Toward an in Vivo Understanding of Addiction and Neuromodulation: Electrophysiologic Correlates of Neurochemicals During Opioid Administration in a Swine Model of Tractography-Guided Deep Brain Stimulation

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Abstract

Introduction: Dysregulation of mesolimbic dopamine pathways contributes to the pathophysiology of opioid addiction. Although intraoperative electrophysiology is routinely performed during deep brain stimulation (DBS), no existing clinical platform can record both electrophysiologic and neurochemical signals in parallel. Identifying electrophysiologic signatures of dopamine dynamics could clarify addiction mechanisms and support development of closed-loop DBS therapies.

Method: The Multifunctional Apparatus for Voltammetry, Electrophysiology, and Neuromodulation (MAVEN) was used in an anesthetized swine model of frame-based, tractography-guided ventral tegmental area (VTA) DBS. A carbon fiber microelectrode (CFM) was stereotactically implanted in the swine nucleus accumbens (NAc) to record both tonic dopamine concentrations and local field potentials (LFPs). Tonic dopamine concentrations were measured using multiple cyclic square wave voltammetry (MCSWV) with the following parameters: initial potential -0.2 V, staircase increment +25 mV, square wave amplitude ±0.4 V, pulse duration 1.0 ms, five cyclic square waves per scan, and scan rate 0.1 Hz. Baseline and post-fentanyl recordings were performed.

Results: Fentanyl administration resulted in increases in tonic dopamine concentrations in the NAc. Concurrent electrophysiologic recordings revealed increased power in lower-frequency LFP bands. Pre- and post-operative in vitro testing confirmed dopamine detection by the CFM.

Discussion: This study demonstrates the feasibility of simultaneous neurochemical and electrophysiologic recording using MAVEN during tractography-guided DBS in a large-animal model of opioid administration.

Conclusions: These results support the potential for neurotransmitters to serve as biomarkers of opioid intake in the development of closed-loop neuromodulation systems for opioid addiction and other neuropsychiatric disorders.

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