Seizure Threshold in ECT : I. Initial Seizure Threshold†

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Abstract

Seizure threshold determination is of crucial importance in optimizing electrical stimulus dosage during administering electroconvulsive therapy (ECT). We measured initial seizure threshold by means of Srinakharinwirot University titration schedule in 150 psychotic patients. Initial seizure threshold was approximately 104 millicoulombs on average, but varied widely (12-fold) across patients. Motor seizure duration was inversely related to initial seizure threshold. Seizure threshold could be strongly predicted by age. The results may have important clinical implications for stimulus dosing strategy in ECT.

Key word : Electroconvulsive Therapy (ECT), Initial Seizure Threshold, Age, Srinakharinwirot University (SWU) Titration Schedule

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The most fundamental view of the mechanisms of action of electroconvulsive therapy (ECT) originated from the elegant research conducted by Ottosson[1-3]. This classic work led to the conclusions that 1) the production of an adequate generalized seizure is both necessary and sufficient for ECT therapeutic efficacy; and, 2) increasing the electrical stimulus intensity above that necessary to produce an adequate seizure does not contribute to either the number of patients who respond to ECT nor to the speed of their clinical response, but results in increased cognitive side effects.

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These principles have had a great impact on clinical practice that optimization of ECT is to insure that each patient has an adequate seizure at each treatment, using the minimum amount of electrical stimulus intensity. The National Institute of Health Consensus Conference of ECT (1985) also concluded that the lowest amount of electrical energy to induce an adequate seizure should be used[4].

Research conducted over the past few decades has demonstrated that each of these central beliefs is wrong. Several lines of evidence indicate that both the efficacy and the cognitive side effects of ECT may depend on the extent to which the stimulus dosage exceeds the patient's seizure threshold[5-15]. These findings suggest that optimizing stimulus dosage during ECT must have a determination of seizure threshold.

Recent studies on estimating seizure threshold suggests a wide range in initial seizure threshold, varying from 4-fold[16-18] to 6-[19,20], 12-[10,11,21], or up to 40-fold[12]. Higher seizure threshold is related to bilateral electrode placement [12,17-19,21], male gender[12,18-21], age[12,18-24], anesthetic agents[12,14,15,23,24], and concurrent medications[12,18,23,24].

This study was designed to address these issues and to replicate previous work in a large clinical sample of psychotic patients referred for ECT.

METHODS

Subjects

The subject sample included 150 patients with DSM-IV[25] schizophrenia (n = 120) or major depressive disorders (n = 20) or bipolar disorder (n = 4) or schizoaffective disorder (n = 4) or dementia with psychosis (n = 2). They received ECT during 3 years period (1996-8), at the participating hospitals. Patients who had received either ECT or depot neuroleptics within the past six months and who were receiving medicines that inhibit seizures (e.g., antiepileptics, benzodiazepines, beta-blockers) were excluded.

Previous psychotropic medications were discontinued prior to the first ECT. Flupenthixol (12 mg/day) and benzhexol (6 mg/day) were prescribed to all patients with schizophrenia and schizoaffective disorders, the rest of the patients did not receive any medication. All data were collected during the first two ECT sessions.

ECT technique

ECT was administered three times per week. The ECT devices were MECTA SR1 and Thymatron DGx. After atropine 0.4 mg intravenously, anesthesia was given with a minimal dosage of thiopental (2-4 mg/kg) and 0.5-1 mg/kg of succinylcholine. Patients were oxygenated from the time of administration of anesthetic until postictal resumption of spontaneous respiration. Bitemporal bilateral electrode placement was used exclusively. The tourniquet method and two channels of prefrontal electroencephalogram (EEG) were used to assess seizure duration. In each treatment one adequate seizure was elicited. An adequate seizure was defined as a tonic-clonic convulsion occurring bilaterally for at least 30 seconds plus EEG evidence of cerebral seizure.

Determination of seizure threshold

Seizure threshold was quantified at the first two treatment sessions, and was defined as the minimal electrical stimulus (in millicoulombs, mC) used to produce an adequate seizure. Srinakharinwirot University titration schedule was used (Table 1). The first stimulus intensity level (10%) was applied to all patients. If this failed to elicit such a seizure, the patient was then restimulated with stimulus charge one level above, and up to 4 stimulations were used with an interval of at least 40 seconds between each without giving additional thiopental. At the second treatment session, the stimulus dose given was 5 per cent lower than at the first session. If an adequate seizure occurred, that dose was taken as the threshold; if not, the first session's stimulus dose was so taken.

Statistical analysis

Correlations between continuous variables were examined with the Pearson correlation coefficients. Differences between groups on the continuous variables were evaluated with analysis of variance (ANOVA). The degree to which variables could predict initial seizure threshold was examined by stepwise multiple regression analysis. Values were given as mean $\pm$ SD. All significant levels were for two-tailed. SPSS 7.5 (1996 SPSS Inc.) was used for all analyses.

RESULTS

Table 2 provides the characteristics of 150 patients who participated in our study. Initial seizure

Table 1. Srinakharinwirot University (SWU) dosing schedule for MECTA SR1 and Thymatron DGx.
Initial and successive treatments (25-100% increments)

	MECTA SR1					Thymatron DGx	
Level*	Pulse width	Frequency	Duration	Current	Charge (mC)	%	Charge (mC)
1	1.0	40	1.25	0.6	60	10	50.4
2	1.0	40	2.0	0.75	120	20	100.8
3	1.0	60	2.0	0.75	180	30	151.2
4	1.2	60	2.0	0.8	230.4	40	201.6
5	1.0	90	2.0	0.8	288	50	252
6	1.4	90	2.0	0.8	403.2	70	352.8
7	2.0	90	2.0	0.8	576	100	504
Extra level**							
1	1.0	40	0.5	0.8	32	5	25.2
2	1.0	40	1.5	0.7	84	15	75.6
3	1.0	90	1.0	0.8	144	25	126
4	1.0	60	2.0	0.8	192	35	176.4
5	1.2	70	2.0	0.75	252	45	226.8
6	1.2	90	2.0	0.8	345.6	60	302.4
7	1.6	90	2.0	0.8	460.8	80	403.2
8	1.8	90	2.0	0.8	518.4	90	453.6

* Increase by one level is recommended for use in either dose titration of the first or subsequent treatments.
** The extra level is only used when a finer estimation of seizure threshold is needed, i.e., in children and adolescents, comparison of the effects of different stimulus dosages.

Table 2. Patient characteristics.

	Value	Range
Age (years, mean ± SD)	38.4 ± 10.8	20-67
Gender (n, %)		
Men	61 (40.7)	
Women	89 (59.3)	
History of prior ECT (n, %)	117 (78)	
Diagnosis (n, %)		
Schizophrenia	120 (80)	
Major depressive disorder	20 (13)	
Bipolar disorder	4 (2.7)	
Schizoaffective disorder	4 (2.7)	
Dementia with psychosis	2 (1)	
Pre-ECT BPRS scores (n = 145, mean ± SD)	49.7 ± 9.1	34-77

threshold was 104.2 ± 49.6 mC. There was a substantial variability in patient's seizure threshold, the range observed was from 25.2 mC to 288 mC (12-fold). Seizure threshold of male patients (106.3 ± 53.4 mC, n = 61) was almost equal to that of female patients (103.1 ± 46.7 mC, n = 89).

Figure 1 shows the distribution of initial seizure threshold in 150 patients. One hundred and forty eight patients seized at the first session, the number of patients who seized at each level of stimulation (1- 4) were 36 (24%), 85 (57%), 14 (9%), and 13 (9%) patients, respectively. Two patients seized at the second session using the fifth level (252 mC and 288 mC). Initial seizure threshold could be determined at the first session in the majority of patients (n= 88, or 59%). The average num-

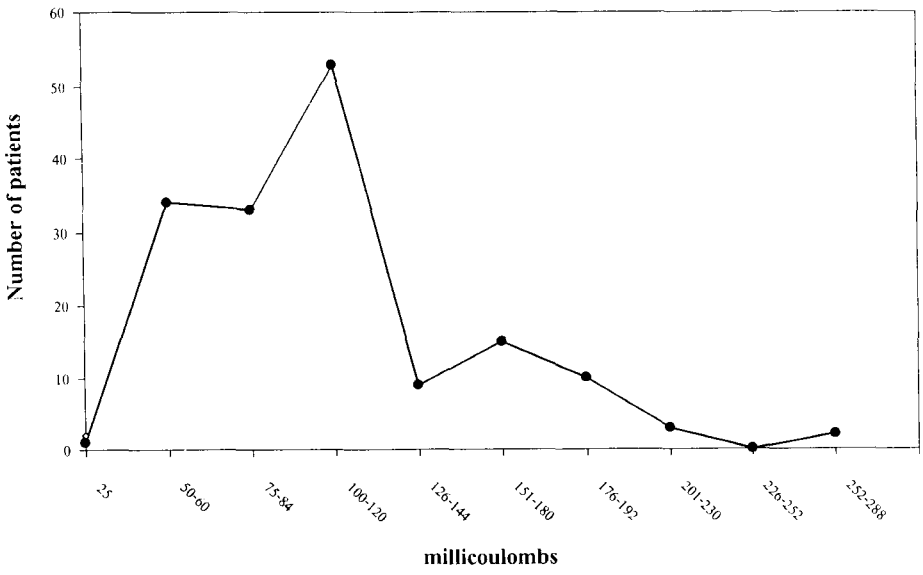

Fig. 1. Initial seizure threshold in 150 patients.

ber of stimulations was 2.0 ± 0.8. Anesthetic procedure required an average dose of 143.8 ± 38.3 mg of thiopental and 24.8 ± 6.7 mg of succinylcholine.

Only age had significant main effects in estimating seizure threshold [F (2,149) = 11.5, p < 0.0001). There were no two-way interactions between any of the variables. Before inclusion in the multivariate model, the relationship between each variable and seizure threshold was investigated (Pearson's product-moment correlation). Age was significantly associated with seizure threshold (r = 0.48, p <0.001, R^2 = 0.23, p <0.001). Motor seizure duration (50.1 ± 16.0 seconds) was negatively related to seizure threshold (r = 0.2, p < 0.05), this apparent relationship did not persist after regression analysis.

DISCUSSION

In our study of a clinical sample of 150 psychotic patients who received treatment with a brief-pulse, constant current, bilateral ECT, we found that the average initial seizure threshold was 104.2 ± 49.6 mC. This estimate is in the middle of the range of mean seizure thresholds observed by other investigators using the stimulus dose titration technique[9,17,19-21,26,27], and is close to that of two recent studies (96.8 mC [28] and 110.5 mC [21]). The range in initial seizure thresholds observed in our study was from 25.2 mC to 288 mC (12-fold), compared to that of prior studies which had a low of 12 mC[29] and a high of more than 700 mC[12]. Seizure threshold could only be predicted by age.

The seizure threshold is not a fixed, invariant, or inherent property of a neural tissue, but rather a highly variable phenomenon that is a function of the methods used to measure it[30,31]. The use of either a more efficient stimulus configuration or a more rigorous titration schedule will definitely lead to lower seizure threshold estimates[31]. The seizure threshold is also known to depend on several factors such as age[12,18-24], gender[12,18-21], electrode placement[12,17-19,21], anesthetic agents [12,14,15,23,24], concomitant medications[12,18, 23,24], ECT course[10,12] and frequency[32], diagnosis[29,33], laterality[10], and head measurement[27].

These factors may account for a wide range in estimating initial seizure threshold. Therefore, it is clear that average seizure threshold data represent an approximation, and patients' true seizure threshold values were actually somewhere below that dosage level. Only 24 per cent of our sample (19 men, 17 women) seized at the first level (10% of charge) in which two women seized at 5 per cent charge. The majority of patients (76%, n = 114) had adequate seizures at higher levels, in which 75 per cent (n = 85) did at the second level.

There are two major differences between our methodology and the methods used in prior reports of ECT stimulus dosing. First, we estimated the seizure threshold at the first two treatment sessions instead of only one as in all prior studies. There were 60 patients (40%) whose threshold could be determined at the second session. This titration strategy raises an important question that only a 5 per cent difference of charge between these two sessions could give us any academic interest? Given the known risks of using repeated subconvulsive stimulations, do these patients really benefit from our method? However, several recent reports (including the present one) have found much more benign cardiovascular effects of subconvulsive stimuli[18,21,34-36]. The use of anticholinergic premedication may be particularly important in patients undergoing stimulus dose titration, since it is protective against sinus arrests[37] and was routinely used in all studies. The average number of stimulations in our study was 2.0 ± 0.8. In practical use, we recommend that seizure threshold determination should be performed only at the first session. Second, we have no results from patients receiving ECT with unilateral electrode placement for a comparison as in prior studies[13,19-21].

In summary, initial seizure threshold was approximately 104 mC on average, and had a 12-fold variation across patients. Motor seizure duration was inversely related to seizure threshold. Only age was found to predict seizure threshold.

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ปริมาณไฟที่เหมาะสมในการรักษาด้วยไฟฟ้า: I. ปริมาณไฟในการรักษาครั้งแรก†

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การหาปริมาณไฟที่เหมาะสมที่ใช้ในการรักษาด้วยไฟฟ้าเป็นสิ่งที่มีความสำคัญมากเพื่อให้ได้ประสิทธิภาพของการรักษาสูงสุดและเกิดผลข้างเคียงน้อยที่สุด คณะผู้วิจัยได้ทำการหาปริมาณไฟที่เหมาะสมที่ใช้เริ่มต้นในการรักษาผู้ป่วยโรคจิตชนิดต่าง ๆ จำนวน 150 คน โดยการใช้เกณฑ์ของมหาวิทยาลัยศรีนครินทรวิโรฒ

พบว่าค่าเฉลี่ยของปริมาณไฟที่เหมาะสมในการเริ่มต้นการรักษามีค่าเท่ากับ 104 มิลลิคูลอมบ์ ปริมาณไฟที่เหมาะสมในการรักษาผู้ป่วยแต่ละรายนี้มีค่าแตกต่างกันมากถึง 12 เท่า พบว่าระยะเวลาของการชักแปรผันกลับกับปริมาณไฟที่ใช้ และอายุของผู้ป่วยสามารถใช้ทำนายปริมาณไฟที่ใช้ได้

ผลการศึกษามีความสำคัญมากในการกำหนดเกณฑ์เพื่อใช้ในการหาปริมาณไฟที่เหมาะสมในการรักษาด้วยไฟฟ้า

คำสำคัญ : ปริมาณไฟต่ำสุดที่ใช้เริ่มต้นการรักษา, การรักษาด้วยไฟฟ้า, เกณฑ์ปรับไฟของมหาวิทยาลัยศรีนครินทรวิโรฒ

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