Autism and ADHD in NF1: Insights from a Mouse Model

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Background and Hypothesis: Children with Neurofibromatosis type 1 (NF1) suffer from a significantly higher incidence of ADHD and Autism. Deletion of a single *Nf1* allele (*Nf1+/-*) in mice is a well-established model of NF1 that recapitulates the peripheral tumors phenotype. We have shown that *Nf1+/-* mice demonstrate autism-like social and communication deficits and that increased activation of the Ras pathway in the basolateral amygdala (BLA) causes social deficits. We hypothesized that *Nf1+/-* mice will exhibit ADHD-like behaviors.
Experimental Design: To further test the role of BLA, we activated this region in WT mice or inhibited the BLA of *Nf1+/-* mice through optogenetic stimulation following acquisition of a social memory in the social preference test. Dual immunofluorescence was then used to map pERK activation and GFP expression in the BLA. In a second experiment, we examined impulsive choice in WT and *Nf1+/-* mice using a delayed discounting task.
Results: Long-term memory of WT mice was disrupted after optogenetic BLA stimulation and pERK expression in the BLA was increased in *Experiment 1*. In contrast, BLA inhibition of *Nf1+/-* mice did not rescue social learning deficits. In *Experiment 2*, *Nf1+/-* mice choose a higher percentage of smaller rewards when a 10 s and 20 s delay was administered compared to WT mice, suggesting *Nf1+/-* mice are more impulsive.
Conclusion and Potential Impact: These data provide the first genetic mouse model to study ADHD symptoms in NF1 patients and shed further light on the CNS pathways regulating autism-like deficits.