

Japan-U.S. Brain Research Cooperation Program
Researchers Dispatched to the U.S. Program FY2018: Report

Field: 4

1. Researcher

Name: Shintaro Otsuka

Title: PhD

Affiliation: Department of Physiology, School of Medicine, Keio University

2. Research Title: Analysis of synaptogenic disruption in cerebral cortex of fragile-X syndrome using three-dimensional aggregate culture of human iPS cells.

3. U.S. Joint Researchers/Institutes

Please give the name, title and affiliation.

Anis Contractor, Feinberg school of medicine, Department of neurobiology, Department of physiology, Northwestern University

4. Research Period, from/to (mm/dd/yyyy):

18/8/14 – 18/12/24

5. Abstract, Results, and Research Significance (300 Words):

Because of cutting edge free-moving *in vivo* recording of neural activity using head-mounted microscopic (Miniscope) technique is launched and a novel model of autism spectrum disorder (ASD) is established in Contractor's laboratory just after I arrived at the US, I'm studying neural activity during ASD-related behavior of ASD model mouse using miniscope instead of the research using iPS cell because he miniscope study would bring more deep knowledge about etiology of ASD.

Although a behavioral task which is compatible with miniscope and can demonstrate core phenotypes of ASD such as impairments of sociality and perseverative behavior with high reproducibility is essential for this project, it was still remained unknown whether the novel-established ASD model (Mutant mouse which is a model of ASD human patients who have G407R mutant in *CACNA1d*, a alpha1 subunit of voltage-dependent calcium channel Cav1.3) has any impairment in sociality and stickiness. Thus, I established behavioral analysis which can evaluate these cognitive functions and possesses high compatibility with miniscope analysis. I have revealed that G407R mice showed phenotypes in both sociality and perseveration using reciprocal social interaction test and place discrimination test, respectively. In reciprocal social interaction test where active contact with stranger mouse is evaluated, G407R mice showed significantly shorter contact duration with strangers than litter wild type meaning G407R mouse have poor sociality like ASD-patients (Fig. 1). In place discrimination test, the mouse is trained to touch a panel located in a correct position presented with a dummy panel and then correct and dummy location are switched to evaluate how quickly the mouse can adjust their behavior to the new rule (Fig. 2). I have demonstrated that G407R mice show poor adaptation to the new rule (Fig. 3B) while they showed normal learning curve during training phase (Fig. 3A) suggesting they have enhanced perseveration.

Since I can continue this project after dispatch period of Japan-U.S. Brain Research cooperation program, I'm going to study where and how the neural activities are affected during ASD-related behavior in G407R mice.

6. Other (Research concerns, particular points of note):

*Please attach any reference materials as necessary.

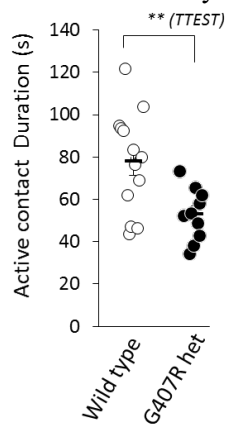


Fig. 1 Active contact durations in the reciprocal social interaction test. G407R heterozygous mice showed shorter duration of active contact.

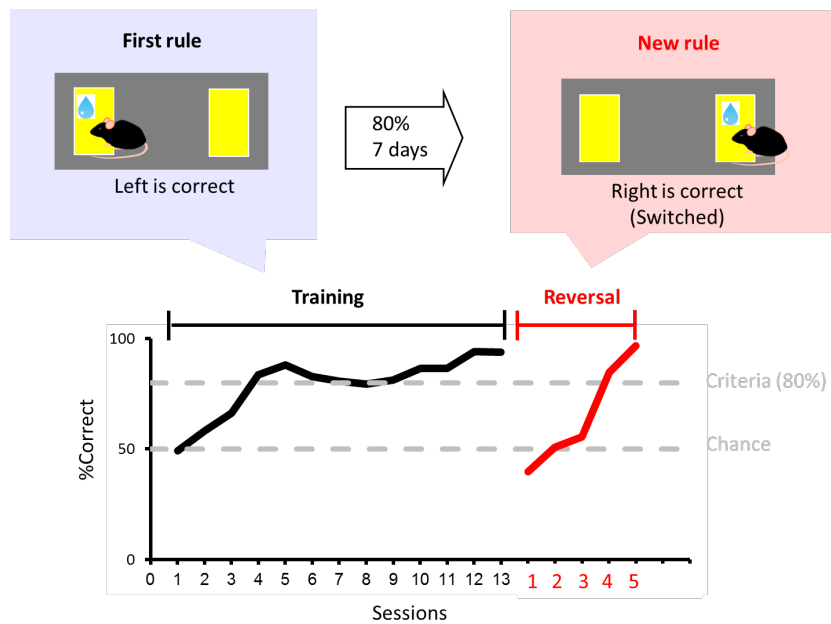


Fig. 2 Schematic of place discrimination task. In this example, the mouse is trained to touch left panel and then correct position is switched to the right.

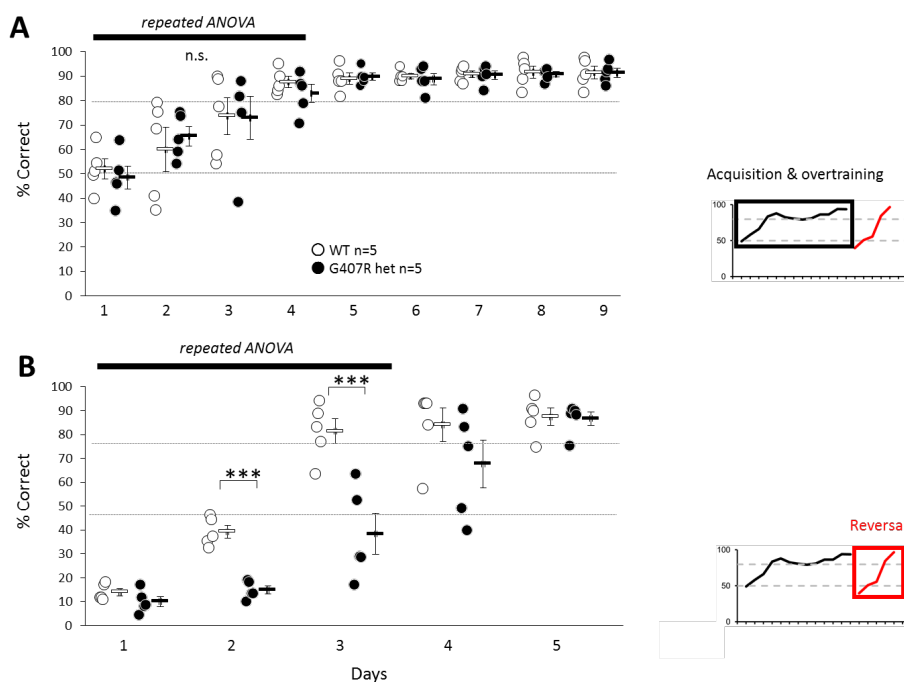


Fig. 3 Result of place discrimination task. Although G407R mice showed normal acquisition in the training period (A), their adaptation to the new rule is significantly delayed (B).