the patients were advised not to take any drugs throughout the entire observation period. On follow-up the patients were asked whether they took any medication in the last month of the observation period.

EEG studies were performed before therapy, and then 2, 4 and 6 weeks, and 3, 6 and 12 months after termination of ECT<sub>s</sub>. The first EEG examination was made 2 weeks after the washing out period. Throughout the investigation time the patients did not receive any psychotropic drugs except for casual administration of diazepam at a daily dose of 5–10 mg. EEG examination were carried out using an 8-channel Medicor-Orion device with bipolar electrode placement. EEG tracings accomplished at rest after hyperventilation (HV) and photostimulation were assessed visually.

Results of EEG analysis were plotted on a specially prepared “Chart of EEG changes after unilateral ECT” comprising 29 points to help characterize the studied tracings. Application of the chart made it possible to compare EEG features in successive investigations as well as to make qualitative and quantitative analyses of tracings.

## Results

Changes in EEG recordings were found in 17 patients two weeks after termination of unilateral ECT<sub>s</sub>. Slowing of the basic activity in 14 patients and theta waves in 12 patients were the most common findings, other EEG abnormalities were less frequent (see Table 1).

Generalized changes were observed in 7 patients, localized – in the temporal re-

Table 1

Kind and frequency of EEG changes 2 weeks after unilateral ECT courses

Kind of EEG changes	Slowing of the basic function	Theta waves	Del/b waves	Sharp waves	Paroxysmal activity	HV intensifies changes	Changes only after HV
Number of patients (n=37)	14	12	4	2	4	5	2

gion in 4, and in the frontal brain regions in 3 patients. Abnormal EEG recordings in 5 patients were found four weeks after termination of a unilateral ECT course, and in 2 patients after six weeks. EEG performed six months after termination of a unilateral

ECT course revealed generalized slowing of the basic activity in 1 patient (Table 2), and a year after ECT this change disappeared.

It was found (Table 3) that the number of patients with EEG changes increased

Table 2

EEG changes after a course of unilateral ECT throughout a one-year observation period

Time elapsing from ECT termination	2 weeks	4 weeks	6 weeks	3 months	6 months	12 months
Number of patients (n=37)	17	5	2	1	1	0

Table 3

Number of patients with EEG changes and number of electroconvulsions

Number of UECT	Patients with EEG changes	Patients with EEG changes	Statistical value $\chi^2$	Critical value $\chi^2_{0.05}$
up to 8	5	16	4.743	3.841
more than 8	12	7		

when the number of ECT<sub>s</sub>, on average, was greater than 8 ( $\alpha=0.05$ ). However, no significant correlation between the persistence of EEG changes and the number of ECT<sub>s</sub> in one course of treatment was observed. No interrelationship between the persistence of EEG changes and the number of ECT courses before the start of the study was found, either (Table 4).

After completing treatment, 28 patients showed remission and improvement

Table 4

EEG changes and the number of past ECT courses on interview

Number of past ECT courses on interview	Elapse of time after ECT termination		Statistical value $\chi^2$ (with Yates correction) ( $\alpha=0.05$ )	Critical value $\chi^2_{0.05}$
	2 weeks (number of patients)	4 weeks (number of patients)		
-	12	2	1.798	7.815
1	2	1		
2	1	1		
3	2	1		

( $x < 12$  pts in HDRS), and 31 patients assessed by CGI. No significant relationship was observed between the results of therapy and frequency or persistence of EEG changes.

## Discussion

The longest, 3-year periods of observation of EEG recordings after termination of an ECT course were those described in the works of Karliner (1956) or Assel et al (1967) [7]. These authors noticed that EEG changes in some patients subsided as late as 3 years after termination of ECT<sub>s</sub>. Persistence of EEG changes described in the quoted works could possibly result from the application of a different mode of ECT, and the use of long, sinusoidal waveform stimuli, in particular.

Klotz (1955), [7] and Weiner et al [29] report on shorter, 6-month observation periods. Klotz observed slow function in EEG in 2% of patients half a year after ECT completion. The quoted paper of Weiner et al is, as yet, the most elaborate study on this issue, it covers as many as 74 patients. EEG recordings were assessed visually as well as by means of computer analysis and EEG mapping. These investigations showed, among others, that EEG changes following bilateral ECT<sub>s</sub> were greater and lasted longer than those after unilateral ECT. The same authors also found residual slowing of the basic function in EEG recordings in 3 patients as late as six months after ECT termination. They stressed that longer periods of observation were necessary to elucidate the problem of reversibility of EEG changes after ECT.

In the present paper the observation period of EEG recordings lasted one year. Frequency and kind of the observed EEG changes in patients after a unilateral ECT course are consistent with the literature data [2, 7, 13, 29]. A month after termination of a unilateral ECT course, normal EEG tracing was found in the majority of patients i. e. in 32 cases (86.5%). This finding is in accord with observations of the authors, who underline that EEG changes easily subside after electroconvulsions and after unilateral ECT<sub>s</sub> in particular [7, 13, 29]. Reversibility of EEG changes over a 1-year observation period deserves special attention. Similar results of long-term observation of EEG recordings are reported by other authors [7]. It should be emphasized that, after termination of ECT course, the patients were found to have persistent EEG changes on successive follow-up examinations. Metabolic, endocrinological and hydroelectrolytic disturbances, which could produce nonspecific changes in EEG recordings, were excluded. The patients denied ever taking any drugs throughout the one-year observation period.

As mentioned in the introduction, there are only a few reports on permanent EEG abnormalities after a course of ECT, which, in turn, are a manifestation of post electroconvulsive encephalopathy [12, 13, 23, 28]. Most reports on the subject were published in the 1940s and 1950s.

At that time ECT was accomplished with the use of alternating sinusoidal current at 80-115 V, pulse width of 0.5–0.7s., and 0.3-0.6 A.

The electric current used during ECT<sub>s</sub> was in the range of 400–840 J [7, 13, 14]. General anaesthesia, muscle relaxation and oxygenation of patients prior and during electroconvulsions were applied only occasionally in those days. That kind of management could sometimes lead to impairment of cerebral tissues, specifically in patients with arterial hypertension or other illnesses affecting cerebral circulation [7, 13, 17].

Today, unidirectional or bidirectional current changed into brief-pulse stimuli (width most frequently 1–2 ms, total stimulus duration 0.5–2s) is used in ECT<sub>s</sub>. It is recommended that the electric stimulus passed during the procedure should be low energetic, i.e. within the range of 10–25 J [28]. According to most authors it is very unlikely that electroconvulsions accomplished by means of the stimuli described above, and under general anesthesia, muscle relaxation and oxygenation could lead to impairment of cerebral tissues [4, 5, 11, 15, 17, 22, 27].

The device used in this study facilitated application of a low energetic stimulus at a short exposure time, and large width of the pulse – 6 ms is its only disadvantage. According to the literature data it should range between 1–4 ms [25].

The results of our investigations indicate, (Table 3) that a significantly greater number of patients with EEG changes received more than 8 unilateral ECT<sub>s</sub> ( $\alpha=0.05$ ). This finding collaborates with those reported in literature [8,23]. No significant correlation between the duration of EEG changes and the number of electroconvulsions was shown. The literature data suggest that there is positive correlation between the number of ECT<sub>s</sub> and the duration of EEG changes [17, 26].

It should be mentioned that studies upon this problem were carried out in the years 1942-1951 [7,27], when other ECT methods were used. It is still an open question whether this kind of interrelationship exists between the number of ECT<sub>s</sub> and the persistence of EEG changes when modern ECT methodology is applied.

The origin of persistent EEG changes after a course of ECT requires further elucidation [28, 29]. In several cases these changes could occur in individuals with special bioelectric sensitivity of some brain structures, e.g. the limbic system [17]. In others, however, pathophysiological disturbances resulting from poor cerebral circulation, e.g., in arterial hypertension, cerebral atherosclerosis, could be the underlying cause of EEG changes. Effect of other pathologic factors within the cerebral tissue should also be taken into account [7, 17].

It is worth noting that our studies showed no correlation between the number of past ECT courses and the persistence of EEG changes in the currently treated patients. In the available literature no attempts to investigate this kind of correlation have been found. This finding could provide support against possible worsening of the cerebral tissue damage after successive ECT courses.

Results of this work, with regard to the duration of EEG changes after ECT courses, can be related only to unilateral electroconvulsions and EEG recordings assessed visually. Application of bilateral electroconvulsions and more sensitive methods in the analysis of EEG recordings could reveal longer-lasting EEG changes.

Our results may also support the hypothesis that changes in the brain bioelectric function following ECT<sub>s</sub> are not symptomatic of encephalopathy; they are reversible. Most probably, they reflect functional changes of the neurons at a molecular level.

### Conclusions

1. One month after termination of a unilateral ECT course, normal EEG recordings were found in the majority of patients.

2. Changes in EEG recordings were observed in 2 patients six weeks after unilateral ECT<sub>s</sub>, and EEG follow-up performed six months after termination of therapy revealed generalized slowing of the basic function in 1 patient.
3. None of the above listed changes were found in EEG recordings 12 months after completion of unilateral ECT.
4. Number of patients with EEG changes was significantly ( $\alpha=0.05$ ) greater among those who received more than 8 unilateral ECT<sub>s</sub>.
5. No significant correlation between the duration of EEG changes and the number of unilateral ECT<sub>s</sub> was found.
6. No significant correlation between the duration of EEG changes and the number of past courses of ECT<sub>s</sub> was observed.
7. Results of this work may support the hypothesis that changes in the bioelectric function of the brain after ECT<sub>s</sub> are not symptomatic of encephalopathy; they are reversible.

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Address:

Robert Teodor Hese  
Katedra i Oddział Kliniczny Psychiatrii Śląskiej Akademii Medycznej  
Wielospecjalistyczny Szpital Rejonowy im. dr B.Hagera  
ul. Pyskowicka 47, 42-600 Tarnowskie Góry  
tel/fax 285-43-58