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Rapid anxiolytic effect of electroconvulsive treatment via serotonin 5-HT₄ receptor

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Anxiety disorders represent the most prevalent mental health problem. While pharmacological and cognitive-behavioral therapies are effective for these disorders, approximately one third of patients show treatment resistance. Electroconvulsive treatment (ECT) could be a candidate treatment option for the medication-resistant anxiety disorders. However its anxiolytic efficacy and mechanism of action are poorly understood. Here we characterized a potential anxiolytic effect of ECT and investigated its neuronal basis using mice. We found that a few times of ECT produced a robust anxiolytic-like behavioral effect. Further repetition of ECT additionally induced an antidepressant-like effect. Repeated ECT also strongly enhanced serotonin 5-HT₄ receptor-dependent synaptic modulation mediated by endogenous serotonin in the hippocampus. In mice lacking the 5-HT₄ receptor, the anxiolytic-like, but not antidepressant-like, effect of ECT was significantly attenuated. These results suggest a specific involvement of the enhanced 5-HT₄-dependent neuromodulation in the anxiolytic effect of ECT. Our finding suggests that ECT can be a plausible treatment option for anxiety disorders with onset of action faster than its antidepressant effect.