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Comments on Brain Damage and Memory Loss from Electroconvulsive Shock.

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As a neuroscientist I have studied the structure and function of the mammalian brain for more than 30 years. I also teach this subject to medical students and graduate students in Neuroscience at the University of Pennsylvania.

My concern regarding effects of electroconvulsive shock (ECS) on the brain began more than 25 years ago when I read in the **New Yorker** magazine about Marilyn Rice, a bright, professional woman whose past memories were destroyed by a series of ECS treatments. This led me to study the literature on ECS, both the clinical literature regarding possible efficacy and negative side-effects and also the experimental literature -- the application of ECS to animals in order to study the basis for the possible efficacy and side effects. I have continued to follow this literature over several decades. Here I wish to summarize my main conclusions as they are relevant to the issue of "informed consent".

ECS unquestionably damages the brain. The damage is due to a variety of known mechanisms:

- (1) The electric shock delivered by a standard ECS machine to the skull is roughly comparable to what you would get from a common electrical outlet, but the voltage is stepped up from 110 V to 150 V. The total power drawn is about 60 Watts -- enough for a conventional light bulb. It is commonly stated that modern ECS is kinder and gentler than the original version, but here is its application in a recent study: "*Electroconvulsive therapy was given 3 times per week with a **customized** MECTA SR1 device ...which had **double the maximal charge output** of commercial devices in the United States.*" (Sackeim et al, 2001). It is obvious, prima facie that repeated application of such electrical shocks to the brain would cause damage.

There has been an effort to restrict application of the ECS to the right hemisphere, most recently to the right frontal lobes. This treatment seems to produce less retrograde memory loss, and so is thought to be "safer". But most likely this is because language capacity is expressed in the left hemisphere, so damage to the right hemisphere, while almost certainly present, is simply harder to evaluate. Neuroscience learned this lesson during the lobotomy period of the 1940s: the right frontal lobe is essential to human cognitive and emotional functioning.

- (2) ECS is designed to evoke a *grand mal* epileptic seizure. This involves massive excitation of cortical neurons that also deliver excitation to lower brain structures. The seizure causes an acute rise in blood pressure, well into the hypertensive range, and this frequently causes small hemorrhages in the brain. Wherever a hemorrhage occurs in the brain, nerve cells die -- and are not replaced.

- (3) ECS ruptures the “blood-brain barrier”. This barrier normally protects the brain from potentially damaging substances in the blood. Because the brain is our most chemically sensitive organ, breach of this barrier exposes nerve cells to chemical insults which can also kill them. Rupture of the blood-brain barrier also leads to brain “edema” (swelling). Since the brain is enclosed by the rigid skull, swelling leads to local arrest of blood supply, anoxia, and neuron death.
- (4) ECS causes neurons to release large quantities of the excitatory neurotransmitter, glutamate. This chemical excites further neuronal activity which releases still more glutamate, leading to “excito-toxicity” -- neurons literally die from overactivity. Such excito-toxicity has been recognized relatively recently and is now a major topic of research because it accompanies epileptic seizures and cerebral hemorrhages. Glutamate excito-toxicity is probably a major contributor to the brain damage that accumulates over repeated episodes of ECS.
- (5) ECS releases myriad other neurotransmitters and hormones within the brain. These substances are normally released in small amounts under strict spatial and temporal regulation. Therefore, their massive release would be expected to cause damage. For example, ECS sharply elevates corticosteroids in the brain. These “stress” hormones affect memory, possibly by “remodeling” neuronal connections in the hippocampus (McEwen, 2000). Thus, toxicity from brain steroids may well be another contributor to the damage that accumulates over repeated episodes of ECS.

The degree of damage consequent to ECS varies between individuals. It can be catastrophic in response to a single series, as for Marilyn Rice and Ann Donohue (see below), or it can appear more gradually following repeated series. This resembles the damage to boxers -- who may occasionally die in the ring due to massive cerebral hemorrhage -- but who more commonly accumulate damage until the impairment becomes obvious. Because the possible therapeutic effect of ECS is temporary, the treatment is usually repeated, leading inevitably to chronic brain damage.

The key manifestation of damage is “retrograde” memory loss.

“Retrograde” refers to loss of memories already formed. This can extend quite far back in time -- years and decades -- so that an individual no longer remembers family members, friends, professional skills and knowledge, etc. Needless to say this is disorienting, terrifying, and ...depressing. For most of the 28 years that I have followed this issue, practitioners of ECS have largely denied that this is an issue, terming these losses “complaints”, and attributing them to an underlying mental illness. Thus a recent review of the book, *Electroshock: Restoring the Mind*, states that ECT “has proved to be one of the safest procedures in medicine.” (Nature 401,327, 1999).

Fortunately, the tide has turned, and at least one leading proponent of ECS, Dr. Harold Sackeim now acknowledges that the memory and cognitive losses are real. This seems so important, that I here excerpt from Dr. Sackeim’s recent editorial in the *Journal of ECT* (Sackeim, 2000):

“... virtually all patients experience some degree of persistent and, likely, permanent retrograde amnesia. A series of recent studies demonstrates that retrograde amnesia is persistent, and that this long-term memory loss is substantially greater with bilateral than right unilateral ECT (Weiner et al., 1986; McElhiney et al., 1995; Lisanby et al., 2000; Sackeim et al. 2000) ”

“... adverse effects on cognition are by far ECT’s most common side effects.”

“... some patients experience profound memory loss due to ECT. Most ECT practitioners have encountered fully credible patients who are distressed by the magnitude of their persistent post-ECT amnesia. Skeptics will argue that ...we have no objective “dipstick” to verify that memory is truly impaired. On the other hand, there is no dearth of patients who have received ECT who believe that the treatment was valuable, often life saving, who are not litigious, who return to productive activities, and yet report that a large segment of their life is lost. These patients often report a classic temporal gradient in their retrograde amnesia, with the memory loss most accentuated for the time period (months and years) closest in time to the treatment, with sparing of more remote memories. It is hard to imagine that such reports of a classic retrograde amnesic syndrome, with sparing of other cognitive functions, are simply fabricated.”

“Electroconvulsive shock (ECS) is the most common procedure used to induce amnesia in animals to screen pharmacological compounds for protective effects on memory.”

“Prospective patients, family members, and the public often want to know the frequency with which patients report substantial memory impairment following ECT. While we believe that such reports are infrequent, there is little objective evidence to support this judgment or to even broadly estimate base rates... This should be a readily resolvable issue, and calls for a large sample study in community settings.”

The same issue of this journal prints a poignant account by Ann Donohue of her major retrograde memory loss, similar to Marilyn Rices’ description more than a quarter century ago. Both Dr. Sackeim and Ann Donohue, though eminently aware of the danger of ECS, nevertheless believe it to be valuable.

How efficacious is ECS?

On this point, Dr. Sackeim provides an important new study that fully documents two key points. Sackeim et al (2001) initially treated 290 patients with a round of ECS. Of these, 114 patients did not respond at all; 17 patients, who responded initially, showed no remission after 4-8 days, and were dropped from the study. Thus, 45 % of the group received the deleterious effects of a round of ECT but no benefit. Eighty-five patients received the full course of ECS and remained in the study for follow-up over 26 weeks (6 months). The study concludes:

*“...without active treatment, **virtually all remitted patients relapse within 6 months of stopping ECT. Monotherapy with nortriptyline has limited efficacy. The combination of nortriptyline and lithium is more effective, but the relapse rate is still high...**”.*

(emphasis added)

This supports my point that the benefit of ECS (to half the patients in the study) is only temporary -- even with strong drug treatment-- so it tends to be repeated, and the accumulating ECS does more brain damage.

What should be done?

The physician's first injunction is "Do no harm.". This treatment clearly does harm, and this should certainly be explained to patients before their treatment in a way that fairly and honestly conveys the risks, the modest level of efficacy, and the virtual certainty of relapse.

The reason that psychiatrists have for so long remained unaware of accumulating memory loss is that they do not routinely test for it. Testing is required when patients take certain drugs, such as lithium. High blood levels of lithium can be toxic; and lithium can damage the blood-forming cells in the bone marrow. Therefore, blood levels of the drug and the state of the bone marrow are monitored. Memory loss could be monitored just as easily -- by asking patients before ECS about early events in their lives and then questioning the patients following each series of ECS. When this was done by Dr. Edward Janis (almost 50 years ago), losses were marked and prolonged. Janis' simple test should be performed on every patient before and after ECT so that retrograde memory loss could be tracked and documented for each individual. No effort has been made since then to do this simple test.

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