EFFECTS OF BOTULINUM NEUROTOXINS IN THE CENTRAL NERVOUS SYSTEM: ANTI-EPILEPTIC ACTIONS.

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Botulinum neurotoxins A and E (BoNT/A and BoNT/E) are bacterial enzymes that exert a long-lasting inhibition of transmitter release via the cleavage of the synaptic protein SNAP-25. We have studied the effects of BoNT/E after *in vivo* injection into the rodent hippocampus and visual cortex. We found that BoNT/E inhibits glutamate release and silences both spontaneous and evoked activity of pyramidal neurons. The effects of BoNT/E persist for at least two weeks (as determined by both electrophysiological and neurochemical analysis) with no subsequent deleterious effects on brain function. Thus, BoNT/E is a novel tool to achieve reversible blockade of neuronal activity in the brain. Based on these findings, we explored the potential anti-epileptic effects of *in vivo* administration of BoNT/E. We show that BoNT/E delivery to the rat hippocampus is anticonvulsant on seizures induced by kainic acid. The possible therapeutic implications of these findings will be discussed.