Characterizing Social Memory in Shank3β Deficient Mouse Pups

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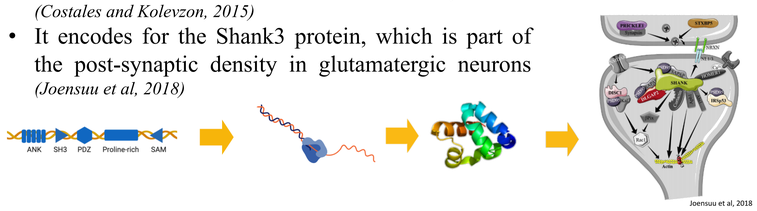
BACKGROUND

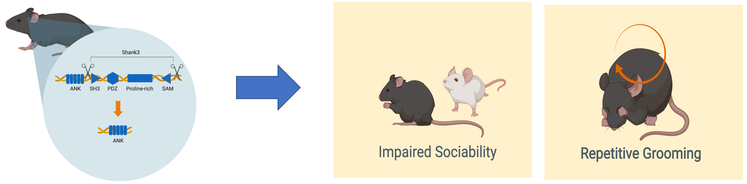
- Autism Spectrum Disorder (ASD) is a common developmental disorder that currently impacts over 3 million people in the United States *(Buescher et al, 2014)*
- ASD is characterized by altered sociability and repetitive behaviors in humans *(National Institute of Mental Health, 2018)*
- Most diagnoses of ASD are the result of numerous factors, including genetic and environmental *(Geschwind, 2011)*
- ASD is highly heritable; there is a concordance of 0.9 between monozygotic twins *(Rosenberg et al, 2009)*
- Shank3 is one gene that has mutations associated with ASD and/or Pheland McDermind Syndrome *(Costales and Kolevzon, 2015)*
- It encodes for the Shank3 protein, which is part of the post-synaptic density in glutamatergic neurons *(Joensuu et al, 2018)*

Rudy, 2019

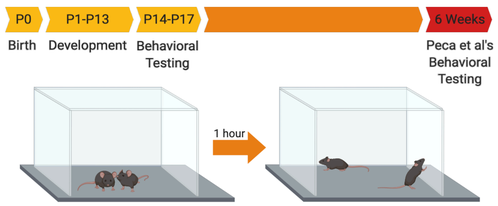


Joensuu et al, 2018

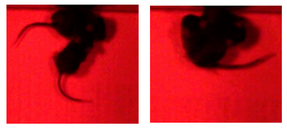
- Previous work has shown that young adult male Shank3B KO mice show decreased sociability, impaired social memory, and repetitive grooming *(Peça et al, 2011)*
- ASD is a developmental disorder; it is important to investigate behavioral changes in early development



METHODS



The direct social interaction paradigm was used to assess the sociability and social memory of P14-P17 mice.



Huddling Sniffing

Behavior was scored for sniffing and huddling. Huddling was scored when two mice sat side by side. Sniffing was scored when one mouse pointed its nose towards the other in active investigation.

Social behavior for WT (n = 7) and KO (n = 5) mice was analyzed by a two-way ANOVA repeated measures followed by a paired t-test post hoc comparison or by unpaired t-tests. The data from WT-littermate (N = 8) social interaction were analyzed by paired t-tests. ** = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$*

RESULTS

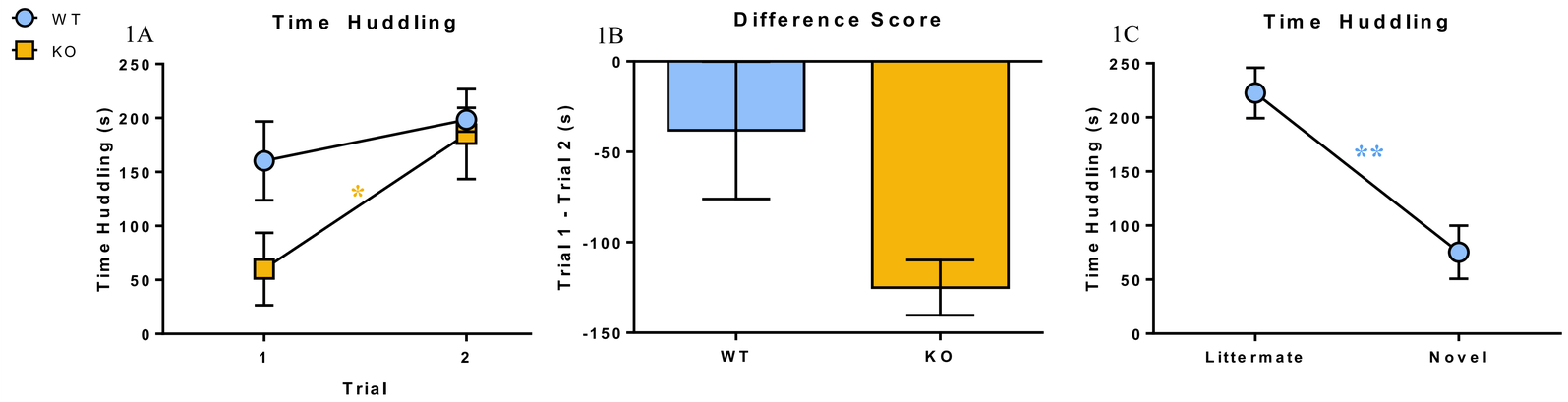


Figure 1: (A) KO mice spent significantly more time huddling with their partner in trial 1 compared to trial 2, whereas WT mice approached significance. In trial 1, the difference in time spent huddling between groups trended towards significance. (B) The difference between the WT vs KO difference scores for huddling approached significance.. (C) WT/Het mice spent significantly less time investigating a littermate compared to a novel mouse.

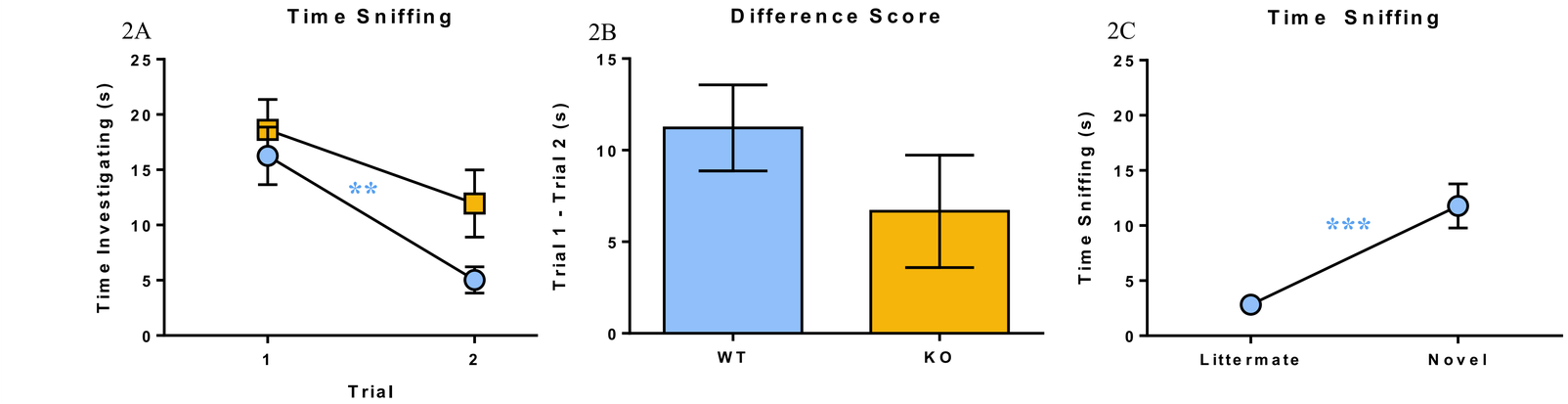
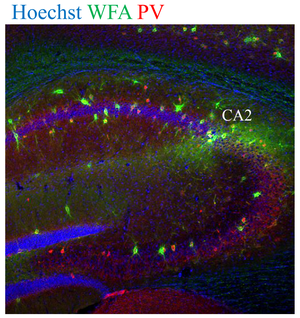


Figure 2: (A) WT mice spent significantly less time sniffing their partner in trial 1 compared to trial 2,, whereas KO mice approached significance. (B) The difference between the WT vs KO difference scores for sniffing approached significance. (C) WT/Het mice spent significantly more time huddling with a littermate compared to a novel mouse.

FUTURE DIRECTIONS

- Conduct social tests at later time points
- Alter the DSI paradigm
- Examine USVs and repetitive behavior
- Analyze Shank3B mouse brains to determine if there are structural and/or cellular abnormalities
  - Social memory paradigms have been linked to the CA2 in the hippocampus

Hoechst WFA PV



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