

Abstract

Electroconvulsive therapy (ECT) is one of the most effective treatments for severe psychiatric disorders. ECT delivers an electrical shock to the cortex to induce brief generalized seizures, ECT requires multiple sessions to be effective. After 80 years, the mechanism of how these seizures impart such robust therapeutic effects remains unknown. Two clinical observations on the properties of ECT via electroencephalogram (EEG) traces contributed to an early hypothesis. First serial ECT increased seizure threshold (more electrical charge was required in subsequent sessions to produce an adequate seizure). Second ECT produced an acute postictal suppression of brain activity which is positively associated with treatment response. These observations led to the “GABA Hypothesis” which stated that ECT’s mechanism of action involved a basal increase in inhibitory brain activity. This hypothesis has been tested with contradicting and inconclusive results. This proposal will specifically interrogate the role of inhibitory interneurons during electroconvulsive shock (ECS; the animal analogue to ECT) in different phases of ECS. The central hypothesis is that GABAergic interneurons (GABA-INs) mediate the effect of ECT via their recruitment during the ictal, postictal, and interictal phases. To test this hypothesis, the following aims propose to determine: (1) the influence of GABA-INs on seizure activity and postictal suppression during ECS and (2) the evolving effect of serial ECS on global GABA-IN activation. These aims are an important first step to collect pilot data to help determine the mechanism of action of ECT, which may lead to novel therapeutics utilizing this mechanism.