

Altered brain activity responsible for cognitive symptoms of schizophrenia

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Cognitive problems with memory and behavior experienced by individuals with schizophrenia are linked with changes in brain activity; however, it is difficult to test whether these changes are the underlying cause or consequence of these symptoms. By altering the brain activity in mice to mimic the decrease in activity seen in patients with schizophrenia, researchers reporting in the Cell Press journal *Neuron* on March 20 reveal that these changes in regional brain activity cause similar cognitive problems in otherwise normal mice. This direct demonstration of the link between changes in brain activity and the behaviors associated with schizophrenia could alter how the disease is treated.

"We artificially decreased activity of the mediodorsal thalamus region of the brain in the mouse and found that it is sufficient to lead to deficits in [working memory](#) and other schizophrenia-like cognitive deficits," says senior author Dr. Christoph Kellendonk of Columbia University in New York City. "Our findings further suggest that decreased thalamic activity interferes with cognition by disrupting communication between the thalamus and the prefrontal cortex, an area of the brain that has already been shown to be important for working memory," he added.

The researchers made their discovery by giving mice a drug that decreased activity selectively in the mediodorsal thalamus region of the brain. They then tested the animals in various [cognitive tasks](#) involving levers and mazes. The investigators found that even a subtle decrease in the activity of the mediodorsal thalamus led to altered connectivity

between this brain region and the prefrontal cortex region and that the altered connectivity was associated with a variety of cognitive impairments experienced by patients with schizophrenia.

The findings likely apply to humans because patients with schizophrenia have decreased thalamic activity as well as altered connectivity between the thalamus and the prefrontal cortex. "Our work suggests that these two findings may be linked," explains co-senior author Dr. Joshua Gordon, also of Columbia University. "One next step would be to examine this relationship in patients. For example, one could ask whether deficits in thalamic activity and connectivity between the thalamus and [prefrontal cortex](#) are correlated with each other."

Cognitive symptoms of schizophrenia include problems with memory and behavioral flexibility, two processes that are essential for activities of daily living. These symptoms are resistant to current treatments, but this study's findings provide new information for the design of potentially more effective therapies that target the neuronal mechanisms underlying patients' cognitive problems.

More information: *Neuron*, Parnaudeau et al.: "Inhibition of medio-dorsal thalamus disrupts thalamo-frontal connectivity and cognition." [dx.doi.org/10.1016/j.neuron.2013.01.038](https://doi.org/10.1016/j.neuron.2013.01.038)

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