Commentary

Commentary: “Electroconvulsive Stimulation (ECS) Increases the Expression of Neuropeptide Y (NPY) in Rat Brains in a Model of Neuropathic Pain: A Quantitative Real-Time Polymerase Chain Reaction (RT-PCR) Study,” by Okabe and Colleagues

The report by Okabe and colleagues in the current issue of *Pain Medicine* investigates whether electroconvulsive therapy (ECT) is useful for the treatment of neuropathic pain, using a lumbar nerve ligation model in the rat. Their methodology mimicked the clinical use of ECT in depressed patients in that treatments were administered every other day for several days. Mechanical and thermal hyperalgesia were measured daily over several days after the nerve ligation surgery and prior to ECT treatments to establish a baseline. Latency to paw withdrawal for mechanical and thermal stimuli was measured in the nerve-ligated (ipsilateral) limb and contralateral limb just prior to ECT treatments. The authors found that ECT produced antinociception to thermal stimuli in the ipsilateral limb after three or four treatments without change in the nociceptive threshold in the contralateral (unaffected) limb. Compared to the control group of animals who had nerve ligation but did not receive ECT, the ECT group had significantly greater hyperalgesia for thermal stimuli, although this began even prior to the ECT treatments. For the mechanical nociceptive stimuli, while differences emerged between the limbs and between groups, these differences appeared even prior to the ECT treatment. The authors also found that neuropeptide Y was expressed to a greater degree in the ECT group, compared to the control group who had nerve ligation, but did not receive ECT.

Multiple human case reports and small sample series suggest that ECT may have positive analgesic benefits in a variety of chronic painful conditions, including chronic low back pain and complex regional pain syndrome, although few of the studies control for a co-morbid major depression disorder in the use of ECT in a patient with chronic pain. Hence, it is still quite unclear whether ECT has intrinsic analgesic properties independent of its effects on improving major depression, which occurs at a high rate in a chronic pain population, particularly in those patients referred to specialty pain clinics, from which these studies recruited. Improvements in major depression would certainly improve the affective component of pain, for example, the unpleasantness or bothersomeness of the pain perceived by the patient, and thus, may be the mechanism by which pain ratings are modulated after ECT treatment. Neuroimaging studies have shown that blood flow to brain areas involved in the processing of pain is improved after ECT treatment for depression in humans. Evidence suggests that ECT induces changes in neurotransmitter gene expression and levels of neurotransmitters in the neuronal synaptic clefts throughout the brain. Correlation of these observations in humans to similar findings in animals has been lacking, particularly when it comes to understanding the mechanisms by which ECT may be effective for pain. One can call this a need for “reverse translational research.”

The experiment by Okabe and colleagues attempts to remedy this deficit and in this sense they present valuable scientific findings. Furthermore, they establish an animal model by which ECT can be studied for analgesic properties. But, one should not think that we now have more of a scientific basis from animal research to conclude that ECT has analgesic properties. This study, while designed well, presents preliminary, and pilot data at best. It suffers from a small sample size (N = 6 in the ECT group), and only one analgesic measure among several collected, and only one neuropeptide gene expression level among four collected were positive. Hence, even though the authors attempted to correct for multiple comparisons, their findings are still preliminary and require further confirmation in future studies. I wish them luck.

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