Cerebellar Disruptions in Development Interrupt Social Behavior and Spine Maturation in Mice

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Background
- The cerebellum, which is highly interconnected to forebrain structures, often has structural abnormalities in individuals with autism spectrum disorder (ASD)
- Hypothesis: cerebellar activity modulates maturation of downstream targets during sensitive periods of development
- Cerebellar disruptions, specifically to molecular layer interneurons (MLIs) in lobule VI, may lead to ASD-related pathologies

Objective of Research
- Tested lobule specific cerebellar disruptions using Designer Receptors Exclusively Activated by Designer Drugs (DREADDs)
- Observed and quantified behavioral changes
- Analyzed changes in spine morphology and density of pyramidal neurons in layer V of the anterior cingulate cortex (ACC), a region thought to be important for cognitive and social functions

Methods
(a) Experimental Design

(b) Three-chamber Sociability Assay Phases

Results (continued)
(c) Increased Mature Spines in Lob VI MLI Inactivated Mice

(d) Imaging (layer V pyramidal neurons in YFP-H mice)

(e) Tracing using IMARIS

Conclusions
- Inactivating molecular layer interneurons during development in Lob VI by DREADDs resulted in a significant decrease in social preference and alteration in spine maturity
- DREADD inactivation increased the overall amount of mature spines in pyramidal neurons in layer V of the ACC
- Thus, maturation of spines in the ACC may be regulated by cerebellar signaling during development and influence behavior in

Future Experiments
- Electrolytic Lesions: disrupt cerebellar activity bilaterally of hemispheric regions
- PSAM-PSEM: analyze effects of an ion channel manipulator in the cerebellum on forebrain development

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