

## Abstract View

### HIGH-FREQUENCY STIMULATION ABOLISHES NETWORK OSCILLATIONS BY ASTROCYTIC GLUTAMATE RELEASE

[K.H.Lee<sup>1,4\\*</sup>](#); [F.L.Hitti<sup>1,4</sup>](#); [V.L.Tawfik<sup>2</sup>](#); [K.J.Kristic<sup>1,4</sup>](#); [B.T.Harris<sup>3</sup>](#); [J.C.Leiter<sup>4</sup>](#); [D.W.Roberts<sup>1</sup>](#)

1. Neurosurgery, 2. Pharmacology, 3. Pathology, 4. Physiology, Dartmouth-Hitchcock Med. Ctr., Lebanon, NH, USA

The mechanism of action of high frequency deep brain stimulation (DBS) is unknown. We test the hypothesis that high frequency stimulation (HFS) results in glutamate release from astrocytes that is able to abolish neural network oscillations. Glutamate was measured using a dual enzyme-based electrochemical sensor in the rat subthalamic nucleus (STN) and thalamus in vivo, ferret thalamus in vitro, and in rat primary astrocytic cultures. Electrical stimulation (1 s to 5 min duration; 100-2000  $\mu$ A; 5-1000 Hz) was given using a bipolar stimulating electrode. Intracellular and extracellular recordings were made in the nucleus Reticularis thalami (nRt) and in thalamocortical relay (TR) neurons in an in vitro slice preparation from the ferret lateral geniculate nucleus (LGN), which generates spontaneous network oscillations. Stimulation of the STN or thalamus in vivo in rats and in vitro in the ferret thalamus elevated glutamate levels, which reached a plateau after  $\sim$ 5 min and remained elevated for the duration of stimulation. Glutamate release was still evoked after treatment with the Na<sup>+</sup> channel blocker tetrodotoxin or high Mg<sup>++</sup>, low Ca<sup>++</sup> solution, suggesting that the source of glutamate is at least in part non-neuronal. HFS of primary cultures of astrocytes also resulted in glutamate release that was quantitatively similar to the glutamate release observed in vivo and in vitro. HFS of TR neurons generated excitatory post-synaptic potentials (EPSPs), increased the number of action potentials in both TR and nRt neurons during the stimulation period and abolished synchronized oscillations. These results suggest that HFS of the thalamus or STN leads to glutamate release from astrocytes that is insensitive to classic neuronal exocytosis inhibitors. Thus, astrocytic glutamate release may be an important mechanism by which DBS is able to block synchronous neural network oscillations such as those that generate tremor and seizures.

*Support Contributed By: NREF/Medtronic*

**Citation:** K.H. Lee, F.L. Hitti, V.L. Tawfik, K.J. Kristic, B.T. Harris, J.C. Leiter, D.W. Roberts.

HIGH-FREQUENCY STIMULATION ABOLISHES NETWORK OSCILLATIONS BY ASTROCYTIC GLUTAMATE RELEASE Program No. 898.2. 2005 Abstract Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience, 2005. Online.

**2005 Copyright by the Society for Neuroscience all rights reserved. Permission to republish any abstract or part of any abstract in any form must be obtained in writing from the SfN office prior to publication**



Site Design and Programming © ScholarOne, Inc., 2005. All Rights Reserved. Patent Pending.