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Deep Brain Stimulation Of The Medial Prefrontal Cortex Reverses Social Dysfunction In A Mouse Model Of Autism

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Introduction

Social dysfunction plays a prominent role in many developmental, psychiatric, and neurodegenerative disorders. Among the most widespread of these is Autism Spectrum Disorder (ASD). Despite its prevalence, we still have little understanding about what precise neural processes are disrupted in ASD. Furthermore, there is no effective available treatment for ASD.

Methods

We recorded neuronal activity to identify core processes in social function, probed how these processes are disrupted in a mouse model of ASD and tested DBS for mitigating social dysfunction. We developed a novel rodent group foraging paradigm that allowed us to study the social influence on individual behavior. We then recorded the activity of medial prefrontal cortex (mPFC) neurons, an area recently proposed to play a key role in social behavior. Afterward, we tested for differences in single neuron and population responses in wild-type (WT) vs. SHANK3 -/+ mice, the latter served as an ASD model. Finally, we examined the effect of deep-brain-stimulation (DBS) on social behavior.

Results

We found that individuals' behavior was significantly influenced by their social peers. Importantly, the individual's learned to follow positive social influence (towards reward) and ignore negative influence (away from reward). Control tests revealed that non-social cues do not influence behavior. Single-neuron activity in mPFC encoded social biases introduced by peer behavior. However, these signals were broadly absent in SHANK3 -/+ mice. Furthermore, SHANK3 -/+ mice were not influenced by their peers but were much more susceptible to social influence during DBS of the mPFC.

Learning Objectives

1) Peer's behavior influences individual choices, but animals learn to ignore negative bias.

2) Prefrontal cortex neurons encode the directionality of social bias.

3) DBS in autistic (SHANK3 -/+) mice magnified the effect of social bias.

Conclusions

These observations (i) identify a specific group of neurons in the mPFC modulated by social influences, (ii) reveal their selective disruption in an autism mouse model and (iii) demonstrate the prospective use of clinically applicable DBS for treating social dysfunction.