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Responsive Neurostimulation for Impulsivity: Evidence from a Mouse Model of Binge-eating Behavior

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Introduction

Impulsivity is one of the most pervasive and disabling features common to many brain disorders. Heightened responsivity in the nucleus accumbens (NAc) during anticipation of rewarding stimuli predisposes to impulsivity. Electrophysiological correlates have been reported during brief windows of anticipation, which have potential to inform a novel therapeutic to deliver a time-sensitive intervention. But no available neuromodulaion therapy is capable of sensing and therapeutically responding to this vulnerable moment. The objectives of our research are: to identify biomarkers of anticipation of highly-reinforcing food reward in mouse NAc, to use these biomarkers to guide responsive neurostimulation (RNS) to suppress binge-like behavior, and to examine the effect of RNS on other behaviors, such as social interaction.

Methods

Multielectrode arrays were implanted into the mouse NAc, and were put on a limited high-fat (HF) exposure protocol known to induce binge-like behavior. Power spectral density analyses of NAc local field potentials (LFPs) before HF intake were performed to identify electrophysiological biomarkers. Identical analyses were performed before house chow intake. RNS was triggered whenever potential biomarkers appeared, and reduction in HF intake induced by RNS was examined. RNS was applied during juvenile interaction test to assess behavioral specificity.

Results

Increased delta oscillations were observed immediately prior to HF intake after mice developed binge-like behavior, which was not detected immediately prior to chow intake. RNS utilizing delta power as biomarker significantly reduced HF intake. RNS showed no significant effect on juvenile interaction, while continuous deep brain stimulation (DBS) significantly reduced it.

Conclusions

Our findings demonstrate that NAc LFPs carry critical information relevant to reward anticipation, and have the potential to be used as an electrographic biomarker to guide RNS for neuropsychiatric disorders exhibiting impulsivity. Compared to continuous DBS, RNS has the advantage of targeting specific psychiatric symptom while potentially sparing other behaviors.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of neural electrographic biomarker and responsive neurostimulation, 2) Discuss, in small groups, potential applications of RNS in neurological disorders, 3) Identify an effective treatment for impulsivity-related disorders.