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Letters to the editors

No long-lasting effects of electroconvulsive therapy on resistance to seizure induction

Comment by Conrad Melton Swartz

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Dear Sirs,

The observation that patients who receive a repeat course of ECT show more resistance to seizure induction is more simply attributable to several processes that do not require the postulation of a new and "long-lasting effect" of ECT as made by Tomasson et al. (1992).

Firstly, because resistance to seizure induction rises less for patients who fail to benefit from ECT, as mentioned in the paper's introduction, patients with a history of benefit from ECT should show more failed and short seizures than other patients. The smaller rise in resistance to seizure induction among ECT nonresponders is consistent with less benefit, by demonstrating less physiologic impact from ECT in nonresponders, expressed as less anticonvulsant effect. Thus, the observation that patients who receive a repeat course of ECT demonstrate more failed and short seizures can be explained by the usual temporary anticonvulsant effects of ECT.

This simple explanation suggests that the patients who received a repeat course of ECT would have also shown more failed and short seizures during their previous ECT courses than the study group receiving ECT for the first time. Unfortunately, the authors were unable to test this hypothesis because they did not have the essential relevant data. Rather, they made the unstated assumption that during their prior ECT courses these patients resembled the new ECT patients more closely than they resembled their present selves. It is hard to accept this assumption without proof.

Secondly, the customary trial-and-error method of dose regulation defies ordinary clinical impression (Hollister et al. 1980). The knowledge that a patient had responded to ECT in the past might bias the ECT clinician to attempt to minimize the ECT stimulus. In turn, this would lead to more failed and short seizures for patients receiving a repeat ECT course. Therefore, the absence of a set protocol for stimulus selection is a substantial weakness in this study; the authors merely noted "the usual starting frequency was 40 Hz."

Thirdly, depressed patients referred for ECT have an excessively high prevalence of structural brain abnormalities. These include small frontal lobe, subcortical leukoencephalopathy observed as MRI hyperintensity especially in periventricular white matter (Coffey 1993), cortical atrophy, ventricular enlargement, and basal ganglia lesions (Guze & Szuba 1992; Coffey et al. 1991). Prospective measurements made three days after an ECT course demonstrated no changes in brain anatomy from treatment, while measurements made 6 months later suggested progression of leukoencephalopathy in some patients, attributable to progressive cerebrovascular disease (Coffey et al. 1991). Progressive degenerative brain disease might explain both the predisposition to repeated severe depression, with a corresponding need for a repeat course of ECT, and the tendency to greater resistance to seizure induction.

Besides these problems, any study of physiologic resistance to seizure induction that allows research subjects to be influenced by anticonvulsant medications (i.e., diazepam, carbamazepine) is biased. The validity of the authors' assumption that the inconsistent and severe effects of anticonvulsant medications on ECT seizure induction can be accounted for by the use of linear statistical models has never been tested or otherwise established, and appears unrealistic. The authors' application of the linear methods of retrospective epidemiological statistics to explain complex interactions between pharmacology and physiology was rationalized only by analogy rather than justified by preceding studies, i.e., you either believe it or you don't.

The complexity and pathophysiologic obscurity of the authors' assertion of additional and permanent effects of ECT on top of the effects noted above, which are sufficient to explain the findings, make such effects unlikely.

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C. M. Swartz
Department of Psychiatric Medicine
East Carolina University School of Medicine
University of North Carolina
Greenville, NC 27858-4354, USA

Reply to Conrad Melton Swartz's comment

If our findings were explained by the hypothesis that resistance to seizure induction rises less for patients who fail to benefit from ECT, we would expect to see a difference in the number of successful treatments given to patients with a prior history of ECT compared to those receiving the treatments for the first time. This was not the case. The mean number of induced seizures to obtain the preferred clinical results was 10.1 (SD 3.6) amongst those receiving ECT for the first time, but 10.4 (SD 4.6) for those with a prior history of ECT (Tómasson et al. 1992).

Furthermore, due to our relatively large sample size, and statistical control of the variables listed in our paper we assumed that patients with prior ECT responded earlier than patients receiving ECT for the first time.

The treatment protocol in use was standard, allowing only changes in frequency of the current used. Nearly 90% of the patients had a starting frequency of 40 Hz, 1% had a starting frequency of 50 or 60 Hz, and 9% a starting frequency of 30 Hz. The records reflected that those with a lower starting frequency had either a past history of ECT with very hard prolonged seizure or were very frail individuals. Those with a higher starting frequency had a prior history of difficulty with seizure induction.

The third point made by Dr. Swartz is an interesting one. However, we can not view it as likely as our statistical model controlled for number of prior hospitalization, and age at onset of the psychiatric illness; a proxy measure of repeated severe depression.

No preceding studies were available that had solved the statistical problem involved in the study design. We acknowledge that the use of linear methods to explain the complex interaction and gradual change that occurs during ECT is open to question. However, by using such method we were able to elicit other established predictors for difficulties of seizure induction i.e. number of current ECT treatments, age, and electrode placement, a tangential validation of the method used. The impact of prior ECT treatment was still robust.

The last paragraph in Dr. Swartz's letter is unsubstantiated.

In a recent paper about whether ECT permanently altered seizure thresholds (Krueger et al. 1993) the authors, having recognized that the question of long-lasting changes is an important one, tested this possibility, but used a different kind of methodology. They found that there was no evidence that a history of ECT was associated with alterations of seizure thresholds or seizure duration. Their methodology used an estimation of seizure threshold in the first treatment using "the ascending methods of limits procedure we devised". This titration procedure, they say, "involves administering repeated subconvulsive stimulation at progressively higher intensity until an adequate generalized seizure is elicited". This methodology does not directly test the hypothesis because by giving a series of stimulations the investigators may have actually altered the seizure threshold itself. It is a little bit like the Heisenburg uncertainty principle which suggested that you could not both obtain the weight of a submicroscopic particle and the speed, because they influenced each other. Specifically, the methodology itself may have changed the threshold which made it impossible to obtain differences. Do we know whether subconvulsive stimuli may change the threshold? Certainly, when individuals are given ECT for the first time, the seizure threshold goes up and it is possible that this becomes apparent with missed convulsions about the same time in any patient regardless of the original seizure threshold. A reasonable study would be a study of seizure threshold in animals that had a prior set of convulsions. This should not be difficult and would be a very useful test of the possibility of long-lasting changes. Interestingly, simple conditioning shows a long-lasting effect (Gantt 1944). The effect of a prior history of conditioning was noted in an animal after two years of rest when returned to the laboratory situation. If this can occur with a simple conditioning paradigm where no direct stimulation on the central nervous system occurred, why is it not possible that several convulsions might also have an effect. One should note this does not impair the value of ECT as a treatment for depression. If there is a long-lasting or permanent change in seizure threshold, there is no reason to believe that it is relevant to any meaningful cognitive or behavioural aspects of the person.

Finally, as our work raises an important question we elected to present the results despite methodological difficulties involved in a complex model. It is our hope that another research group will attempt to replicate our study.

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Kristinn Tómasson M.D.[1]
George Winokur M.D.[2]
Bruce Pfohl M.D.[2]

[1] National University Hospital
Department of Psychiatry
101 Reykjavík, Iceland
[2] University of Iowa College of Medicine
Department of Psychiatry
Iowa City, IA 52242, USA