Press Release

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Study identifies brain circuit controlling social behavior

A new study in Biological Psychiatry *identifies specific brain circuit that may lead to social impairments in autism spectrum disorder*

Philadelphia, January 11, 2018 – A new study by researchers at Roche in Basel, Switzerland has identified a key brain region of the neural circuit that controls social behavior. Increasing the activity of this region, called the habenula, led to social problems in rodents, whereas decreasing activity of the region prevented social problems.

The study, which appears in *Biological Psychiatry*, suggests that social impairments characteristic of autism spectrum disorder may stem from alteration of activity in this circuit, and that tuning this circuit may help treat the social deficits in the disorder.

"We are excited about this study as it identifies a brain circuit that may play a critical role in social reward, which is affected in autism," said senior author Dr. Anirvan Ghosh, who was the Head of Neuroscience Research at Roche and now serves as Head of Research and Early Development at Biogen. The findings provide clues as to what may be altered in the brain to lead to neurodevelopmental conditions like autism spectrum disorder.

Previous research has linked social function to the prefrontal region of the brain, but circuits that affect prefrontal control of social behavior were unknown. So first author Dr. Madhurima Benekareddy and colleagues activated the prefrontal region in mice and rats, and performed a brain-wide screen to find which regions responded. The screen identified changes in activity in regions related to emotional behavior, particularly in the habenula.

In the study, the researchers then used a combination of different techniques to map the connections from the habenula to the frontal area of the brain, and to precisely control the activity of neurons in these regions. Turning up the activity of neurons in the habenula reduced how much the rats and mice socialized. Turning down habenula activity prevented the social deficits that could be induced by activating the frontal region.

According to the authors, an alteration of the normal activity range for the circuit may cause behavioral function in disorders such as autism spectrum disorder. "Understanding how altered brain function leads to social deficits could help develop novel targeted therapeutics for autism spectrum disorder," said Ghosh, such as by tuning the circuit to correct the altered activity.

The findings also have implications for diseases other than autism spectrum disorder, including schizophrenia and depression. The circuit incorporates brain regions involved in reward and pleasure, leading the authors to consider that social dysfunction may stem from reduced enjoyment in social

interaction. “It is interesting that the circuit implicated in social behavior in this study is also a circuit implicated in the biology of depression,” said Dr. John Krystal, Editor of *Biological Psychiatry*. “Perhaps this circuit represents a pathway through which disruptions in social relationships contribute to negative mood states and depression.”

Notes for editors

The article is "Identification of a cortico-habenular circuit regulating socially-directed behavior," by Madhurima Benekareddy, Tevye Jason Stachniak, Andreas Bruns, Frederic Knoflach, Markus von Kienlin, Basil Künnecke, and Anirvan Ghosh (http://dx.doi.org/10.1016/j.biopsych.2017.10.032). It appears in *Biological Psychiatry*, published by Elsevier.

Copies of this paper are available to credentialed journalists upon request; please contact Rhiannon Bugno at Biol.Psych@UTSouthwestern.edu or +1 214 648 0880. Journalists wishing to interview the authors may contact Anirvan Ghosh at anirvan.ghosh@biogen.com.

The authors’ affiliations and disclosures of financial and conflicts of interests are available in the article.

John H. Krystal, M.D., is Chairman of the Department of Psychiatry at the Yale University School of Medicine, Chief of Psychiatry at Yale-New Haven Hospital, and a research psychiatrist at the VA Connecticut Healthcare System. His disclosures of financial and conflicts of interests are available here.

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