Effects of Thalamic Deep Brain Stimulation on Motor Cortical Perfusion

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ELECTRICAL stimulation applied to deep brain structures, or deep brain stimulation (DBS), has revolutionized the management of movement disorders, such as Parkinson's disease and tremor. Despite widespread clinical use, its mechanisms of action are not well understood. While there is some knowledge of the local effects of stimulation [1], less is known about remote or network effects of DBS. DBS applied in VL-thalamus stops tremor, and this nucleus projects to and receives major input from the primary motor cortex (M1) [2]. Therefore thalamic DBS may influence neural activity, and thereby blood flow/ tissue perfusion in M1. In this study we sought to determine how thalamic DBS affects motor cortex perfusion in the anesthetized rat. Because intrinsic optical properties of brain tissue are correlated with cortical perfusion [3-5], we utilized intrinsic optical imaging using a 5mm x 5mm cranial window created over M1 (AP: +2mm, ML: -2mm from bregma). The camera was mounted over the craniotomy and focused on the cortical vasculature.

Initially, we determined whether electrical stimulation had any direct non-neural mediated effects on blood vessels. We blocked M1 neuronal activity by administering tetradotoxin (TTX) before applying epidural electrical stimulation to M1. TTX blocks voltage-gated sodium channels but does not directly affect vascular smooth muscle [6]. Epidural electrical stimulation, which significantly altered M1 perfusion at baseline, did not alter perfusion in the presence of TTX. Therefore, DBS does not appear to have direct effects on tissue perfusion in the absence of neural activity. Next, we delivered DBS to VL thalamus (AP: -2.3 mm, ML: 1.66 mm from bregma) while imaging over M1. After 10 sec of baseline imaging, bipolar, constant current stimulation of set frequency (10, 50, 100, 150, 200, 400, 750Hz), pulse width (0.1, 0.2 and 0.35 ms) and amplitude (0.5mA) was delivered for 10 sec. Imaging continued for 40 sec after the end of stimulation. DBS increased M1 cortical perfusion, which was dependent on the amplitude and frequency of stimulation applied. Higher frequencies and pulse widths evoked larger increases in tissue perfusion, with longer times required to return to baseline perfusion. Stimulation outside of VL thalamus did not change M1 perfusion. In conclusion, optical imaging allowed reliable measurement of the remote effects of DBS and will permit future experiments correlating different parameters of stimulation with the dynamics of cortical activity.

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