Psychological Medicine, 1999, **29**, 1417–1423. Printed in the United Kingdom

Value of the initial stimulus dose in right unilateral and bifrontal electroconvulsive therapy

P. HEIKMAN,[1] A. TUUNAINEN AND K. KUOPPASALMI

From the Department of Psychiatry, Helsinki University Central Hospital and KTL, National Public Health Institute, Helsinki, Finland

ABSTRACT

Background. The outcome of electroconvulsive therapy (ECT) is affected by the placement and dose of the stimulus. In general, the ECT dose can be selected either by the dose-titration method (on which the measured seizure threshold level is based), or the method of predetermined dose (e.g. the age-based dosing and the fixed high dose method).

Methods. Seizure thresholds were measured in 50 patients with right unilateral (RUL) and in 30 patients with experimental bifrontal (BF) ECT stimulus. The ECT dose (mC) of the age-based dosing was calculated by multiplying the age (years) by 5·0 (age method) or 2·5 (half-age method). The fixed high dose was set to 378 mC.

Results. The seizure thresholds had only a moderate correlation with the age of the patients. The methods based on the predetermined dose would have led us to give patients with the lowest seizure thresholds in the RUL ECT group very high stimulus doses, up to 12 (age method) or 15 (fixed high dose method) times the individual seizure threshold. In contrast, the RUL ECT patients with the highest seizure thresholds would have received low stimulus doses down to 1·5 times (half-age method) the initial seizure threshold. In the BF ECT group the-age based dose would have been similarly dependent on the initial seizure threshold level.

Conclusion. The use of the dose-titration method is recommended, because it is the only method that allows for the individual selection of ECT stimulus dose relative to the seizure threshold.

INTRODUCTION

Electroconvulsive therapy (ECT) is a powerful tool for the treatment of depression. Technical aspects of this method, however, need to be considered (Abrams, 1997*a*). Weiner *et al.* (1986) have found that sine-wave stimuli induce more cognitive side-effects in the treatment of depressive patients than modern brief-pulse stimuli. Regarding stimulus placement, right unilateral (RUL) ECT (Abrams, 1997*b*) induces less cognitive-side-effects than the conventional bilateral (BL) positioning of electrodes. More anteriorly placed bilateral stimulus (bifrontal, BF) has been shown to spare both verbal and non-verbal cognitive functions better than BL and RUL ECT treatment if the stimulus is dosed just above individual seizure threshold (Lawson *et al.* 1990). On the other hand, Sackeim *et al.* (1993) has found that RUL ECT at the threshold-level dose has an extremely poor efficacy. Increasing the dose to 2·5 the seizure threshold level increases the efficacy of the RUL ECT, although not to the level of the BL ECT. In addition, changes in brain function corresponding to the efficacy of ECT have been found to be dependent on the amount of the stimulus relative to the seizure threshold level (Sackeim *et al.* 1996). Thus, an important object of ECT research is the dose with respect to the individually measured seizure threshold.

When treating patients with major depression, the initial stimulus dose can be chosen using two

[1] Address for correspondence: Dr Pertti Heikman, Department of Psychiatry, Helsinki University Central Hospital, FIN-00180 Helsinki, Finland.

alternative methods. First, the ECT dose can be given individually as obtained by a dose-titration method (see e.g. Sackeim *et al.* 1987) by which the individual seizure threshold is measured. Secondly, one can use a method of predetermined dose, e.g. a fixed high dose method for RUL ECT treatment (Abrams *et al.* 1991), or a dose based on parameters that have some relationship with the seizure threshold level, e.g. the age of the patient (age-based dosing) (Abrams 1997*c*).

We previously used the age-based dosing based on the manual of the THYMATRON-DGx machine (Swartz & Abrams, 1994). With this method, however, we observed that many patients experienced cognitive side-effects. Consequently, the question arose of whether the patients might have received stimulation excessive to their individual requirements?

The aim of the study was to compare the dose-titration method and the method of predetermined dose in terms of stimulus dose in relation to the initial seizure threshold of the patients. The comparisons between the methods were carried out separately for the patients in the RUL ECT and BE ECT groups.

METHOD

Subjects

We studied 82 consecutive depressive in-patients referred for ECT, 32 out of 56 patients in the preliminary phase and 50 out of 61 patients in the randomized phase of the clinical study. We included, regardless of the severity of the episode, all consecutive depressive (unipolar and bipolar) in-patients in the study. All patients underwent the same dose-titration method (DTM, see seizure threshold measurement) through RUL or BF ECT stimulus electrode placements. If different dose titration methods were used, the patients were excluded from the study. In addition, two patients (BF ECT group) were excluded from statistical calculations. The first (a 54 year-old woman) had at the first subconvulsive stimulus a 20-s asystole which resolved spontaneously without complications. The patient was not restimulated. She had a history of hypertension treated with beta blockers, and prior to ECT, she had had doxepine withdrawal for 6 days. The second (a 63 year-old-woman) did not exhibit a clinical seizure of adequate duration even at the highest stimulation level. Thus, the study group comprised of 80 patients: 50 patients ranging in age from 28 to 69, with a mean age of 49·8 (median 48·5) in the RUL ECT group and 30 patients ranging in age from 24 to 77, with a mean age of 47·3 (median 47) in the BF ECT group. None of the patients had undergone a course of ECT treatment during the 3-month period prior to ECT. Psychotropic medication was either kept stable or reduced by the attending physician. In the first treatment, the majority of patients had some psychotropic medication in both ECT groups: benzodiazepines (35/50 and 23/30 patients); neuroleptics (30/50 and 19/30 patients); and antidepressants (7/50 and 14/30 patients) in the RUL and BF ECT groups, respectively. The patients continued with their somatic medications prescribed prior to ECT. The study was conducted at the Lapinlahti Hospital of the Department of Psychiatry of Helsinki University Central Hospital. All patients gave their informed consent for the study, which was approved by the Ethics Committee of the Department of Psychiatry, Helsinki University Central Hospital.

ECT treatment technique

Medications for standard intravenous anaesthesia comprised atropine (0·4 mg), methohexital (0·75 mg/kg) and succinylcholine (0·5 mg/kg). However, the doses of medications were adjusted individually. The mean dose (range) of methohexital was 0·89 (0·61–1·40) for the RUL ECT group and 0·93 (0·68–1·64) for the BF ECT group and those of succinylcholine 0·55 (0·35–1·02) for the RUL ECT group and 0·60 (0·35–0·98) for the BF ECT group. The doses of succinylcholine used did not prevent the estimation of seizure duration by direct visual observation. One patient (RUL ECT group) was relaxed using mivacurium (0·07 mg/kg iv dose) because of polyneuropathia. The patients were oxygenated (100% O_2), and their cardiovascular function was monitored using a Cardiocap™ II anaesthesia monitor (Datex).

The stimulation sites were cleansed with alcohol, wiped dry, and thereafter conductive gel (Hellige) was applied over the treatment surfaces of the stainless steel electrodes for checking the static impedance (skin-to-electrode contact). The impedance was according to the

https://doi.org/10.1017/S0033291799001245 Published online by Cambridge University Press

Table 1. *The relation of age-base dose and fixed high dose to the initial seizure threshold (ST)*

ST (mC)	Age (years)		Age/ST		HAM/ST		AM/ST		FHDM/ST Ratio
	Median	Range	Median	Range	Median	Range	Median	Range	
RUL ECT									
25·2	46	29–61	1·8*	1·2–2·4	4·4*	2·9–6·1	9·0*	6·0–12·0	15·0
50·4	48	28–68	1·0	0·6–1·4	2·5	1·4–3·4	5·0	3·0–7·0	7·5
75·6	57·5	44–69	0·8	0·6–0·9	1·9	1·5–2·3	4·0	3·0–4·5	5·0
BF ECT									
50·4	41·5	24–63	0·8†	0·5–1·3	2·1†	1·2–3·1	4·1†	2·5–6·5	
100·8	46	32–77	0·5	0·3–0·8	1·1	0·8–1·9	2·3	1·5–4·0	
151·2	66	57–68	0·4	0·4–0·5	1·1	0·9–1·1	2·2	2·0–2·5	

ST, initial seizure threshold by the dose titration method; RUL, right unilateral; BF, bifrontal.
HAM, half-age method: the ECT dose (mC) ~ age (years) of the patient multipled by 2·5.
AM, age method: the ECT dose (mC) ~ age (years) of the patient multiplied by 5·0.
FHDM, fixed high dose method: the ECT dose = 378·0 mC.
* $P < 0{\cdot}0001$; † $P = 0{\cdot}0005$ (Kruskal–Wallis test). The ratio is highest at the lowest ST level ($P < 0{\cdot}05$) in both ECT groups (multiple comparison for the Krustal–Wallis test).

recommendation of the THYMATRON-DGx manual (Swartz & Abrams, 1994) at least 100 and less than 3000 ohms prior to all stimulations. For RUL ECT, a flat and concave stimulus electrode, and for BF ECT, two concave stimulus electrodes, both hand held and ~ 5 cm in diameter, were used. In the RUL ECT, we used d'Elia ECT stimulus placement (d'Elia & Perris, 1970), and in the BF ECT, the midpoints of both electrodes were about 5 cm above the lateral angles of the orbits on both sides (Lawson *et al.* 1990; Letemendia *et al.* 1993).

Seizure threshold measurement

Seizure threshold (ST), in units of charge (millicoulombs, mC), was measured at the first ECT treatment session using the same brief-pulse ECT machine (THYMATRON-DGx™, Somatics Inc., Lake Bluff, IL, USA) for all patients. The initial dose was 25·2 mC (0·9 A, 1·0 ms pulse width, 30 · Hz, 0·47 s duration) for RUL ECT and 50·4 mC (0·9 A, 1·0 ms pulse width, 30 · Hz, 0·93 s duration) for BF ECT. The stimulus (1·0 ms pulse width) was repeated at about 30 s intervals with stepwise increased stimulus doses (50·4, 75·6, and 100·8 mC for RUL ECT; 100·8, 151·2, and 201·6 mC for BF ECT). The seizure threshold was defined as the ECT stimulus dose which elicited a generalized convulsive activity lasting for at least 25 s that could be observed by the ECT treatment team (i.e. the ECT treatment nurse, the treating psychiatrist and the anaesthetist). The mean (range) duration of seizures was 57 s (30–95) in the RUL ECT group and 50 (32–73) in the BF ECT group.

Age seizure threshold ratio

Age-based dosing has two clinical applications. In the age method (AM), the dose (mC) equals the age (years) of the patient multiplied by 5·0 (Swartz & Abrams, 1994) and in the half-age method (HAM) the dose (mC) equals the age (years) of the patient multiplied by 2·5 (Petrides & Fink, 1996). In both ECT groups, we calculated the age/ST, the AM/ST, and HAM/ST ratios (Table 1) at the individually measured ST levels. These calculations show how a patient with a low or high ST is treated by age-based dosing.

Age fixed high dose ratio

We used the same fixed high dose (378·0 mC, FHDM) as Abrams *et al.* (1991). Because Abrams *et al.* (1991) has used the FHDM for RUL ECT only, we did not carry out this calculation in the BF ECT group.

Statistical analysis

Non-parametric tests were used because of three reasons. First, the values both for seizure threshold (Table 1) and for the age-groups (Table 2) are more ordinal than continuous variables. Secondly, the age/ST ratio had a non-normal distribution both in the RUL ECT group (the skewness = 1·56, $P < 0{\cdot}0001$, Wilk–Shapiro test), and in the BF ECT group (the skewness = 1·05, $P = 0{\cdot}0003$). Thirdly, sub-

https://doi.org/10.1017/S0033291799001245 Published online by Cambridge University Press

group comparisons included small number of patients. The tests were two-tailed, and their statistical significance level was set to $\alpha = 0{\cdot}05$. Statistical computations were performed with the BMDP New System (BMDP Statistical, Software, Inc, Los Angeles, California, 1994) except that the multiple comparisons of the Kruskal–Wallis test were done with BMDP Classic Release 7 (1993).

RESULTS

The median (mean, range) seizure threshold (mC) was 50·4 (49·9, 25·2–75·6) in the RUL ECT group and 100·8 (85·7, 50·4–151·2) in the BF ECT group (Table 1). The numbers of patients (male/female) at the different seizure threshold levels were: 2/7 at 25·2 mC, 9/24 at 50·4 mC, 6/2 at 75·6 mC, and 0/0 at 100·8 mC in the RUL ECT group; and 3/9 at 50·4 mC, 6/9 at 100·8 mC, 1/2 at 151·2 mC, and 0/0 at 201·6 mC in the BF ECT group.

Correlation between seizure threshold age

The correlation between the ST and the age was relatively poor both in the RUL ECT group ($r_s = 0{\cdot}31$, $P = 0{\cdot}027$, Spearman rank correlation), and in the BF ECT group ($r_s = 0{\cdot}35$, $P = 0{\cdot}054$) (Table 1). In the RUL ECT group, there was a significant correlation between the seizure threshold level and the age of the men ($r_s = 0{\cdot}64$, $P = 0{\cdot}0061$) whereas there was no correlation between the seizure threshold level and the age of the women ($r_s = 0{\cdot}098$). In the BF ECT group, there was a tendency for inverse correlation between the ST level and the age of the men ($r_s = -0{\cdot}47$, $P = 0{\cdot}17$), and a significant correlation between the ST level and age of the women ($r_s = 0{\cdot}59$, $P = 0{\cdot}0064$).

Age-based dose and seizure threshold

The age of patients tended to increase in relation to their ST level both in the RUL ECT group ($P = 0{\cdot}081$, Kruskal–Wallis test), and in the BF ECT group ($P = 0{\cdot}060$) (Table 1). The age/ST ratio decreased relative to the ST level both in the RUL ECT group ($P < 0{\cdot}0001$, Kruskal–Wallis test), and in the BF ECT group ($P = 0{\cdot}0005$). Using multiple comparison for the Kruskal–Wallis test, the age/ST at the lowest ST level was higher than that at the second or third level both in the RUL ECT and in the BF ECT group. The age/ST at the second level was not different from the age/ST at the third level in the RUL ECT group, or in the BF ECT group.

The age/ST ratio by gender was different relative to the ST level both in the RUL ECT group (for men, 1·5, 0·9 and 0·8, $P = 0{\cdot}034$; for women, 1·8, 1·0 and 0·6, $P = 0{\cdot}0002$, Kruskal–Wallis test), and in the BF ECT group (for men, 1·3, 0·4 and 0·4, $P = 0{\cdot}043$; for women, 0·7, 0·5 and 0·4, $P = 0{\cdot}026$). Using multiple comparison for the Kruskal–Wallis test, both men and women in the RUL ECT group had a higher age/ST ratio at the first level stimulation level than at the third level. The ratio at the first level for women was higher than at the second level. In the BF ECT group, the comparisons between subgroups were not statistically significant.

Seizure threshold by age and gender

The seizure threshold by age was found to be different for men in the RUL ECT group ($P = 0{\cdot}0089$, Kruskal–Wallis test) and for the women in the BF ECT group ($P = 0{\cdot}0078$) (Table 2). Using multiple comparison for the Kruskal–Wallis test, the seizure threshold (BF ECT

Table 2. *Median (range) initial seizure threshold (mC) by age and gender*

	RUL ECT		BF ECT	
Age (years)	Male	Female	Male	Female
10–29	25·2*	50·4 (50·4–50·4)	100·8	50·4 (50·4–50·4)†
	$N = 1$	$N = 2$	$N = 1$	$N = 4$
30–59	50·4 (25·2–75·6)	50·4 (25·2–75·6)	100·8 (50·4–151·2)	100·8 (50·4–100·8)
	$N = 12$	$N = 23$	$N = 8$	$N = 12$
60–85	75·6 (75·6–75·6)	50·4 (25·2–50·4)	50·4	126·0 (100·8–151·2)
	$N = 4$	$N = 8$	$N = 1$	$N = 4$

* $P = 0{\cdot}0089$, † $P = 0{\cdot}0078$ (Kruskal–Wallis test). In the BF ECT group, seizure threshold for women in the youngest age-group is lower than in the oldest age-group ($P < 0{\cdot}05$) (multiple comparison for the Kruskal–Wallis test).

https://doi.org/10.1017/S0033291799001245 Published online by Cambridge University Press

group) for women in the youngest age group was lower than that in the oldest age group. The comparison between other subgroups was not statistically significant.

Fixed high dose method and seizure threshold level

The FHDM/ST ratio was $\geqslant 5$ in the RUL ECT group at all ST levels the highest level being 15 (Table 1).

Psychotropic medication and seizure threshold level

In the RUL ECT group, the patients on neuroleptics had a lower ST level (median 50·4, mean 46·2) than those without the medication (median 50·4, mean 55·4, $P = 0{\cdot}031$, Mann–Whitney U test). In the BF ECT group, the patients on benzodiazepines had a higher ST level (median 100·8 mC, mean 92·0) than those not using benzodiazepines (median 50·4, mean 64·8 mC, $P = 0{\cdot}05$). Other calculations regarding ST by psychotropic medication were statistically non-significant.

DISCUSSION

This study shows that the patients in both the RUL ECT and BF ECT groups with low seizure thresholds would have received a higher dose in relation to the initial seizure threshold than other patients if the age-based dosing or the fixed high dose method (only RUL ECT) had been used. Only a moderate correlation between age and seizure threshold was found in the RUL ECT group as in the previous studies (Sackeim *et al*. 1987; McCall *et al*. 1993*a*; Beale *et al*. 1994; Coffey *et al*. 1995; Enns & Karvelas, 1995). The correlation between age and seizure threshold in the BF ECT group was even poorer. In the RUL ECT group the relation between seizure threshold and age was stronger in men than in women. This finding is in agreement with the findings of Sackeim *et al*. (1991), and Dykes & Scott (1998).

RUL ECT treatment

The lack of information about the optimal stimulus intensity in the RUL ECT is today a significant limitation of the dose-titration method. Whether the stimulus dose should be given individually by a dose-titration method or by a method of predetermined dose is still under debate. Both the age-based dosing and the fixed high dose method would have guided us to give effective RUL ECT treatment to all the patients. In contrast, the half-age method would have led probably us to give ineffective treatment to patients with high seizure thresholds because according to Sackeim *et al*. (1993) the dose in RUL ECT treatment should be 2·5 times or more the initial seizure threshold level. The dose-titration method allows us to give for the second treatment an exact dose relative to the initial seizure threshold. For example, a relatively high dose (5 times the seizure threshold level) would have led us to give our patients a stimulus dose that was at most the same as the fixed high dose (378 mC) used in the study of Abrams *et al*. (1991).

In the patients with the lowest seizure threshold (25·2 mC) the doses based on the age method and the fixed high dose method would have been very high. Furthermore, the doses would have been underestimated in these patients because 'their true seizure threshold' was either at the measured level or somewhere below it. The number of patients who had an adequate seizure at the first stimulus level (18%) is in agreement with the finding (15%) of the Columbia University group (Sackeim *et al*. 1987).

The question arises whether high stimuli relative to the individual seizure threshold may be dangerous? Squire & Zouzounis (1986) have suggested that the advantage of brief-pulse ECT on memory function in clinical practice is probably achieved only if treatment is dosed close to the individual seizure threshold. More recently, Sackeim *et al*. (1993) have shown that RUL ECT treatment with stimuli dosed at 2·5 times the seizure threshold level compared with that to threshold-level treatment induces a longer immediate disorientation phase, which increases the risk of retrograde amnesia following ECT (Sobin *et al*. 1995). On the other hand, Abrams (1997*b*) has stated that there is no clear evidence in the literature that some long-term cognitive side-effects persist after brief-pulse stimuli with RUL electrode placement. However, Abrams (1997*b*) points out that when increasingly higher doses become routine for unilateral ECT in order to maximize therapeutic impact, objective memory deficits may become manifest.

BF ECT treatment

According to Letemendia *et al.* (1993), BF ECT is safe and effective when dosed just above the individual seizure threshold level. The half-age method would have guided us to give almost the dose recommended by Letemendia *et al.* (1993) to patients with moderate (100·8 mC) to high seizure thresholds (151·2 mC). In patients with low seizure thresholds (50·4 mC), both the half-age and the age method would have given significantly higher doses.

Letemendia *et al.* (1993) have suggested that BF ECT by avoiding the temporal regions of the brain may spare both verbal and non-verbal cognitive functioning and by inducing maximal current density in the frontal regions may achieve full therapeutic advantage. Sackeim *et al.* (1996) have, more recently, found that the efficacy of ECT is linked to the induction of EEG slow-wave activity in the prefrontal cortex. Nevertheless, the BF placement has to be considered as experimental, and it can not be recommended for routine clinical use until further trials are completed.

Seizure threshold measurement

The individual seizure threshold is not absolute, but is highly affected e.g. by electrical stimulus parameters such as pulse-width of the ECT stimulus (Abrams 1997*a*), and individual differences in skull thickness, anatomy and resistance (Sackeim *et al.* 1994). The initial seizure threshold of the RUL ECT has been shown to vary in the range from 25 mC to 300 mC (Sackeim *et al.* 1991). Comparison of the initial seizure threshold levels between studies is difficult due to other contributing factors, e.g. the psychotropic medication used (Coffey *et al.* 1995) and the variation in titration schedule (Lock, 1995). In our study, the protocol was the same for both women and men, and the doses at the three first stimulus levels were identical to those of McCall *et al.* (1993*a*) and Rasmussen *et al.* (1994). However, both McCall *et al.* and Rasmussen *et al.* used a shorter interval (20 s *v.* 30 s) between subconvulsive stimuli than we did, and additionally, Rasmussen used a shorter stimulus pulse width (0·5 ms *v.* 1·0 ms). The seizure threshold level in our RUL ECT group is similar to the low values among studies using brief-pulse stimuli and the d'Elia stimulus placement (Malitz *et al.* 1986; Sackeim *et al.* 1987, 1993; McCall *et al.* 1993*b*; Rasmussen *et al.* 1994; Coffey *et al.* 1995; Enns & Karvelas, 1995).

The first stimulus level in our BF ECT group (50·4 mC) was set low relative to the mean initial seizure threshold level in the study of Letemendia *et al.* ($\sim$ 115 mC, 0·8 A, 1·5 ms pulse width, 40 Hz, 1·25 s duration, MECTA device) (1993) because we used a shorter pulse-width (1·0 ms). Despite this, our initial seizure threshold level (median 100·8 mC, mean $\sim$ 86 mC) was at the same level. However, nearly half of our BF ECT patients (40 %, three men and nine women) had an adequate seizure at the lowest stimulus dose level. Therefore, if a Thymatron machine with similar stimulus parameters as in our study is used, a lower starting dose, especially for women, might be sufficient. Apart from finding patients with low seizure thresholds, the dose-titration method is useful in detecting patients with exceptionally high seizure thresholds.

In conclusion, this study indicates that patients with different seizure thresholds would be treated differently if the predetermined dose is used both for RUL ECT and BF ECT groups. Especially, patients with low seizure thresholds are in danger of being treated with supra-high stimulus doses. The safety of such doses is questionable. We recommend the use of the dose-titration method, i.e. measurement of the individual seizure threshold in the first ECT treatment, followed by an ECT treatment relative to it. Only the dose-titration method permits us to standardize the ECT stimulus dose relative to the initial seizure threshold level.

This work was supported by a grant to Dr Heikman from the Orion company. We thank Seppo Sarna, Professor in the Department of Public Health, University of Helsinki, for statistical consultations.

REFERENCES

Abrams, R. (1997*a*). The electroconvulsive therapy stimulus. In *Electroconvulsive Therapy* (ed. R. Abrams), pp. 114–135. Oxford University Press: New York.

Abrams, R. (1997*b*). Memory and cognitive functioning after electroconvulsive therapy. In *Electroconvulsive Therapy* (ed. R. Abrams), pp. 212–250. Oxford University Press: New York.

Abrams, R. (1997*c*). Technique of electroconvulsive therapy: theory. In *Electroconvulsive Therapy* (ed. R. Abrams), pp. 181–182. Oxford University Press: New York.

Abrams, R., Swartz, C. M. & Vedak, C. (1991). Antidepressant effects of high-dose right unilateral electroconvulsive therapy. *Archives of General Psychiatry* **48**, 746–748.

Beale, M. D., Kellner, C. H., Pritchett, J. T., Bernstein, H. J., Burns, C. M. & Knapp, R. (1994). Stimulus dose-titration in ECT: a 2-year clinical experience. *Convulsive Therapy* **10**, 171–176.

Coffey, C. E., Lucke, J., Weiner, R. D., Krystal, A. D. & Aque, M. (1995). Seizure threshold in electroconvulsive therapy: I. Initial seizure threshold. *Biological Psychiatry* **37**, 713–720.

d'Elia, G. & Perris, C. (1970). Comparison of electroconvulsive therapy with unilateral and bilateral stimulation. I. Seizure and post-seizure electroencephalographic pattern. *Acta Psychiatrica Scandinavica* **46** (suppl. 215), 9–29.

Dykes, S. & Scott, A. (1998). Initial seizure threshold in bilateral electroconvulsive therapy. *Psychiatric Bulletin* **22**, 298–299.

Enns, M. & Karvelas, L. (1995). Electrical dose titration for electroconvulsive therapy: a comparison with dose prediction methods. *Convulsive Therapy* **11**, 89–93.

Lawson, J. S., Inglis, J., Delva, N. J., Rodenburg, M., Waldron, J. J. & Letemendia, F. J. J. (1990). Electrode placement in ECT: cognitive effects. *Psychological Medicine* **20**, 335–344.

Letemendia, F. J., Delva, N. J., Rodenburg, M., Lawson, J. S., Inglis, J., Waldron, J. J. & Lywood, D. W. (1993). Therapeutic advantage of bifrontal electrode placement in ECT. *Psychological Medicine* **23**, 349–360.

Lock, T. (1995). Stimulus dosing. In *The ECT Handbook* (ed. C. P. Freeman), pp. 72–87. Royal College of Psychiatrists: London.

McCall, W. V., Reid, S., Rosenquist, P., Foreman, A. & Kiesow-Webb, N. (1993*a*). A reappraisal of the role of caffeine in ECT. *American Journal of Psychiatry* **150**, 1543–1545.

McCall, W. V., Shelp, F. E., Weiner, R. D., Austin, S. & Norris, J. (1993*b*). Convulsive threshold differences in right unilateral and bilateral ECT. *Biological Psychiatry* **34**, 606–611.

Malitz, S., Sackeim, H. A., Decina, P., Kanzler, M. & Kerr, B. (1986). The efficacy of electroconvulsive therapy. Dose-response interactions with modality. *Annals of the New York Academy of Sciences* **462**, 56–64.

Petrides, G. & Fink, M. (1996). The 'half-age' stimulation strategy for ECT dosing. *Convulsive Therapy* **12**, 138–146.

Rasmussen, K. G., Zorumski, C. F. & Jarvis, M. R. (1994). Possible impact of stimulus duration on seizure threshold in ECT. *Convulsive Therapy* **10**, 177–180.

Sackeim, H. A., Decina, P., Prohovnik, I. & Malitz, S. (1987). Seizure threshold in electroconvulsive therapy. Effects of sex, age, electrode placement, and number of treatments. *Archives of General Psychiatry* **44**, 355–360.

Sackeim, H. A., Devanand, D. P. & Prudic, J. (1991). Stimulus intensity, seizure threshold, and seizure duration: impact of the efficacy and safety of electroconvulsive therapy. *Psychiatric Clinics of North America* **14**, 803–843.

Sackeim, H. A., Prudic, J., Devanand, D. P., Kiersky, J. E., Fitzsimons, L., Moody, B. J., McElhiney, M. C., Coleman, E. A. & Settembrino, J. M. (1993). Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *New England Journal of Medicine* **328**, 839–846.

Sackeim, H. A., Long, J., Luber, B., Moeller, J. R., Prohovnik, I. & Nobler, M. S. (1994). Physical properties and quantification of the ECT stimulus: I. Basic principles. *Convulsive Therapy* **10**, 93–123.

Sackeim, H. A., Luber, B., Katzman, G. P., Moeller, J. R., Prudic, J. & Devanand, D. P. (1996). The effects of electroconvulsive therapy on quantitative electroencephalograms; relationship to clinical outcome. *Archives of General Psychiatry* **53**, 814–824.

Sobin, C., Sackeim, H. A., Prudic, J., Devanand, D. P., Moody, B. J. & McElhiney, M. C. (1995). Predictors of retrograde amnesia following ECT. *American Journal of Psychiatry* **152**, 995–1001.

Squire, L. & Zouzounis, J. A. (1986). ECT and memory: brief pulse versus sine wave. *American Journal of Psychiatry* **143**, 596–601.

Swartz, C. M. & Abrams, R. (1994). *ECT Instruction Manual*, *5th edn*. Somatics Inc: Lake Bluff, Illinois.

Weiner, R. D., Rogers, H. J., Davidson, J. R. & Squire, L. R. (1986). Effects of stimulus parameters on cognitive side effects. *Annals of the New York Academy of Sciences* **462**, 315–325.