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When to switch from bilateral to unilateral electroconvulsive therapy: A simple way to elicit seizures in high seizure threshold cases

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Abstract

Aims: Although electroconvulsive therapy (ECT) is effective for various psychiatric disorders, its therapeutic effect depends on the occurrence of adequate seizures. Thus, the management of inadequate seizures remains a clinical problem. Here, we aimed to develop a simple method to elicit adequate seizures in high seizure threshold patients during ECT sessions.

Methods: Right unilateral ECT was performed in 87 sessions (22 inpatients) in which 504 millicoulombs bilateral (bitemporal or bifrontal) electrical stimulation had failed to induce adequate seizures. A Thymatron® System IV (Somatics LLC, Lake Bluff, IL, USA) and the LOW 0.5 program were used in accordance with the manufacturer's instructions. The electrode placement was bitemporal, bifrontal, or right unilateral (d'Elia placement). The minimum duration for an adequate seizure was 15 seconds in the electroencephalogram record of the Thymatron® stimulator. The efficacy of treatment was estimated by the Global Assessment of Functioning at the time of admission and discharge. Cognitive assessment was not performed.

Results: By switching to right unilateral stimulation immediately after failure of bilateral stimulation, adequate seizures were achieved in 71 of 87 (81.6%) sessions. Improvement in the Global Assessment of Functioning was observed in 23 of 28 (82.1%) treatment courses.

Conclusion: Switching from bilateral to unilateral electrode placement may be a simple clinical option for eliciting adequate seizures in high seizure threshold cases.

KEYWORDS
bilateral, electroconvulsive therapy, high seizure threshold, seizure augmentation, unilateral

1 | INTRODUCTION

Electroconvulsive therapy (ECT) is an effective and widely practiced therapeutic procedure in clinical psychiatry.[1] Since its origins in the 16th century, it has become recognized that generalized epileptic seizures are essential for the therapeutic efficacy of ECT. To maximize the benefit and minimize the risk of ECT, many technical variations have been developed.[2] One form of variation is the placement of the electrode, which may be bitemporal, bifrontal, or right unilateral.[3] In general, bilateral (ie, bitemporal and bifrontal) placement is

Clinical Trial Registration: This report consists of the accumulation of clinical experience. It was not intended to be a research project, and thus, it was not registered in databases.

preferred when rapid improvement of clinical symptoms is needed, whereas right unilateral placement is selected in cases where cognitive side effects should be minimized.[4,5] Furthermore, the intensity of the electric stimulation can be adjusted. Though many practitioners use an empirical titration procedure, the simplest formulas adjust the initial intensity to the patient's age (eg, a 40-year-old patient receives 40% stimulus in %Energy dial of Thymatron® System IV), adjust it to half of the patient's age (eg, a 40-year-old patient receives 20% stimulus), or use a fixed electrical dosage (eg, 100%).[6] However, as with any formula, the seizure threshold may rise during the treatment courses of ECT and clinicians sometimes encounter patients for whom adequate seizures cannot be elicited.[7] Several techniques currently exist to induce seizures in such difficult cases,[6,8,9] but they do not always succeed. Thus, a simple clinical method to elicit adequate seizures in high seizure threshold patients is needed. We tried to solve this problem based on accumulated clinical experience and propose a promising procedure in this report.

2 | METHODS

2.1 | Subjects

The study population comprises 22 inpatients (12 men and 10 women) treated with 0.5 millisecond (ms) right unilateral ECT at Hokkaido Prefectural Midorigaoka Hospital between September 2013 and September 2017 who did not develop adequate seizures with 504 millicoulombs (mC) bilateral electrical stimulation. The total number of sessions was 87. The mean age of the patients was 61.7 years (min. 31 and max. 76). Their diagnoses encompassed various psychiatric disorders (Table 1), and all patients were taking psychotropic medications (eg, antidepressants, mood stabilizers, antipsychotics, and anticonvulsants). This study was reviewed and approved by the review board of Hokkaido Prefectural Midorigaoka Hospital, and all participants provided informed consent prior to ECT courses.

2.2 | ECT administration

A Thymatron® System IV (Somatics LLC) and its LOW 0.5 program (0.5 ms pulse width) were used in accordance with the manufacturer's instructions. The specifications of the Thymatron® System IV hardware and software in Japan are identical to those in the USA (ie, the maximum 100% %Energy dial delivers 504 mC stimulation). Routine anesthetic agents used during treatment included thiamylal sodium 1.3-7.7 mg/kg, rocuronium bromide 0.5-1.1 mg/kg, and sugammadex sodium 2.3-5.4 mg/kg with 100% oxygen per mask. The initial intensity of electric stimulus in each treatment course was determined according to the patient's age, half the patient's age, or empirically, regarding the balance of risk (eg, elevation of seizure threshold) and benefit (eg, speed of recovery). During each ECT course, the stimulus intensity was increased according to the urgency of clinical situation if an adequate seizure was not elicited. The minimum duration for an adequate seizure was 15 seconds in the electroencephalogram record of the Thymatron® stimulator.[6] All sessions started with bilateral electrode placement (bitemporal or bifrontal). If 504 mC bilateral stimulation failed to induce an adequate seizure, the position of the left electrode was changed from left temporal or frontal to right vertex, followed by right unilateral stimulation with 504 mC without titration, referring to the concept of Thymatron® Instruction Manual. The right vertex electrode was placed according to the description by d'Elia.[10] The maximal number of stimulations in a single session was three.

TABLE 1 Subjects' diagnoses

Diagnosis	ICD-10	Number of patients	%
Schizophrenia	F20	13	58
Schizoaffective disorder	F25	3	14
Bipolar disorder	F31	2	9
Major depressive disorder, single episode	F32	2	9
Major depressive disorder, recurrent	F33	1	5
Others		1	5
Total		22	100

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision.

2.3 | Therapeutic outcome measurement

The efficacy of the treatment was estimated by the Global Assessment of Functioning (GAF) score[11] at the time of admission and discharge. No cognitive assessments were performed.

3 | RESULTS

By changing the left electrode to a right vertex placement, adequate seizures were obtained in 71 out of 87 sessions (81.6%). This switching method induced at least one adequate seizure in 26 of 28 treatment courses (92.9%), namely 20 out of 22 patients (90.9%). Two patients did not respond to serial switching trials, namely a 56-year-old male with a schizoaffective disorder who did not develop adequate seizures in three switching sessions and a 75-year-old female with schizophrenia who did not respond to two serial switching trials. However, she later developed adequate seizures with 504 mC bilateral stimulation. We typically needed to use this switching procedure in the middle of each treatment course (the fifth session, on average; min. first session, max. 12th session). In three courses, switching was needed from the first session; in these cases, the seizure thresholds were already known to be high.

The outcomes of our 22 inpatients were generally good. One patient remained hospitalized, but the rest were discharged. For 23 of 28 ECT courses (ie, 23 of 28 hospitalizations), GAF scores at the time of admission and discharge were available. Reasons for unavailability included ongoing hospitalization or missing/incomplete GAF

score recordings. A comparison of GAF scores on admission and discharge showed improvement in 23 courses (82.1%) by an average of 152% (min. 39% and max. 286%). The data of the patients reported are summarized in Table 2.

4 | DISCUSSION

The reason why right unilateral stimulation can elicit seizures in cases unresponsive to bilateral stimulation is likely related to differences in seizure thresholds between the types of stimulus and electrode placement. The seizure threshold is reported to be lower in unilateral ECT than in bilateral ECT,[7,12,13] and this phenomenon may be the mechanism of our findings.

We employed a simple criterion of <15 seconds in the duration of seizures on EEG recordings as the hallmark of inadequate seizures. This method is based upon the description of UpToDate® topic named "Technique for performing electroconvulsive therapy (ECT) in adults" updated on May 20, 2018. Though there are some other ways to evaluate the therapeutic efficacy of seizures (eg, synchronous regular activity and postictal suppression on EEG), we preferred the simplicity and applicability to clinical practice. Short seizures are usually caused by the shortage of electrical stimulation (resulting in clinical non-effectiveness) but sometimes by the excess of electrical stimulation (rarely causing clinical non-effectiveness).[14,15] In our report, except for a minority of cases in which the seizure thresholds were known to be high in advance, most cases became unresponsive to the maximum bilateral stimuli in the middle of the

TABLE 2 Summary of the patients reported

Patient	Age	Sex	Hospitalization (days)	Bilateral ECT (sessions)	Right unilateral ECT (sessions)	GAF score (admission)	GAF score (discharge)
1	56	M	1409	56	5	21	NA
2	56	M	214	29	3	21	81
3	51	F	257	40	1	30	NA
4	59	M	80	6	5	51	71
			13	6	1	51	71
5	73	M	18	11	1	51	71
			18	8	3	31	71
			20	4	8	41	81
			19	4	8	31	NA
6	72	F	15	10	1	21	81
			27	6	6	21	71
7	59	F	102	13	8	21	71
8	60	M	40	10	2	31	NA
9	69	M	208	6	4	30	60
10	70	M	24	8	4	41	71
11	75	F	19	10	2	21	71
12	61	M	NA	26	3	NA	NA
13	70	M	69	8	1	30	70
14	72	F	72	8	4	41	81
15	46	M	47	9	2	41	71
16	76	F	76	9	1	41	71
17	31	F	12	7	2	21	71
18	48	M	71	8	4	41	91
19	66	M	85	13	1	31	61
20	75	F	23	9	1	21	71
			76	11	1	21	71
21	44	F	88	8	2	11	40
22	69	F	63	6	3	31	71
Max						51	91
Min						11	40
Average						31.3	71.3

ECT, electroconvulsive therapy; GAF, global assessment of functioning.

treatment course. Thus, it is reasonable to presume that inadequate seizures in our patients were caused not by low seizure threshold and excess stimulation but by high seizure threshold and relatively insufficient electric stimulation. Seizure threshold varies greatly from person to person and from treatment to treatment, with a number of influencing factors such as patient's age, gender, anesthetic agents, psychotropic medications, the number and recency of previous ECT treatments.[9] In our cases, anticonvulsive medications (including benzodiazepines) and relatively strong electric stimuli in the initial sessions (eg, patient's age-dose method) might provoke the elevation of seizure threshold. Our findings suggest that even when maximum bilateral ECT stimuli fail to induce adequate seizures, there is still a high likelihood of obtaining adequate seizures by switching to right unilateral stimulation.

The role and selection of bilateral and unilateral ECT has become a subject of debate.[4,5,16–19] Our report suggesting a simple new method for eliciting adequate seizures during ECT in high seizure threshold cases may add a new viewpoint to this controversy. There are already several techniques to induce adequate seizures when ictal response is insufficient, including hyperventilation, decreasing or changing the anesthesia, decreasing or discontinuing anticonvulsive medications (including benzodiazepines), and the use of flumazenil, caffeine, or theophylline.[6,8,9] However, these methods do not always succeed, caffeine and theophylline may cause other problems,[20–25] and changes to medication or anesthesia require time. Our method of switching from bilateral to right unilateral ECT is promising because it is very simple, is not time-consuming or costly, and does not have any side effects. In addition, it does not interfere with other techniques for seizure augmentation, and they can thus be used in combination. A recent case report by Kawashima et al[26] employed a similar concept, switching from 0.5 ms pulse width bilateral ECT to 0.25 ms pulse width (ultrabrief pulse) right unilateral ECT and successfully eliciting effective seizures. Our report supports their finding and may enhance the clinical application of such switching.

Although our study population consisted mainly of chronic schizophrenia patients, it also included patients with mood disorders. In addition, both sexes were represented, and patients were of wide ages, ranging from 30s to 70s. Thus, it is expected that this switching method is capable of inducing adequate seizures in a wide range of patients if bilateral stimulation at maximum intensity fails. In Japan, where the maximal electrical intensity of ECT stimulation is limited to 504 mC, we often encounter patients who do not develop adequate seizures even with the strongest stimuli.

Although we can induce seizures by the switching method even when bilateral maximum stimulation fails, the efficacy of such seizures requires further evaluation. Although most cases in our study showed improvement in GAF score, this is an indirect estimation that may result from the summation of various kinds of psychiatric therapies, including unilateral ECT, bilateral ECT, psychotropic medication, and psychotherapy. It has been pointed out that right unilateral stimuli barely above the threshold are therapeutically weak.[27–30] In our switching method, right unilateral ECT was performed in patients whose thresholds are high enough not to develop adequate seizures even with maximum bilateral stimulations. Thus, in our case, the intensity of stimulation may not have reached the desirable level, which is thought to be 2.5-8 times greater than the seizure threshold.[30,31] The optimization of the electrical intensity in these situations needs further study including dose titration of stimuli. Cases have been described where initial right unilateral ECT was ineffective and bilateral ECT was required later in the treatment course.[17,32] In these cases, switching back to unilateral ECT may not be effective (however, in Japan, starting an ECT course with right unilateral stimulation is not common). Though Kawashima et al[26] reported a case of remission with bilateral to unilateral switching, future studies with more elaborate designs and specific ratings of symptoms are needed to determine the efficacy of this switching method. More homogenous subjects (eg, a diagnosis restricted to depression) might demonstrate the efficacy more clearly.

We believe that the most practical clinical application of our findings is as follows. In an emergent psychiatric case, bilateral ECT is started, but elevation of seizure threshold interrupts the occurrence of adequate seizures even with maximal stimulation. In this situation, switching from bilateral to right unilateral ECT may elicit adequate seizures and allow for completion of the treatment course. Although right unilateral ECT was previously regarded as a safer but less effective method,[9] it might be useful in this particular application.

In summary, switching from bilateral to unilateral electrode placement may be a simple clinical option for eliciting adequate seizures in high seizure threshold cases.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

R.M. acquired and analyzed the data. M.E. contributed to remainder of the work.

DATA REPOSITORY

Table 2 corresponds to the raw data which are analyzed in this article.

APPROVAL OF THE RESEARCH PROTOCOL BY AN INSTITUTIONAL REVIEWER BOARD

This study was reviewed and approved by the review board of Hokkaido Prefectural Midorigaoka Hospital.

INFORMED CONSENT

All participants provided informed consent prior to ECT courses.

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