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## Analysis of long-term electroconvulsive treatment parameters in schizophrenia: two case reports

Analiza parametrów długoterminowego leczenia elektrowstrząsami w schizofrenii: dwa opisy przypadków

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### Abstract

There is limited data on the long-term use of maintenance electroconvulsive therapy in schizophrenia. This report examines the extended course of maintenance electroconvulsive therapy in two male patients with schizophrenia, treated over periods exceeding 19 and 11 years, respectively. Clinical data were extracted from medical records and electroconvulsive therapy printouts. Electroencephalogram recordings captured during electroconvulsive therapy were digitised and analysed using spectral analysis. Both patients showed high tolerance and good safety of maintenance electroconvulsive therapy. Adverse events were minimal. The majority of maintenance electroconvulsive therapy sessions were effective. Spectral analysis of electroencephalogram recordings indicated a stable pattern of changes in low-frequency band power during ictal activity. Long-term maintenance electroconvulsive therapy appears to be highly effective, safe, and well-tolerated in patients with schizophrenia. Alternative parameters, such as the postictal suppression index, may offer more accurate measures of electroconvulsive therapy efficacy. Further research is needed to explore the potential of the postictal suppression index in evaluating electroconvulsive therapy effectiveness and to validate these findings in larger cohorts.

**Keywords:** schizophrenia, electroencephalogram, electroconvulsive therapy, postictal suppression index

### Streszczenie

Dostępne są jedynie ograniczone dane na temat długoterminowego stosowania podtrzymującej terapii elektrowstrząsowej w schizofrenii. W niniejszym opisie dwóch przypadków autorzy przeanalizowali jej długoterminowy przebieg u dwóch mężczyzn leczonych odpowiednio przez ponad 19 i 11 lat. Dane kliniczne i parametry terapii elektrowstrząsowej zostały zebrane z historii chorób i wydruków terapii elektrowstrząsowej. Zapisy elektroencefalografii uzyskane podczas terapii elektrowstrząsowej zostały zdigitalizowane i poddane analizie spektralnej. U obu pacjentów wykazano wysoką tolerancję i bezpieczeństwo podtrzymującej terapii elektrowstrząsowej w schizofrenii. Zdarzenia niepożądane były minimalne. Większość sesji podtrzymującej terapii elektrowstrząsowej zakończyła się powodzeniem. Analiza spektralna zapisów elektroencefalografii wykazała stabilny wzorec zmian mocy pasm niskich częstotliwości podczas aktywności napadowej. Długoterminowe leczenie podtrzymującą terapią elektrowstrząsową w schizofrenii jest wysoce skuteczne, bezpieczne i dobrze tolerowane przez pacjentów ze schizofrenią. Alternatywne parametry, takie jak wskaźnik supresji ponapadowej, mogą umożliwiać dokładniejszą ocenę skuteczności terapii. Konieczne są dalsze badania, aby ocenić potencjał tego wskaźnika w ocenie skuteczności terapii elektrowstrząsowej oraz potwierdzić przedstawione w artykule ustalenia w większych kohortach.

**Słowa kluczowe:** schizofrenia, elektroencefalografia, terapia elektrowstrząsowa, wskaźnik supresji ponapadowej

## INTRODUCTION

For more than 80 years, electroconvulsive therapy (ECT) has been used with great success in the treatment of affective disorders (mostly depression) and schizophrenia. It is widely recognised as a highly effective and very safe therapeutic method (Madero et al., 2022). In 2001, it was reported that approximately 1 million ECT treatments are performed annually worldwide (Prudic et al., 2001). At the clinical hospital where this study was conducted, ECT has been used since 1997, and approximately 1,000 procedures are performed annually, resulting in the total number of ~25,000 ECT sessions performed to date, mostly for depression, schizophrenia, and catatonia.

The mechanism of ECT is not completely recognised, but available data indicates that ECT alters regional cerebral blood flow, modifies neuronal metabolism, and increases the permeability of the blood–brain barrier (this mechanism may explain why ECT seems to increase the efficacy of pharmacological treatments administered concurrently with ECT). After chronic treatment, transcription of selected genes is increased. Also, maintenance ECT alters levels of neurotrophic factors (such as brain-derived neurotrophic factor) and regulates noradrenergic, serotonergic, dopaminergic, and glutamatergic neurotransmission (Maffioletti et al., 2021). The combined effect of many overlapping processes results in increased neurogenesis and neuroplasticity of neurons. In the direct mechanism of ECT, an electrical impulse generates a wave of action potentials that spreads across neurons. If the applied electric stimulus is too low, an abortive seizure occurs, and neurons are not stimulated or are induced only in the area of electrode placement. Such excitation does not produce beneficial clinical effects. A seizure is considered unsuccessful when the duration of ictal activity is shorter than 20 seconds. It is assumed that this is one of the key parameters for evaluating the effectiveness of ECT (Miller et al., 2022).

Depending on the length of treatment continuation ECT (cECT), defined as treatment till six months from the onset, and maintenance ECT (mECT), which is performed for more than six months, are distinguished (Kolar, 2017).

About 30% of patients have treatment-resistant schizophrenia. In this group, ECT is an effective therapeutic option, especially for reducing positive symptoms (Plahouras et al., 2021). There are recommendations for the use of mECT in the treatment of affective disorders, including pre- and postpartum affective disorders, major depression (Gazdag and Ungvari, 2019), bipolar depression (Miller et al., 2019), psychotic states such as pre- and postpartum psychotic disorders, catatonia, and schizophrenia, where it may also serve as an additive augmentation strategy to antipsychotic drugs (Gazdag and Ungvari, 2019). In addition to these indications, ECT has a proven anti-suicidal protection effect (Kellner et al., 2005) and is therefore recommended as the first-line treatment for suicidal patients (Fink et al., 2014). From the review of medical publications available over the past decade, it follows that there is very limited data regarding

the efficacy and safety of mECT treatment for schizophrenia. Therefore, the objective of this report was to describe two cases of schizophrenia treated with long-term (>19 years and >11 years) mECT. Clinical characteristics, a summary of ECT parameters across all ECT sessions, and spectral analyses of selected EEG recordings during ECT are presented.

## MATERIAL AND METHODS

In this retrospective study, the course of mECT was analysed in two patients with paranoid schizophrenia treated with mECT. mECT procedures performed between December 2003 and February 2021 were studied. A total of 160 ECT sessions were reviewed for the first subject (male, age 19 years at the start of ECT treatment), conducted from December 2003 to July 2019, and 90 ECT sessions for the second subject (male, age 21 years at the start of ECT treatment), conducted from September 2011 to February 2021. Both patients had ECT initiated due to treatment resistance, after adequate trials of antipsychotic medication. No formal evaluations of psychopathology were performed during their treatment; therefore, it was not possible to collect any objective data regarding symptom severity and longitudinal changes.

At the study site, the Mecta stimulator (Mecta LLC, USA) was used for ECT procedures from December 2003 to December 2005. It was then replaced by the Thymatron System IV (Somatics LLC, USA), which has been used since January 2006. Therefore, some procedures for the first patient were performed using the Mecta stimulator. However, the majority of his sessions and all sessions for the second patient were performed using the Thymatron System IV. Both patients were qualified and prepared for ECT procedures using a standardised protocol.

Medical records of both patients for every individual ECT procedure were reviewed. Paper printouts of ECT stimulations were also collected and analysed for automatically calculated parameters and EEG recordings (two-channel electrodes placed at prefrontal and mastoid locations) during ECT procedures.

Clinical data extracted from medical histories included electrode placement, duration of ECT, ECT effectiveness, use of re-stimulation, administration of benzodiazepines to terminate a seizure (if required), interval between ECT treatments [days], changes from the scheduled interval [days], and the presence of delirium or other complications after the procedure. Information on the type of anaesthetic agents used during ECT and psychotropic drugs taken by the patients on a daily basis was also included.

From ECT printouts, the following parameters were collected: current [A], stimulus duration [s], frequency [Hz], pulse width [ms], dynamic impedance [ $\Omega$ ] (available for both devices) and average voltage [V], dynamic energy [J] (available only for Mecta) and energy set [%], charge delivered [mC], static impedance [ $\Omega$ ], EEG endpoint [s], base heart rate [beats/min], peak heart rate [beats/min], average seizure energy index [ $\mu\text{V}^2$ ], postictal suppression index [%],

		<b>P1</b>	<b>P2</b>
<b>Number of ECT procedures</b>		160	90
<b>Number of mECT procedures</b>		141 (88.1%)	71 (78.9%)
<b>Number of ECT procedures in the initial series</b>		19 (13.5%)	19 (21.1%)
<b>Interval between ECT procedures [days]</b>		45.5 ± 16.5	37.0 ± 27.3
<b>Intravenous anaesthetic: propofol</b>		157 (98.1%)	90 (100%)
<b>Intravenous anaesthetic: etomidate</b>		3 (1.9%)	0
<b>Medications [mg/day]</b>	<b>Olanzapine</b>	23.4 ± 3.59	NA
	<b>Risperidone</b>	2.9 ± 0.74	NA
	<b>Aripiprazole</b>	15 ± 0	NA
	<b>Clozapine</b>	NA	112.8 ± 59.6
	<b>Quetiapine</b>	NA	615.6 ± 102.1
	<b>Mirtazapine</b>	NA	30 ± 0
	<b>Sertraline</b>	NA	51.7 ± 9.0
	<b>Citalopram</b>	NA	14 ± 8.2
	<b>Lamotrigine</b>	NA	81 ± 32.5
	<b>Valproic acid</b>	768.0 ± 251.7	957.1 ± 240.9
	<b>Alprazolam</b>	2.2 ± 1.75	0.4 ± 0.13
<b>Hydroxyzine</b>	95.5 ± 15.1	NA	
<b>Location of ECT electrodes</b>	Bi-temporal	147 (91.9%)	52 (57.8%)
	Bi-frontal	0 (0%)	33 (36.7%)
<b>Effective ECT stimulation</b>	Yes	151 (94.4%)	85 (94.4%)
	No	6 (3.7%)	3 (3.3%)
<b>Re-stimulation</b>	Yes	3 (1.9%)	2 (2.2%)
	No	151 (94.4%)	88 (97.8%)
<b>Benzodiazepines after ECT</b>	Yes	2 (1.2%)	18 (20.0%)
	No	156 (97.5%)	72 (80.0%)
<b>Interval modification</b>	Yes	3 (1.9%)	4 (4.4%)
	No	155 (96.9%)	86 (95.6%)
<b>Delirium</b>	Yes	0 (0%)	1 (1.1%)
	No	158 (98.75%)	89 (98.89%)
<b>Other adverse events</b>	Yes	1 (0.63%)	3 (3.33%)
	No	157 (98.13%)	87 (96.67%)

**P1** – patient 1; **P2** – patient 2.  
Data given as mean ± standard deviation or *n* (%). Some data were not available; therefore, numbers may not sum up to the total number of ECT procedures.  
**NA** – not applicable.

Tab. 1. Clinical details of the ECT procedures

maximum sustained power [ $\mu\text{V}^2$ ], time to peak power [s], maximum sustained coherence [%], and time to peak coherence [s] (available only for Thymatron). In the applied protocol, ECT stimulation was considered effective when EEG ictal activity was >20 seconds.

For every 20<sup>th</sup> ECT session, EEG printouts were analysed, including pre-ECT, ictal, and post-ECT segments. Canon i-SENSYS MF8580Cdw (Canon Inc., Japan) flatbed scanner was used to scan paper printouts of ECT EEGs to PNG files at 100 DPI resolution. EEG fragments (490 × 100 pixels, with 0  $\mu\text{V}$  line in the middle of the image) were extracted using Gimp software. Next, the scanned EEG recordings were automatically converted into digital signals using the EEG\_ADC program (Wysokiński, 2023). Next, digital signals were analysed with the NeuroAnalyzer toolbox. Spectral analysis was performed, and signal power across the

delta (0.1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz) frequency bands were calculated using Welch's periodogram and summed using Simpson's numerical rule of integration.

## RESULTS

Details of the ECT procedures for patient 1 (P1) and patient 2 (P2) are presented in the tables. Tab. 1 contains a summary of ECT parameters, including the number of procedures performed, the number of successful procedures, pharmacotherapy used during treatment, complications after the procedures, number of re-stimulations, use of benzodiazepines, and episodes of delirium after ECT. Detailed ECT parameters are shown in Tab. 2. Tab. 3 contains the results of the spectral analysis of EEG recordings obtained during ECT.

	P1	P2
<b>Stimulation parameters</b>		
Energy set [%]	24.5 ± 19.03	24.3 ± 16.89
Average voltage [V]	129.2 ± 14.67	NA
Dynamic energy [J]	19.5 ± 5.59	NA
Charge delivered [mC]	136.1 ± 111.1	123.2 ± 85.7
Current [A]	0.8 ± 0.10	0.9 ± 0.01
Stimulus duration [s]	4.3 ± 2.4	5.6 ± 1.1
Frequency [Hz]	39.9 ± 25.8	23.9 ± 11.1
Pulse width [ms]	0.8 ± 0.47	0.5 ± 0.06
Static impedance [Ω]	996.2 ± 341.3	792.8 ± 239.4
Dynamic impedance [Ω]	191.0 ± 21.4	204.1 ± 29.9
<b>Procedure results</b>		
EEG endpoint: assessed manual [s]	45.3 ± 22.6	62.7 ± 30.0
EEG endpoint: automatic detection [s]	36.2 ± 11.8	25.2 ± 33.8
Average seizure energy index [uV <sup>2</sup> ]	13,592.2 ± 14,921.0	27,453.4 ± 16,858.3
Postictal suppression index [%]	66.4 ± 20.2	68.2 ± 26.9
Maximum sustained power [uV <sup>2</sup> ]	20,263.7 ± 21,442.5	39,523.7 ± 23,294.7
Time to peak power [s]	22.4 ± 11.9	33.7 ± 18.9
Maximum sustained coherence [%]	88.3 ± 12.3	94.0 ± 9.9
Time to peak coherence [s]	25.3 ± 15.5	32.1 ± 15.3
<b>ECG parameters</b>		
Base heart rate [beats/min]	139.1 ± 24.19	86.9 ± 13.19
Peak heart rate [beats/min]	163.1 ± 17.72	132.0 ± 22.34
<b>P1</b> – patient 1; <b>P2</b> – patient 2. Data presented as mean ± standard deviation. <b>NA</b> – not available. Some data were not available due to being specific for the ECT equipment used during that period.		

Tab. 2. Summary of the ECT procedures

## DISCUSSION

Initially, ECT was the main method of treatment for psychotic disorders. Since antipsychotic drugs were introduced, the use of ECT has declined in many countries, such as the United States, the UK, and parts of Europe (Sanghani et al., 2018). In 1941, ECT was also established as an effective treatment method for depression (Leiknes et al., 2012). Nowadays, there are just a few countries in Asia, such as China and India, where schizophrenia remains the most common indication for ECT, and where ECT is still recommended as a first-line treatment (Xiang et al., 2015). In the UK, ECT is not recommended for schizophrenia and is used only marginally for affective disorders. A similar situation occurs in Ireland and New Zealand (Kolar, 2017). Presumably, this is due to the fact that the National Institute for Health and Care Excellence (NICE) recommends ECT only for short-term treatment of life-threatening catatonia and severe manic episodes, when other conventional treatments have failed (National Institute for Health and Care Excellence, 2003). More recent NICE recommendations mention ECT only as the method of treatment of severe depression (National Institute for Health and Care Excellence, 2009). NICE does not refer at all to mECT. This limited use may also be reinforced by the fact that there

are only two official guidelines for maintenance electroconvulsive treatment: the American Psychiatric Association Recommendations from 2001 and The ECT Handbook by Waite and Easton from 2013 (Krepela et al., 2019). Consequently, while ECT is a very effective therapeutic method for affective disorders, such as psychotic depression and acute mania, as well as for schizophrenia, especially in treatment-resistant patients, it remains underused in many centres around the world. Also, according to several studies, post-treatment remission persists after the first six months in 60% of patients, and after a year in about 50% (Cabelguen et al., 2020). This is a strong argument to consider the advantages of long-term mECT. On the other hand, the number of reports of long-term mECT use is very limited. For P1, a single (0.6%) adverse event was recorded across 160 procedures performed. For P2, one episode of delirium (1.1%) and three adverse events (3.3%) were recorded during 90 ECT sessions. This, together with the fact that patients were on their ECT treatment for many years (and in both cases they still are), confirms that the procedures have very good safety and tolerability profiles for both patients. The patients required relatively low and comparable electrical charges (energy set [%] 24.5 ± 19.0 for P1 and 24.3 ± 16.9 for P2), which likely facilitated the execution of a greater number of procedures. ECT stimulations were effective in

Frequency band	Procedure							
	1	20	40	60	80	101	121	141
<b>P1</b>								
Delta 1	83.15	16.84	4.99	3,781.53	77.02	20.72	112.05	114.18
Delta 2	649.36	40.92	124.51	2,623.08	1,700.92	3,947.23	3,648.88	1,389.09
Delta 3	73.06	14.38	29.01	1,235.34	179.17	263.93	410.93	733.26
Theta 1	24.03	2.40	3.11	1,157.36	16.43	33.20	47.39	28.93
Theta 2	82.19	60.51	91.51	1,657.77	1,136.98	375.27	2,436.04	3,003.77
Theta 3	31.18	6.43	1.31	91.15	14.53	68.77	56.68	14.72
Alpha 1	2.66	1.40	0.51	110.73	7.03	11.89	7.53	29.40
Alpha 2	11.40	8.57	18.44	57.74	60.36	32.25	182.78	140.51
Alpha 3	3.58	1.82	0.96	19.20	6.15	6.75	13.42	4.41
Beta 1	3.23	1.09	0.70	124.75	2.28	3.49	2.82	6.87
Beta 2	6.71	3.70	5.05	86.66	41.46	46.84	205.15	177
Beta 3	1.95	0.88	0.53	10.32	6.65	5.30	5.73	3.10
Gamma 1	1.29	0.36	0.37	36.59	0.95	1.29	1.33	3.23
Gamma 2	3.83	2.03	2.69	26.72	10.22	14.46	89.39	27.16
Gamma 3	1.22	0.53	0.33	3.46	1.50	1.78	2.32	1.74
<b>P2</b>								
Delta 1	80.59	104.72	184.84	113.44	49.91	NA	NA	NA
Delta 2	3,142.02	,1016.16	1,455.29	1,175.78	848.01	NA	NA	NA
Delta 3	493.01	34.53	33.58	109.07	177.34	NA	NA	NA
Theta 1	37.11	32.91	48.12	20.09	12	NA	NA	NA
Theta 2	841.7	2,960.97	764.4	2,273.89	959.94	NA	NA	NA
Theta 3	7.08	12.75	4.63	17.8	28.12	NA	NA	NA
Alpha 1	4.17	3.92	12.66	10.51	19.26	NA	NA	NA
Alpha 2	48.92	109.07	49.18	27.06	102.15	NA	NA	NA
Alpha 3	4.6	5.9	2.74	5.07	4.93	NA	NA	NA
Beta 1	2.55	2.13	6.54	5.78	2.35	NA	NA	NA
Beta 2	104.31	207.04	72.04	107.83	81	NA	NA	NA
Beta 3	3.26	2.02	1.37	1.99	2.58	NA	NA	NA
Gamma 1	1.43	1.13	2.62	2.55	1.67	NA	NA	NA
Gamma 2	30.87	38.44	14.24	12.29	19.89	NA	NA	NA
Gamma 3	1.45	0.86	1.04	1.32	1.4	NA	NA	NA
<b>P1</b> – patient 1; <b>P2</b> – patient 2. Data are presented as total power across each band (in mV <sup>2</sup> /Hz). Number at the band name indicates pre-ECT stimulation (1), ictal activity (2), and post-ictal activity (3). <b>NA</b> – not available.								

Tab. 3. Spectral analysis of the ECT procedures

151 procedures (94.4%) for patient P1 and in 85 procedures (94.4%) for patient P2. Re-stimulations were performed three times (1.9%) for P1 and twice (2.2%) for P2.

Both patients maintained longer durations in maintenance treatments, receiving comparable values of delivered current. Despite this, the ECT procedures performed were characterised by varied durations, but quite similar post-ictal suppression index (PSI) values (the ratio of pre-ECT to post-ECT EEG amplitudes). These observations merit further investigation to determine whether PSI correlates more closely with the energy delivered during ECT than with the duration of ictal activity.

There are many indicators of ECT effectiveness, but PSI and burst suppression (BS) seem to be the most valuable (Singh and Kar, 2017). PSI describes the intensity of electrical suppression, ranging from 0% to 100%, and is calculated and recorded automatically, while BS is defined as the percentage of suppressed waves within a unit of time (Kranaster et al., 2013). Regarding PSI, there is no established threshold value for that parameter. The two patients had comparable PSI [%] values ( $66.4 \pm 20.2$  for P1 and  $68.2 \pm 26.9$  for P2), despite a marked difference in the average duration [s] of ictal activity ( $36.2 \pm 11.8$  for P1 and  $58.1 \pm 25.0$  for P2). Within the range of mean  $\pm 1$  SD (which contains 67% of the

procedures), PSI values for P1 ranged from 46.2 to 86.6, and for P2 from 41.3 to 95.1, indicating that these values significantly overlap. These findings suggest that PSI is probably the best indicator of the effectiveness of ECT procedures and demonstrates that ictal duration does not correlate with more precise parameters describing the efficacy of the treatment.

During the ECT procedure, after achieving the depolarisation of nerve cells, there is a phase of epileptic recruiting, initially in the area of electrode placement, visible on EEG as low-voltage activity with a frequency of 18–22 HZ, which then spreads to other areas of the brain as a tonic phase with high-voltage polyspikes with a frequency of 10–20 HZ. The third period is the clonic phase with slow-wave spike complexes, followed by seizure termination (Miller et al., 2022). In the spectral analysis of EEG recordings, ictal activity consistently shows a marked increase in power (which is amplitude squared), particularly in the low-frequency bands (delta and theta). This pattern has been very stable over time in both cases. Spectral analysis of ECT EEG signals, especially if automated, may therefore facilitate the determination of neurophysiological effectiveness of ECT, e.g. as an auxiliary method for determining the end of ictal activity.

If the duration of ictal activity shows greater variability, from a practical standpoint it may not be the optimal parameter for determining the proper amount of delivered energy. This is further evidenced by patient P1, who consistently exhibited high variability of ictal activity durations yet very stable PSI values. Additionally, the varied (and changing) psychotropic medications taken by both patients suggest that pharmacotherapy had no significant effect on PSI values. Based on the compilation of these results and observations, it is apparent that the duration of ictal activity (especially when determined manually) may not be the most accurate parameter for assessing the efficacy of ECT and should be supplemented with other, more objective parameters. PSI may provide a more effective solution, warranting further research into its application in evaluating ECT effectiveness.

In conclusion, long-term treatment with ECT in two patients with schizophrenia was presented. In both cases, the treatment was highly effective, safe, and well tolerated. Alternative methods of evaluating the efficacy of ECT stimulation were discussed. Based on these data and clinical experience, mECT should always be considered in long-term therapeutic planning for schizophrenia.

### Conflict of interest

*The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.*

### Ethics statement

*As this was a retrospective study, the Bioethics Committee approval was not required. Both study participants signed informed consent for the use of their medical documentation for the purpose of this publication.*

### Author contribution

*Original concept of study; analysis and interpretation of data; writing of manuscript; critical review of manuscript; final approval of manuscript: AW, BD. Collection, recording and/or compilation of data: BD.*

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