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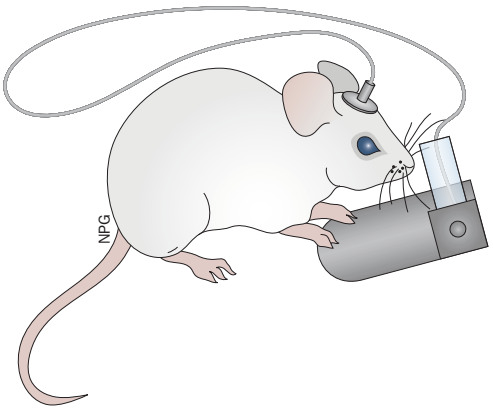
NEURODEVELOPMENTAL DISORDERS

Deep brain stimulation alleviates hippocampal memory deficit in a mouse model of Rett syndrome

Deep brain stimulation (DBS) of the fornix can increase neural activity and mitigate memory deficit in a mouse model of Rett syndrome, according to new research published in *Nature*. "These findings provide hope that DBS might enhance the cognitive abilities of individuals with Rett syndrome," comment Huda Zoghbi and Jianrong Tang, who led the study.

Forniceal DBS has previously been reported to improve memory in healthy individuals, and to retard the progression of Alzheimer disease in early trials. Inspired by these findings, Zoghbi, Tang and colleagues from the Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute (Houston, TX, USA) set out to study the effects of forniceal DBS on hippocampus-dependent memory in female *Mecp2*$^{+/-}$ mice, a well-characterized mouse model of Rett syndrome that reproduces the broad phenotype of the disorder, including cognitive deficits and motor dysfunction.



The investigators applied DBS in the fornix of awake, freely moving mice, using a stimulation frequency similar to that used in humans. Stimulation intensities were adjusted individually for each mouse to avoid seizures.

DBS restored hippocampus-dependent contextual fear and spatial memory in the Rett model mice to a level similar to that seen in sham-treated wild-type mice. No effect was seen on hippocampus-independent behaviours, such as cue-dependent fear memory, motor learning or anxiety.

"This might be the first study to show that neuromodulation improves the cognitive deficits and plasticity in an animal model of intellectual disability disorder," comments Zoghbi. Currently, only symptomatic treatment is available for Rett syndrome and other intellectual disability disorders.

The mechanisms through which DBS improved hippocampal learning remain elusive. "We found that DBS in the fornix increased hippocampal neurogenesis, which has been demonstrated to contribute to learning and memory," says Tang. The investigators plan to explore additional DBS targets to assess whether DBS could improve other symptoms of Rett disorder, such as dystonia and poor coordination.

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Original article Hao, S. *et al.* Forniceal deep brain stimulation rescues hippocampal memory in Rett syndrome mice. *Nature* doi:10.1038/nature15694