Objective: To critically review data relating the seizure duration in electroconvulsive therapy (ECT) to its therapeutic effect in the treatment of depressive illness.

Method: The authors used MEDLINE, PSYCHINFO on CDROM, and their own knowledge of the literature to find studies or reviews concerning the role of seizure duration in ECT efficacy.

Results: Rigorous studies cast doubt on the usefulness of seizure duration as a clinical marker. Some medications that decrease seizure time have deleterious treatment effects but also affect other seizure dynamics. Several medications dramatically shorten seizures but have no influence on treatment efficacy.

Conclusion: The guidelines of ECT seizure length are arbitrary, suggesting exaggerated durations for ECT treatment.

(Can J Psychiatry 1996;41:299–304)

Key Words: electroconvulsive therapy, seizure duration, efficacy, medication, anesthesia, lidocaine, caffeine, benzodiazepines

Perhaps no frequently used somatic therapy in psychiatry sparks as much debate and controversy as electroconvulsive therapy (ECT) (1). The psychiatric research community has made formidable strides in proving ECT to be an indispensable treatment without permanent neurological effects (2). There is, however, considerable debate on how to administer ECT most effectively and what constitutes its mode of action (3–9).

An early clinical controversy regarding ECT concerned which features of the treatment made for an adequate seizure, one that would aid a patient quickly and with the fewest applications (10–16). Cerletti (14) himself did not believe that the duration of motor manifestations was an efficacy marker. In fact, Androp (15) and Lowenbach (16) were the first to detect suppressed postictal electroencephalography (EEG) voltages consistent with therapeutic benefit.

The monitoring of seizure duration remains an important part of ECT practice. Modern ECT stimulators incorporate EEG devices that measure and record seizure length. Current clinical studies, however, challenge the status of seizure duration as a therapeutic parameter and question guidelines for when seizures should be medically terminated (3–9,17). Using the evidence available, we evaluate the appropriateness of current guidelines and comment on future directions in ECT research.

Method

Review of the Literature

Our review covered the literature concerning the role of seizure duration in ECT efficacy over the last 50 years. There are several pieces of evidence suggesting that seizure duration is related to ECT efficacy. First, seizure duration is an easily determined parameter, and clinicians are inclined to believe that a readily measurable feature of the treatment can help explain its therapeutic effect (17). Second, motor seizures of less than 15 seconds in duration do not exhibit tonic–clonic phases and are ineffective in treatment (17,18). This finding has been misinterpreted to imply that more is better and that a longer seizure is more therapeutic. Medications given during ECT that decrease seizure duration also slow or complicate a patient’s improvement; more sessions or larger electrical stimuli are needed in such cases (19–22). Third, a number of retrospective and prospective studies of the last 2 decades have found a correlation between total seizure duration during a course of treatment and patient response (23,24).
A number of technique, electroencephalograph, endocrine, and medication factors correlate with the therapeutic adequacy of ECT (18–23, 25–49). These have been systematically studied and compared to seizure duration as predictors of efficacy. We will review the scientific data on each category of findings (Table I).

**Clinical Studies: Seizure Duration and Improvement in Hospitalized Patients**

The few clinical studies that document a correlation between ECT efficacy and seizure duration have suffered from design difficulties (23,24). Maletzky’s retrospective study of ward patients (23), for example, found that positive clinical outcome from depressive symptoms correlated with accumulated seizure time in the course of therapy. Stimulus intensity, diagnosis, and concurrent medication parameters, however, were not adequately considered (17,52,53), and the study was neither randomized nor well controlled.

The only relevant study we found supporting a correlation was by Zorumski and others (24). His group found that 88% of patients with a cumulative seizure time of 300 seconds or greater had a favourable response. Their data were collected retrospectively and prospectively in the setting of a university hospital. The feature common to all patients was ECT treatment for depressive symptoms, regardless of primary diagnosis. The authors noted significant difficulties in the study, including the variable number of ECT sessions received, a confounding effect of medication, and the unilateral versus bilateral treatment of different patients.

In a prospective study, Miller and colleagues (34) followed a sample of depressed patients receiving ECT and found that seizure durations did not correlate with Hamilton Depression Rating Scale (HDRS) scores after treatment. The group did, however, find that significant nonverbal memory deficits correlated with seizure duration.

To demonstrate that seizure duration is a variable correlated with efficacy, one would have to show that patients with longer seizures require fewer ECTs. Weiner and Coffey (41) and Sackeim and others (40,50,51) have found no such correlation in studies using HDRS scores for a sizeable number of patients. While short seizures may signal that a medical condition or drug is interfering with the ECT process, it should be noted that shortening seizure times is a normal consequence of a progressing course of treatment, a result of ECT’s anticonvulsant effect (52).

In summary, well-designed clinical studies with depressed patients do not generally show a correlation between total seizure time and ECT efficacy.

**ECT Practice Factors and Seizure Duration**

**Bilateral Stimulation.** Sackeim’s insightful review of the literature (17) has outlined the technical parameters that make ECT successful. He found that it is the degree to which the electrical stimulus exceeds seizure threshold and not the absolute dose that determines clinical outcome, especially in unilateral models. His rigorous studies (38–40,50,51) showed that right unilateral (RUL) treatment at low or high dose can produce seizures of equivalent duration to bilateral (BL) treatment. With low levels of electrical stimulation, RUL patients showed only a 17% improvement in HDRS score versus 70% in the BL group, despite the same mean seizure duration in each group (39). RUL treatment outcome can be ameliorated by increasing stimulus intensity (38,40,41).

**Multiple ECT.** In an attempt to achieve longer cumulative seizure durations for a given course of therapy, investigators have given multiple ECT stimuli (MECT) in the same session. Total seizure time for MECT patients correlates with clinical improvement in depression (26,27). Nevertheless, treatment studies have not disentangled the benefits of increased seizure time from the increased number of stimuli administered to achieve it (17,46,53,54). Further, second or third seizures evoked in the same session do not generalize well and are associated with medical and cognitive side effects (54).

In summary, well-designed clinical studies with depressed patients do not generally show a correlation between total seizure time and ECT efficacy.

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While the degree to which electrical stimulus exceeds the seizure threshold has proved to be an important parameter in predicting clinical response, the length of the seizure has not generally done so (40,52,53). The practice of maintaining an adequate seizure duration is a complicated treatment issue. For example, an adequate ECT stimulus in the elderly is high as compared with other age groups and predisposes to
cognitive side effects (5,35,36,55). Despite clinical improvement, seizure duration shortens over time, and the tendency is for clinicians to increase the stimulus to maintain duration, which increases the likelihood of complications (9,17,40,55,56).

In summary, while increasing the electrical stimulus or inducing multiple seizures within the same treatment session may increase duration and help efficacy, there is little evidence that the former is responsible for the latter.

**EEG Findings**

**Voltage Suppression Studies.** Postictal voltage suppression refers to the decrease in resting EEG voltage after seizure activity as compared with baseline. Well-generalized seizures invoke voltage-suppressing neural mechanisms intended to terminate and prevent further seizure activity. This suppression is seen as a lower baseline on the EEG postictus (5,9,57). Studies have found that the degree of suppression correlates with seizure generalization (57), therapeutic adequacy (10), and bilateral stimulation (44,46,58). Nobler and Sackeim (59) studied the effects of bilaterality and stimulus intensity on EEG changes and seizure duration. While bioelectric suppression correlated with ECT efficacy, seizure duration had no bearing on type of administration or patient recovery.

**EEG Waveform Features.** Greater ictal EEG amplitude, intensity, and symmetry obtained with bilateral ECT are not more common with longer seizures, but they are related to antidepressant outcome (10,59). Krystal and colleagues (43,58) have found that the immediate poststimulus and midictal EEG amplitudes correlated well with seizure therapeutic adequacy in depression. The symmetry of the waveforms about the midpoint on the EEG tracing was also predictive. Nobler’s experiments confirmed these findings and found seizure duration had no impact as an EEG measure of treatment adequacy (59).

**Seizure Charge.** Total seizure charge (the calculated product of EEG voltage, seizure uniformity throughout the brain, and seizure duration) is hypothesized to be a measure of treatment intensity and efficacy (42,43,53). The 3 variables it includes may not be physiologically independent of one another, so that a longer seizure duration would not guarantee a greater result. Systematic controlled studies on this index are not evident in the literature.

In summary, EEG findings can be used to identify therapeutically active ECT seizures with a degree of accuracy and reliability. Seizure duration as measured by EEG has not been found to be one of these predictive indices in the studies reviewed.

**Endocrine Measures**

Several authors have demonstrated a series of hypothalamic-pituitary axis abnormalities in the acutely depressed patient (47,48,60–62).

**Oxytocin.** Scott and others found that measures of oxytocin release from the posterior pituitary correlated with HDRS-measured improvement in depression (49). Serum concentrations of oxytocin-associated neurophysin (OAN) were calculated before and after the first treatment in a course of ECT. The increase in OAN correlated strongly with improvement on the HDRS. This neurophysin response to ECT did not correlate with EEG-measured seizure duration. These results countered the hypothesis that patients exhibiting the highest increases in oxytocin might have done so as a result of longer duration.

**Prolactin.** Several authors have found that the surge of prolactin released by ECT may be an indicator of clinical improvement. Abrams and Swartz (45) found that seizure duration (53) was possibly related to the rise in prolactin. Contradictory findings from the same researchers, however, have yet to show a relationship between the magnitude of prolactin release and ECT benefits (9,47).

In conclusion, while there is considerable controversy over endocrine measures of ECT efficacy—the most rigorous study to date (49) has shown that hormone measures predict therapeutic response—this efficacy seems to be independent of seizure duration.

**Medication Factors**

Many medications have been tried as anesthetics and adjuvants in ECT. Though they may shorten seizure duration, some of these medications have an adverse effect on therapeutic adequacy (18–22,63–65).

**Lidocaine.** Lidocaine pretreatment (18,65) results in short seizure duration and poor efficacy of ECT in a dose-dependent fashion; it also causes less postictal voltage suppression. Lidocaine inhibits seizure dynamics by diminishing EEG spike activity, causing escapes of spike-wave complexes, and decreasing voltage amplitude (52). A distinct relationship between seizure duration and therapeutic efficacy was found in a lidocaine-pretreated group, but not in experimental controls (64). The patients least helped by ECT had the shortest seizure durations, but also received the most lidocaine (53).

**Anesthesia.** Another complication of granting seizure duration an important place in the prediction of adequate ECT is outlined by Fear and others (66), who studied the potential utility of propofol anesthesia in ECT. The American Psychiatric Association (APA) guidelines (4,67) do not consider propofol suitable for use in the induction process because it shortens seizure duration. In a well-designed prospective clinical trial, Fear treated patients with ECT using...
propofol as an induction agent. Though a significant decrease in mean seizure duration was found compared with his control group using methohexital induction (17.5 versus 25.5 seconds, respectively), both groups had the same endpoints on the Hamilton and Beck depression scales. Malsch’s data (68) have shown that propofol- or methohexital-treated ECT patients ameliorate from depression at the same rate. Strengths of this latter study include researcher blinding and the avoidance of concurrent medications that might interfere with treatment. Propofol is well tolerated by patients, provides greater autonomic stability than methohexital, and is easy to use. An unjustified assumption about seizure duration may impede the use of this medication in ECT.

Benzodiazepines. Recent data implicate benzodiazepines as inhibitors of effective ECT based on their ability to decrease seizure duration (19–21). Benzodiazepines (BDZ) may inhibit ECT efficacy by 2 mechanisms: the raising of seizure threshold and the inhibition of seizure propagation (22). Greenberg, Pettinati, and their colleagues (20,22) reviewed all clinical studies relating BDZ effects to ECT efficacy and found that none satisfied basic research criteria to correlate decreased seizure duration and therapeutic effectiveness. This occurred because, a priori, research efforts were designed to prove benzodiazepines decreased ECT effectiveness. When this effect was proved, decreased seizure duration was invoked as a cause, regardless of whether it was statistically analyzed or not (22).

Pettinati and others (69) retrospectively found that bedtime benzodiazepine use hinders ECT response. Treatment was unilateral, however, and seizure duration was not analyzed. When the treatment-resistant patients were switched to bilateral ECT, they rapidly responded, implying that overcoming an increased seizure threshold rather than obtaining a sufficient length of treatment was more important therapeutically.

Strömgren’s group (70) found that patients taking BDZ underwent a longer series of ECT treatments to achieve adequate therapeutic response. Seizure duration times were statistically less in the experimental group. Sedative drug doses, however, were not quantified. The study was retrospective, the patient diagnostic groups were poorly defined, and it is likely that sicker (more ECT-resistant) patients were taking the BDZ, although this could not be confirmed (22).

Caffeine. Caffeine predictably increases seizure duration with no measurable effect on threshold (69,71). It is recommended as an adjunctive medication by the APA task force on ECT (67). A recent prospective controlled study, however, did not find therapeutic benefit to the combination (72). Further, Rosenquist and colleagues found no benefit of caffeine pretreatment on measures of seizure efficacy such as EEG voltage suppression or seizure regularity (73).

In summary, a large body of evidence from 4 classes of medication demonstrates that the manipulation of seizure duration alone does not alter the efficacy of treatment. Those medications that decrease the therapeutic benefits of ECT appear to do so by inhibiting the adequate initiation and propagation of the seizure.

Discussion

We have reviewed studies for the literature examining the relationship between seizure duration and ECT clinical outcome. Most investigations focus on the treatment of unipolar depression in hospitalized patients and parameters related to treatment success. Studies that document a relationship between duration and outcome are few and are fraught with major design flaws such as selection bias, uncontrolled medication use, and an inability to distinguish between seizure time and number of treatments (4,17,46,52,53).

No prospective controlled study reviewed found a relationship between longer duration and faster or more favourable outcome in depression. Seizures of less than 15 seconds are associated with postictal autonomic complications and poor clinical results (17,18), but there is little evidence that a length of convolution greater than 20 seconds is necessary. In a few studies, ECT with propofol anesthesia achieved average durations of well below 20 seconds and had outcome equivalent to controls (66,68). While a shorter seizure can signal decreased efficacy when drugs such as lidocaine or benzodiazepines are used, the duration itself does not appear to be the responsible physiological factor (52).

Given these findings, the guidelines concerning ECT seizure length appear to exaggerate the required seizure duration. The APA task force (67) advocates seizure lengths greater than 20 seconds and encourages the termination of seizures of 3 minutes or more. Given the medical and cognitive complications of not terminating seizures earlier (34,74,75) and the questionable benefit of allowing them to continue for that long, the clinical rules about ECT treatment duration could be rethought. Revising guidelines to decrease optimal and maximal seizure times would decrease cognitive and medical complications (34). Similarly, the practice of avoiding or withholding potentially helpful medications because they shorten seizure duration should be reconsidered.

Further clinical research in this field requires the selection of more homogeneous study populations and the use of statistical techniques to measure and filter confounding variables. Results obtained should be correlated with reliable efficacy markers: the stimulus intensity, EEG morphology, and post-ictal voltage suppression, for example. A number of new sedative and inductive anesthetic agents can be used to manipulate seizure threshold or duration in order to verify what constitutes safe, effective ECT practice. Lastly, research is needed on the basic neurophysiology of seizure initiation and propagation.
Clinical Implications

- No rigorous clinical studies support the contention that longer ECT seizures are more efficacious.
- Longer seizures exacerbate the cognitive and medical comorbidity of the treatment.
- Medications that shorten ECT seizures do not invariably alter efficacy.

Limitations

- The number of well-conducted clinical studies in this field is small.
- The optimal minimum seizure duration for adequate treatment response has yet to be elucidated.
- Some ECT practice guidelines appear arbitrary or exaggerated.

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References

Résumé

Objectif : Analyse critique des données qui font le lien entre la durée des convulsions dans le traitement aux électrochocs et leur effet thérapeutique contre la dépression.

Méthode : Les auteurs ont utilisé MEDLINE, PSYCHINFO sur CD-ROM et leurs propres connaissances de la littérature afin de repérer des études ou des comptes rendus sur le rôle de la durée des convulsions dans l’efficacité des électrochocs.


Conclusion : Les directives sur la durée des convulsions provoquées par électrochocs sont arbitraires, ce qui laisse présager une durée excessive du traitement aux électrochocs.