

The Effects of Object Play and Social Interaction on GLUR1 Levels in a Mouse Model of Autism (FMR1 KO)

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Outline

1. An Overview of Autism Spectrum Disorders
2. Hypothesis and Rationale for Experiment
3. Methodology
4. Data-Results and Analysis
5. Conclusion

Autism Spectrum Disorder

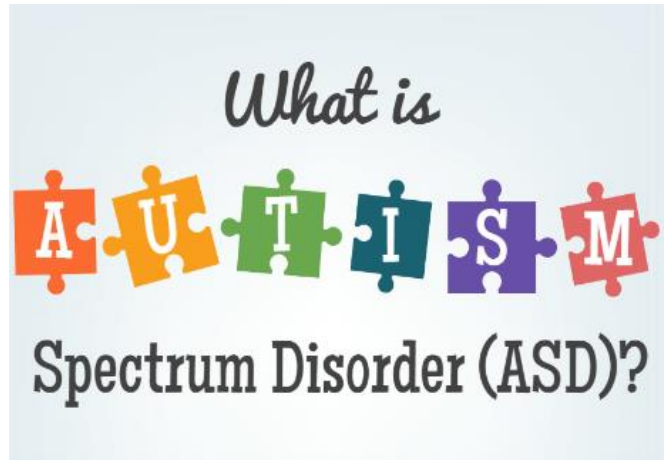


Figure 1.1

Symptoms

Social impairment

Cognitive impairment

Communication difficulties

Repetitive behaviors

The Prefrontal Cortex: The Reward Pathway



Figure 1.2

Engagement in pleasurable activity triggers VTA

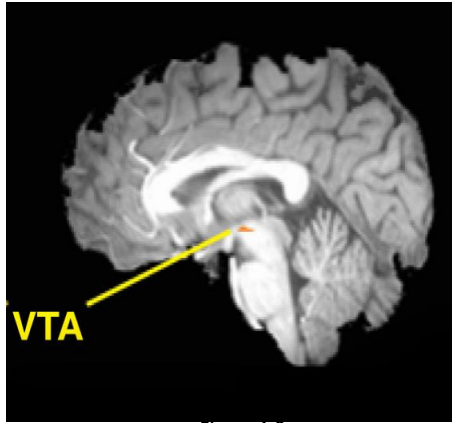


Figure 1.3

VTA releases neurotransmitter



Figure 1.4

Neurotransmitter is sent to the Prefrontal Cortex

Seamans, J., & Yang, C. (2004). Progress in Neurobiology, Forbes, C. E., & Grafman, J. (2010). Annual Review of Neuroscience, Chevallier, C., Kohls, G., Troiani, V., Brodtkin, E. S., & Schultz, R. T. (2012). Trends in Cognitive Sciences, Figure 1.1: Trost, R. (2011, April 11). Developmental Skills While Playing With Cars [Cognition while playing with cars]. Figure 1.3: Writers, S. (2008, February 28). Horizontal (left) and vertical (right) slices of brain show increased blood flow (red region) in brainstem (VTA or ventral tegmental area) in measurements made by functional magnetic resonance imaging. Figure 1.4: Klein, C. (2016, January 22). Prefrontal Cortex ["Ceo of the brain"]

Introduction to Experiment

Aim: We sought to investigate the link between **social motivation** and ASD by comparing GLUR1 (**dopamine** correlate) levels in wild-type and FMR1 KO mice after interaction with an object to the GLUR1 levels of a group of mice without any object play.

Hypothesis: Compared to wild-type mice, FMR1 knockout mice will have a greater increase in GLUR1 levels after interacting with objects because the KO mice will be more stimulated by the objects than they are by interactions with other mice.

Approach: To test this hypothesis, we used immunohistochemistry to measure GLUR1 levels in the **prefrontal cortex** of KO mice and wild-type mice after only interacting with another mouse and after interacting with several toys.

Methodology (Behavior)

Fmr1^{-/-} & WT



Social Interaction



Three Trials per
10 minutes



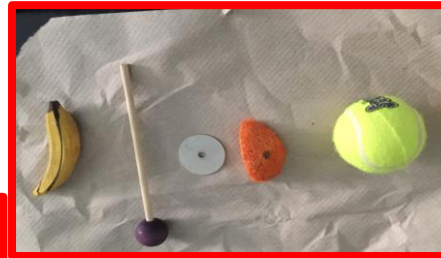
Habituation (One Day)



Social Interaction
One trial
10 minutes



*Five trials
One toy at a
time per 10
minutes with 4
minutes interval*



Fmr1^{-/-} & WT



Social Interaction



Three Trials per
10 minutes



Habituation (One Day)



Social Interaction
One trial
10 minutes

Methodology (Immunohistochemistry)

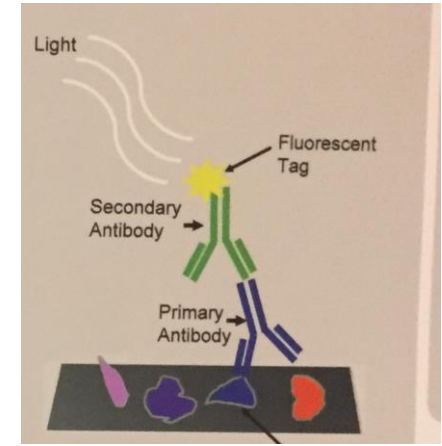
Slices were fixed and washed in PBST to permeabilize them.

Non-specific binding sites were blocked with albumin serum and bovine serum.

They were incubated with primary and secondary antibodies.

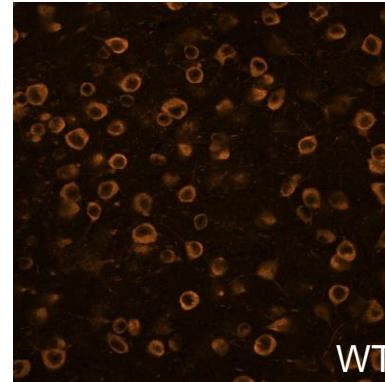
Antibodies selected were for FMRP and GluR1.

DNA staining: Hoechst

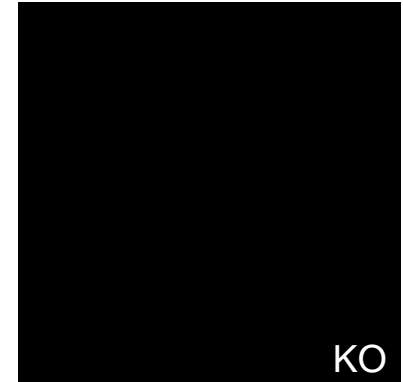


GLUR1

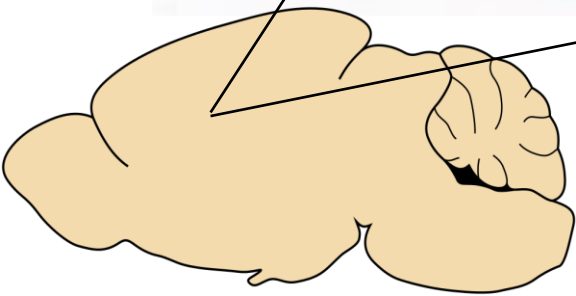
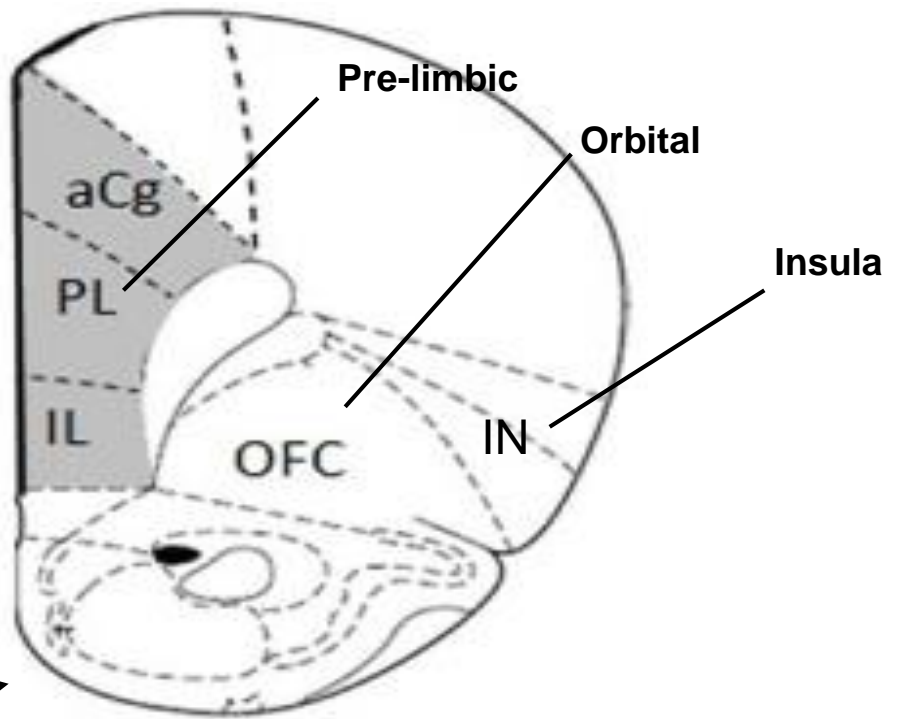
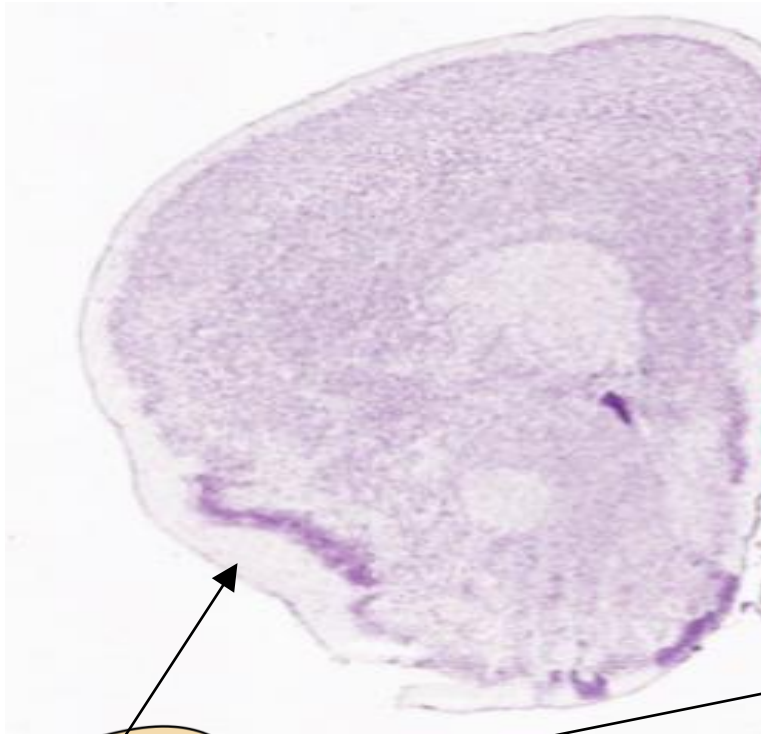
FMRP:



WT

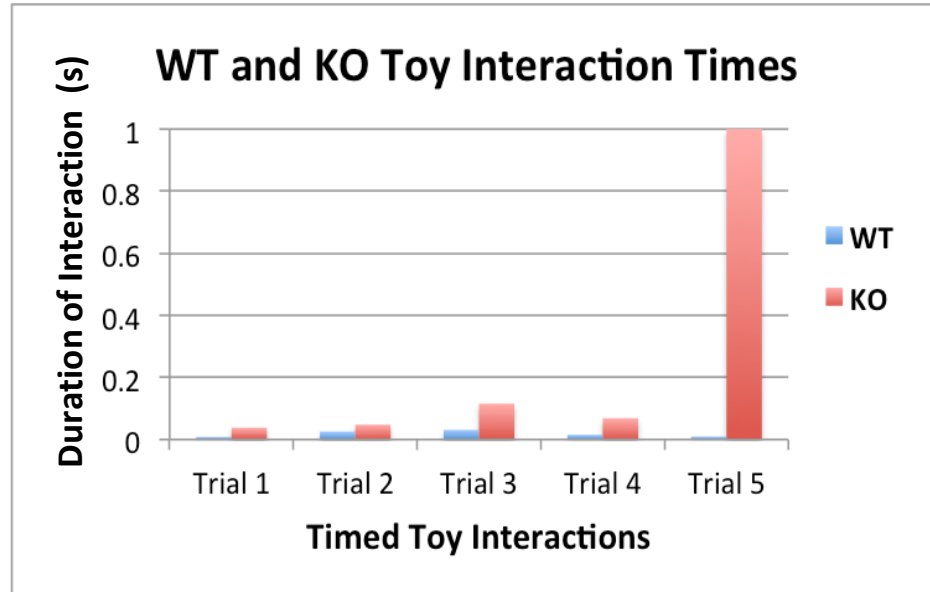


KO



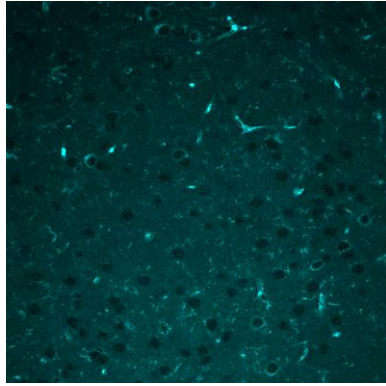
Results and Analysis (Behavior)

Social Interaction + Toys

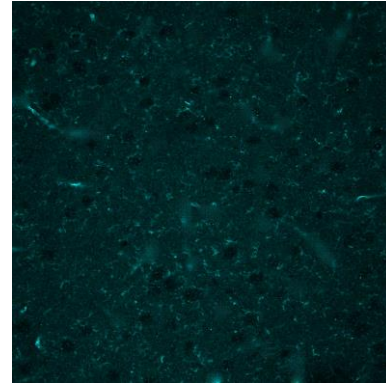


Results and Analysis (Immunohistochemistry)

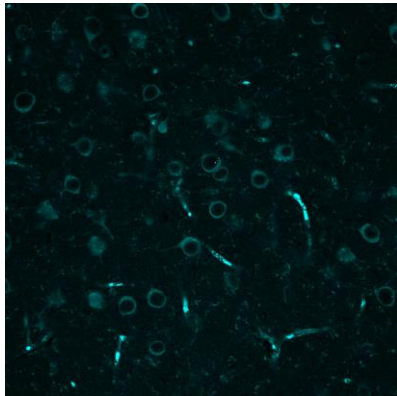
WT Insula - SI Only



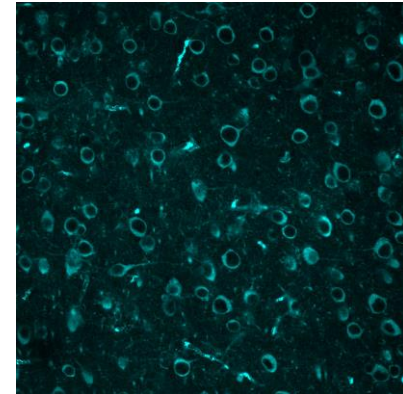
WT Insula - SI+Toys



KO Insula - SI Only



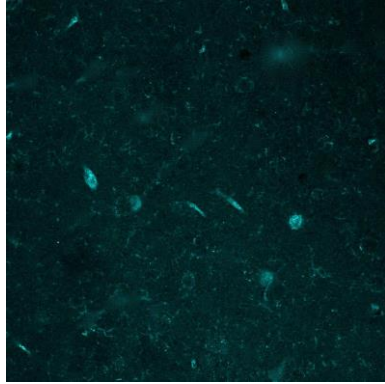
KO Insula - SI+Toys



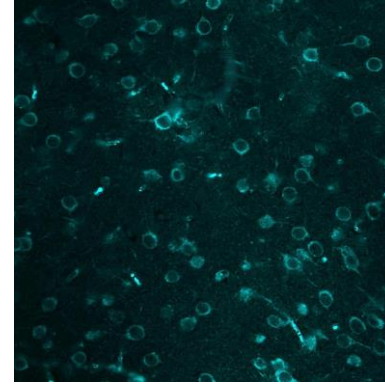
GLUR1

Results and Analysis (Immunohistochemistry)

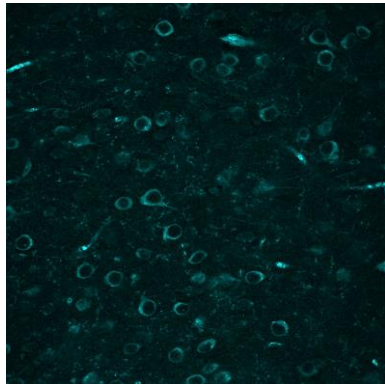
WT Orbital - SI Only



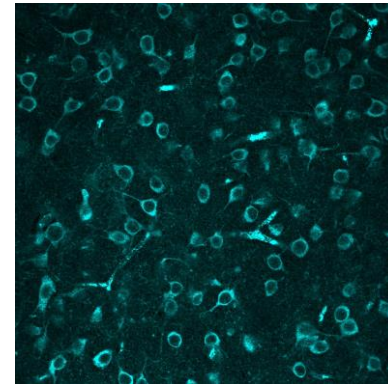
WT Orbital - SI+Toys



KO Orbital - SI Only



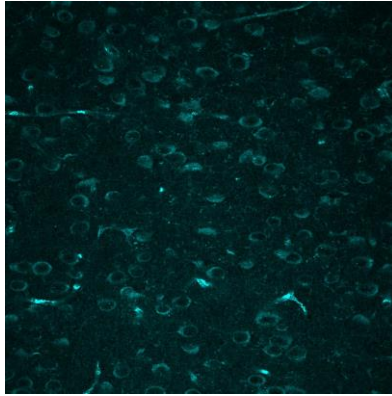
KO Orbital - SI+Toys



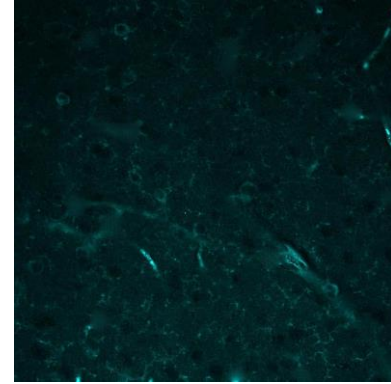
GLUR1

Results and Analysis (Immunohistochemistry)

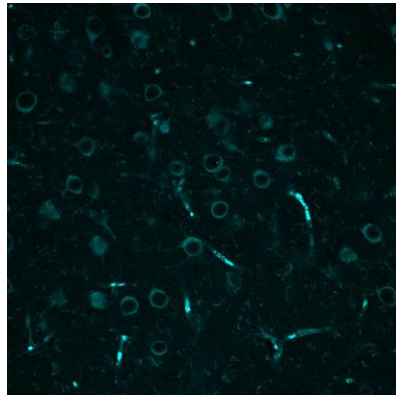
WT Prelimbic - SI Only



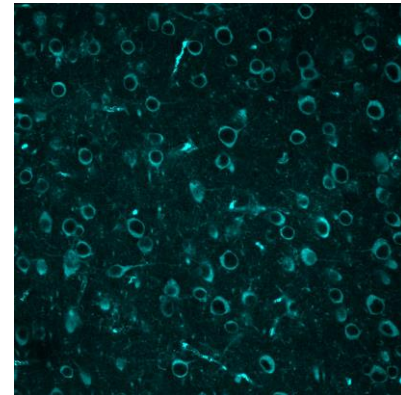
WT Prelimbic - SI+Toys



KO Prelimbic - SI Only

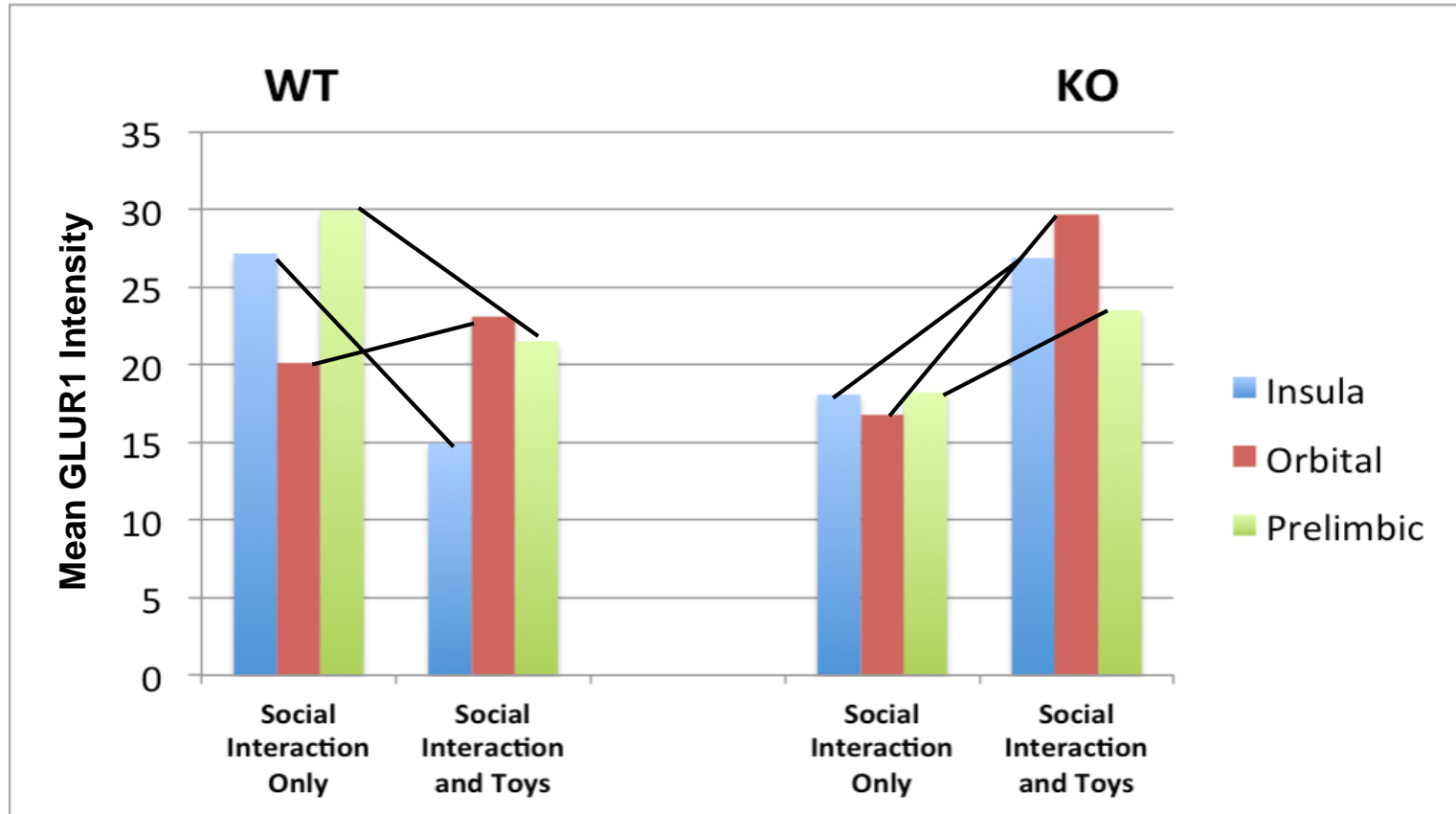


KO Prelimbic - SI+Toys



GLUR1

Results and Analysis (Immunohistochemistry)



Summary and Discussion

Our research is consistent with our hypothesis.

The dynamic nature of the wild-type results show the regulating effect of FMRP.

The absence of FMRP regulation in knockout mice is reflected in the consistency of the knockout results.

Concluding Remarks

Consistency with human individuals with autism or fragile X syndrome

Limitations: The mice may not have liked those kinds of toys

Further research

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