Neurotransmitter modulation in rat hippocampus via extracranial focal electrical stimulation

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EPILEPSY is a neurological disorder that affects approximately one percent of the world population with up to three-fourths of all persons with epilepsy in developing countries [1]. Besio et al. have been analyzing the effects of noninvasive transcutaneous focal electrical stimulation (TFS) for the control of seizures [2]. The TFS has been very successful in controlling acute seizures in penicillin [3], pilocarpine status epilepticus [2], and pentylenetetrazole [4] rat seizure models. To understand what stimulation parameters may be most effective at controlling seizures it would be beneficial to understand the mechanism(s) of action of the TFS. Towards this end we conducted the following experiments.

We followed a very similar procedure as Luna-Munguía [5] where they applied 130 Hz deep brain stimulation in the hippocampus of rats and used microdialysis to quantify several neurotransmitters in the direct vicinity of the stimulating electrode. Male Wistar rats (250 – 300 g body weight), individually housed and maintained under environmentally controlled conditions with experiments conducted according to the Mexican Official Norm

Rats (n = 2) were anesthetized with a mixture of ketamine and xylazine. Then, bipolar electrodes, consisting of two twisted strands of stainless steel wire, insulated except at the cross-section of their tips, were stereotactically implanted into the left ventral hippocampus. A microdialysis guide cannula was attached to the bipolar electrode. Stainless steel screws were threaded into the cranium over the frontal cortex to fix the electrode assembly.

A 6.0 mm diameter TCRE [6] was centered on the top of the skull with the front ring behind the bregma. The bipolar electrode was just outside the outer ring of the TCRE with the bare conductors inside the hippocampus. The electrodes assembly was fixed to the skull with dental acrylic. Animals were allowed to recover with water and food provided *ad libitum* for one week before any further manipulation.

After recovery a continuously perfused dialysis probe was inserted into the guide cannula and anchored with dental acrylic. The Focal Stimulation (FS), on the skull, was delivered at 300 Hz with 200 μS biphasic pulses starting at 100 μA and gradually increased by 20% at a time. The FS application was discontinued when motor behaviors occurred during short (15 s) stimulation trains with 2 min pauses. On the following day background neurotransmitter levels were measured then a 20% subthreshold current was applied for 20 or 30 minutes. Dialysate samples were continued for 1.5 hours after the FS to see if there were any lasting effects on the neurotransmitters.

Fig. 1. is an example of possible neurotransmitter modulation (Taurine) due to the FS. We noticed similar curves for Aspartate as well with the increased levels in the hippocampus present after the FS was discontinued. Further experiments must be conducted to see how consistent the results are and for analyzing FS parameters.

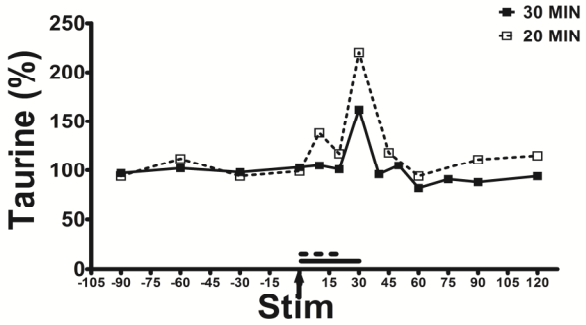

Figure 1: Increase in Taurine during and after the application of FS.

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