THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

UNC COLLEGE OF ARTS AND SCIENCES
Psychology and Neuroscience

Creation of an Automated Behavioral Classifier for Stress Induced Aggression in a Mouse Model for ASD

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Background

- Aggressive behavior (AB) is a major challenge for individuals with Autism Spectrum Disorder (ASD) and their families.
- One study noted that 68% of children and adolescents with ASD had demonstrated aggression to a caregiver[1], and another noted that 30% of individuals with ASD require psychiatric medication to limit behavioral problems as a result[2].
- Current pharmacological treatments often rely on chronic medication reliance on anti-psychotics, with several negative side effects for the general populace, often worse for people with ASD.
- The 16p11.2 gene deletion is one of the most common genetic linkages to ASD, but is also one of the most varying in terms of clinical presentation and phenotypic characterization of symptoms.
- This study proposed a novel approach to automatically identify the phenotypic presentation of stress-induced aggression (SIA) and social in studies utilizing mouse models for ASD.

Issues with Manual Behavior Annotation

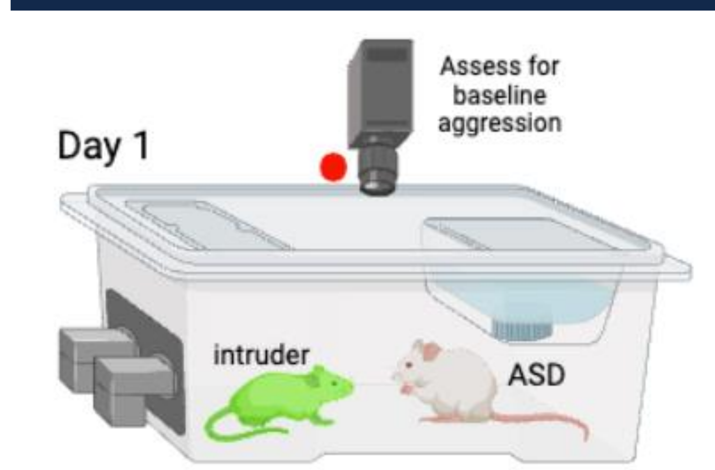
- Time Consuming
- Labor Intensive
- Creates Annotator Fatigue → Leads to Errors
- Largely Subjective
- Not Scalable

Animals

Female Sert-Cre$^{+/-}$:16p11.2$^{flx/flx}$ (KO) mice were selectively bred to allow for control over the deletion of the syntenic region on mouse chromosome 7F3 from 5-HT neurons[3]

C57BL/6 female observer/intruder mice served as (WT)

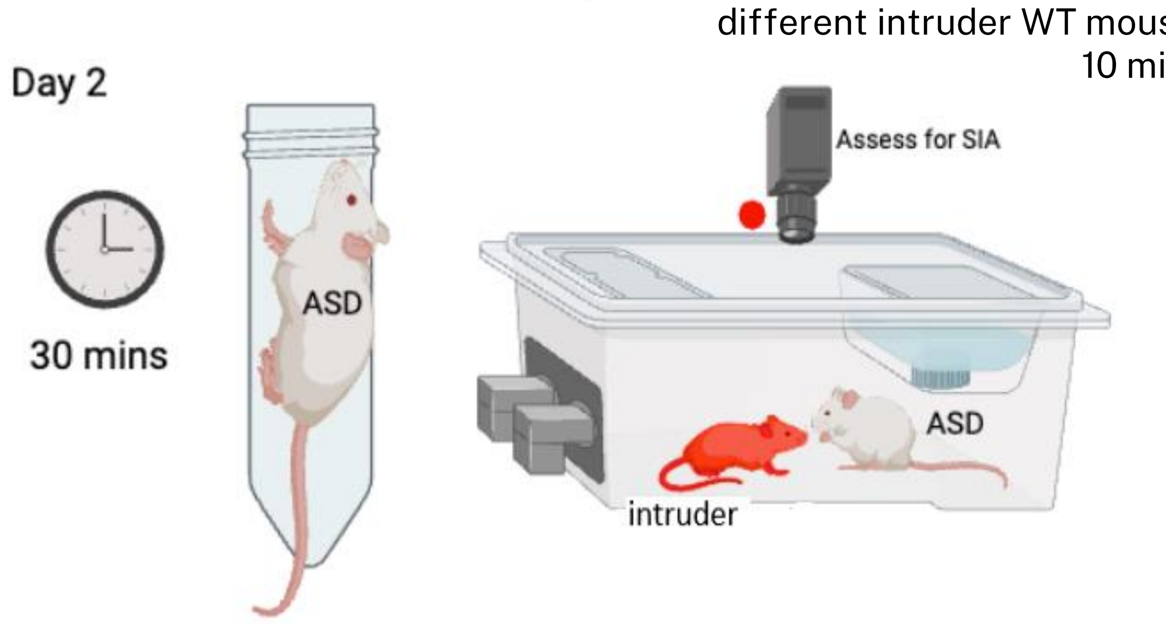
Stress Induction Assay

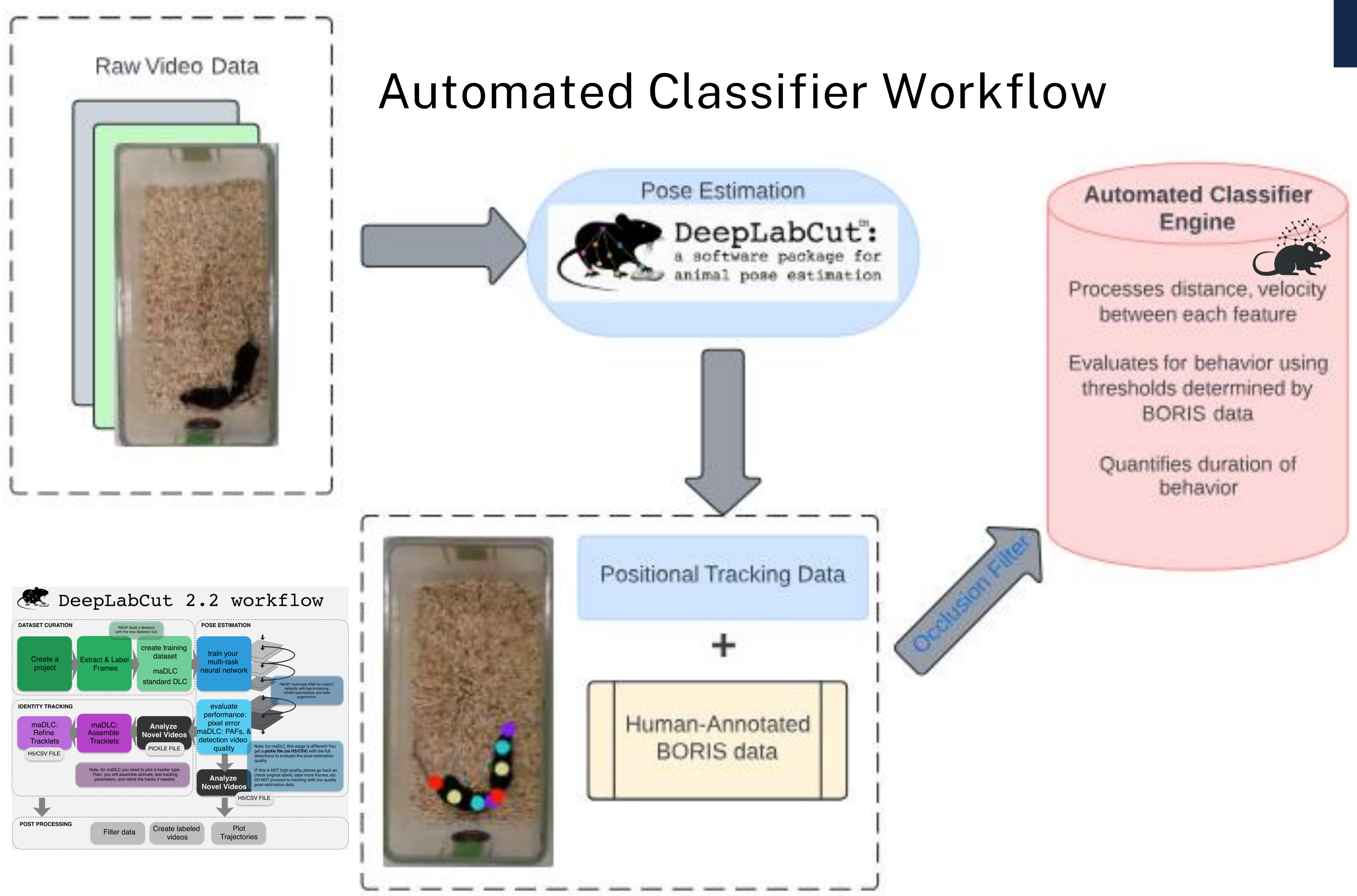


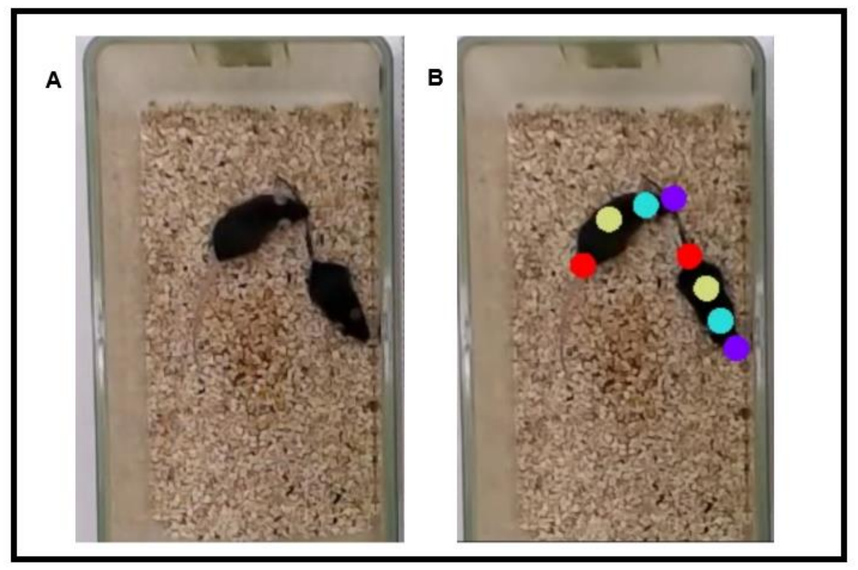
Restraint stress – used to induce anxiety-like behavior in mice through restricting its free movement

Day 1: Test Mouse (KO or WT) Placed in home chamber with intruder WT mouse, interactions recorded for 10 minutes to assess baseline SIA

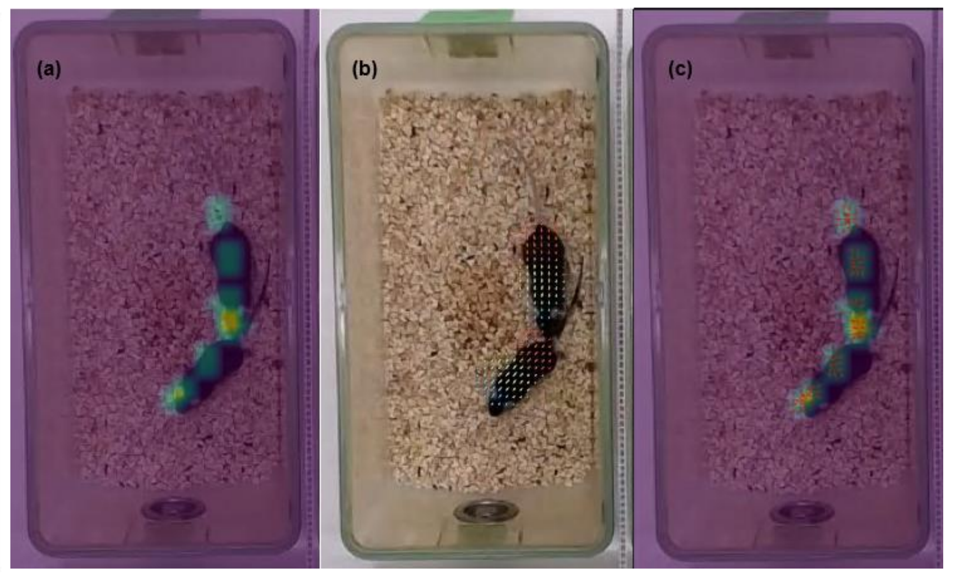
Day 2: Test mouse is placed in 50 mL conical tube to induce restraint stress, physiological distress and aggression is monitored in home chamber with different intruder WT mouse, interactions recorded for 10 minutes.



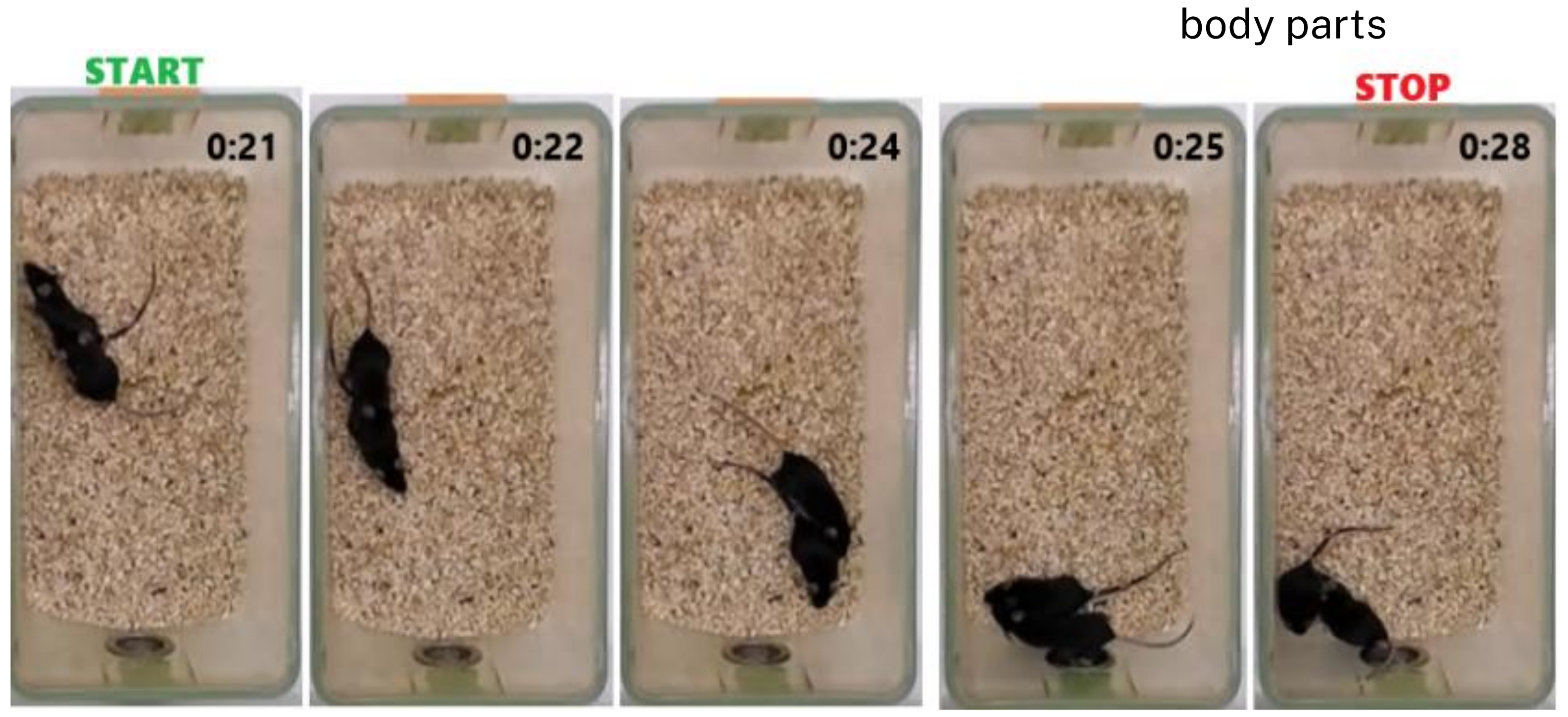




An example of a still frame of raw video data versus the same frame that has been processed through DeepLabCut[4], automatically identifying the mouse's body parts (nose, middleEar, center of mass, and tail base)

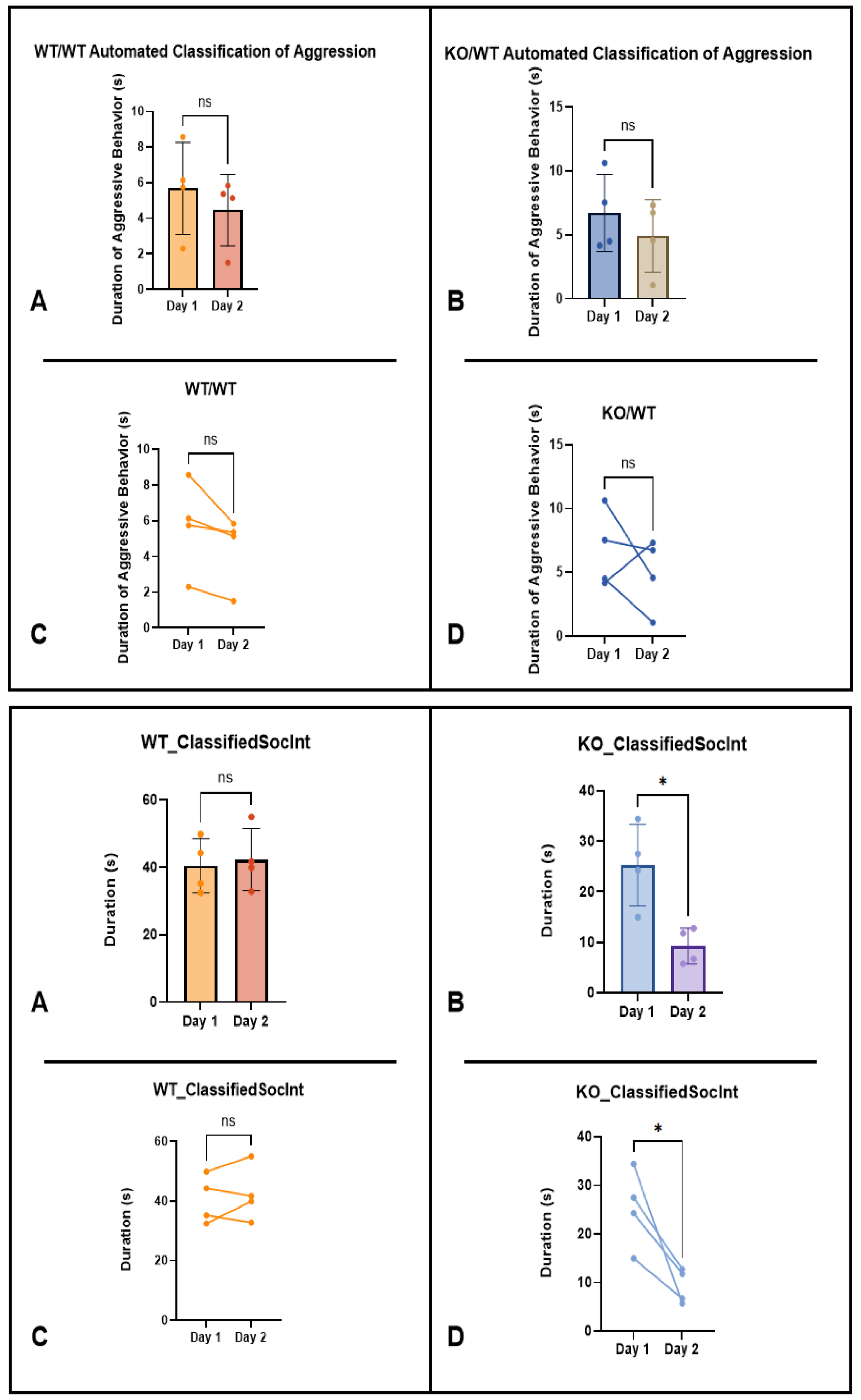


a) Score Map - looks for parts of the image that may have a desired feature b) PAF (Part Affinity Field) - encodes pairwise relationships between body parts, which helps to build the skeleton of the mouse c) Location Refinement layer – uses the two previous layers together, and attempts to find the position of certain features based on their relation to the other body parts



Time series of aggressive behavior as identified by the automated behavioral classifier system

Findings



- Overall, it was difficult to glean any meaningful conclusions about the trends in aggression as a result of our restraint stress protocol given the underpowered *n*, but there was a significantly observed decrease in the level of social interaction (specifically anogenital sniffing) in the 16p11.2 deletion mice, in line with what is known about the ASD-like symptoms exhibited by this specific genotype[5].
- It is a validating measure, though, that this automated classifier was successfully able to detect periods of aggression and social interaction between the two mice of the same coat color, and this same paradigm can be extended to future behavioral studies in this realm.
- Further testing with mice of different genetic backgrounds and alternative stressors may need to be explored in order to truly find a model with the appropriate circuit differences that are attributable to ASD-associated aggression.

References

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