STUDENT SHEET

Obsessive-Compulsive disorder

Name: _____ Date: _____

Bell Ringer activity: Chat with your desk partner and record your ideas.

What do you know about obsessive compulsive disorder (OCD)? Give examples, explain what you think a day in the life of a patient would look like, etc.?	How do you know what you know about OCD?	What additional information do you think you need to help treat patients with OCD?

Enter your top choice into Socrative.

Read the abstract of the following paper and answer the questions that follow.

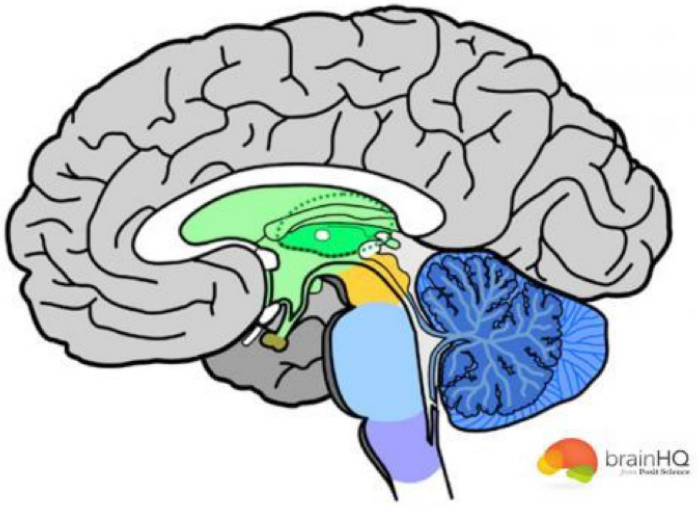
A. Analysis of Abstract

1. What is the question the authors are trying to answer?

2. What is the hypothesis the scientists in this paper proposed?

3. What methods do they use to gather data?

4. Using the image, identify the circuit scientists believe is correlated with OCD in mice on the human brain.



5. What questions do you have, if any, about this paper?

Repeated Cortico-Striatal Stimulation Generates Persistent OCD-Like Behavior

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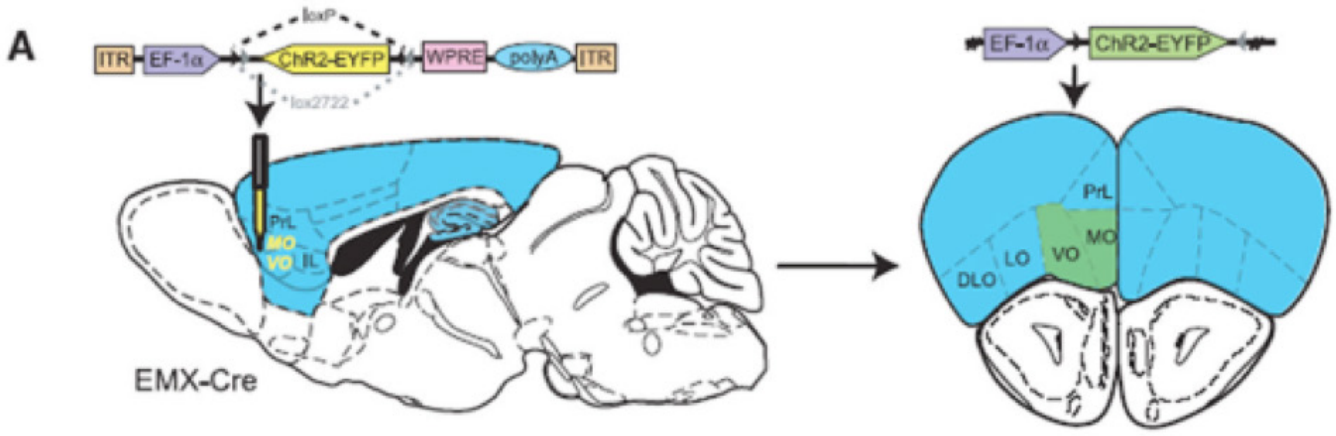
Abstract

Although cortico-striato-thalamo-cortical (CSTC) circuit dysregulation is correlated with obsessive compulsive disorder (OCD), causation cannot be tested in humans. We used optogenetics in mice to simulate CSTC hyperactivation observed in OCD patients. Whereas acute orbitofrontal cortex (OFC)–ventromedial striatum (VMS) stimulation did not produce repetitive behaviors, repeated hyperactivation over multiple days generated a progressive increase in grooming, a mouse behavior related to OCD. Increased grooming persisted for 2 weeks after stimulation cessation. The grooming increase was temporally coupled with a progressive increase in light-evoked firing of postsynaptic VMS cells. Both increased grooming and evoked firing were reversed by chronic fluoxetine, a first-line OCD treatment. Brief but repeated episodes of abnormal circuit activity may thus set the stage for the development of persistent psychopathology.

OCD is characterized by intrusive distressing thoughts (obsessions) and/or repetitive mental or behavioral acts (compulsions) and is a leading cause of illness-related disability (1, 2). Although the pathophysiology underlying OCD is unclear, multiple lines of evidence implicate dysregulation within cortico-striato-thalamo-cortical (CSTC) circuits (3-6). Specifically, functional imaging studies suggest that hyperactivity in orbitofrontal cortex (OFC) and ventromedial striatum (VMS) is associated with OCD pathology (5, 7, 8).

Furthermore, successful treatments are associated with reductions in hyperactivity (9, 10). However, it is not known if OFC-VMS hyperactivity can directly cause OCD symptoms, because increased activity could represent adaptive, homeostatic, or unrelated processes compensating for other primary abnormalities. We therefore used an optogenetic strategy to directly test whether hyperstimulation of glutamatergic OFC-VMS projections leads to OCD-like behaviors in mice.

B. Interpretation of Methods

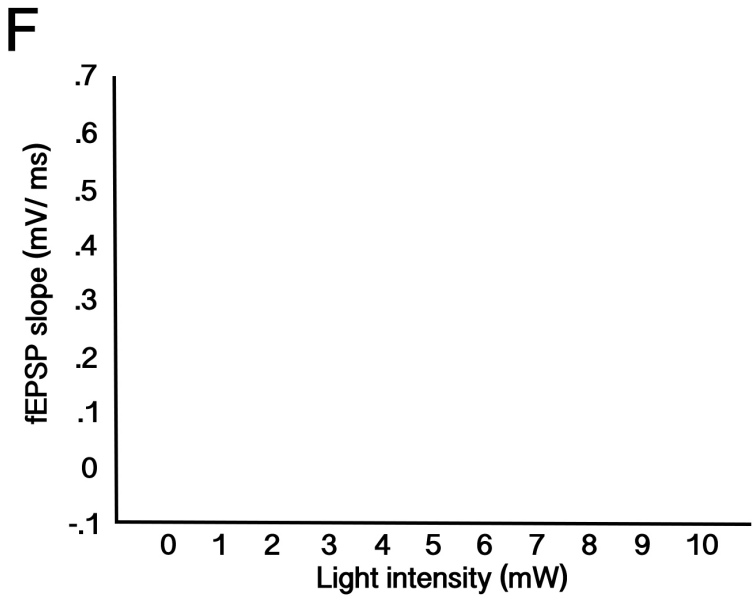


6. According to figure A, which area of the mouse brain is stimulated?

7. What impact do you believe this will have on mouse behavior? Why?

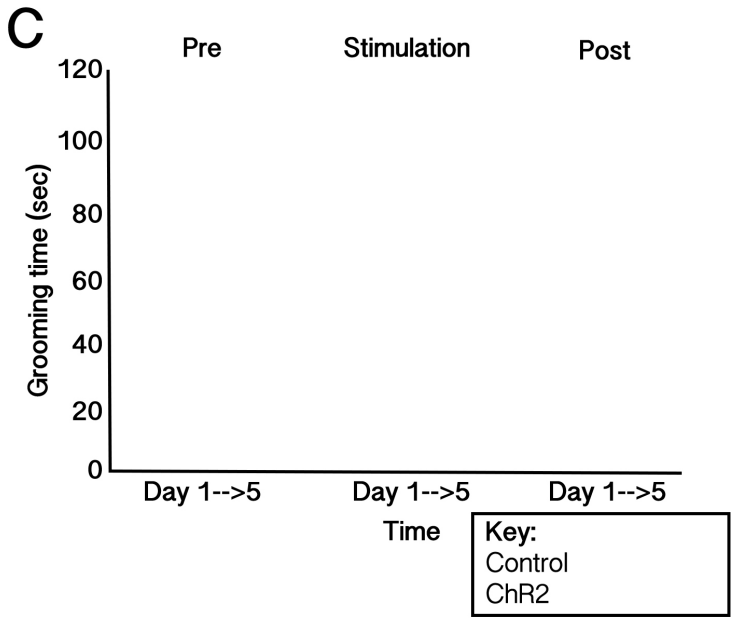
C. Predicting the Results

8. Using your knowledge of neurons and this experiment, predict how light intensity will influence rate of EPSP in the stimulated ventromedial OFC by drawing a trend line on the graph below. Explain your rationale to the right of the graph.

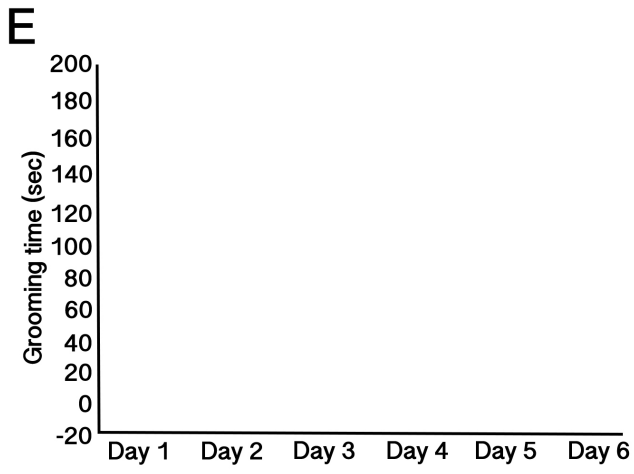


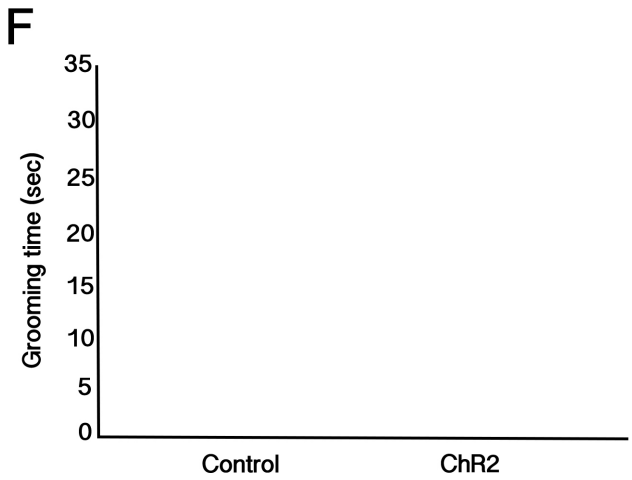
In the next portion of the study, an area of the brain is being stimulated that is believed to initiate OCD compulsions. Total time grooming was assessed for 5 min before (Pre), during (Stim), and after stimulation (Post) for five consecutive days. Data are grouped into Pre, Stim, and Post categories for days 1 to 5 to facilitate examination of changes in behavior over time.

9. Draw trend lines to show how the amount of time spent grooming would change before, during and after stimulation of the neural circuit. Write an explanation of your trend lines to the right of the graph.



10. Predict the grooming time for a new group of mice 1 hour post stimulation for both control and ChR2 mice on graph E. These mice did not have the 5 day stimulation period yet. Predict bar graph results for the mice grooming time in graph F for 2 weeks after the experiment.





Summary:

What do these data tell us about OCD?

If you were the scientists, what would you study next? Explain.