Fornix deep brain stimulation circuit effect is dependent on major excitatory transmission via the nucleus accumbens

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Deep brain stimulation (DBS) is a circuit-based treatment shown to relieve symptoms from multiple neurologic and neuropsychiatric disorders. In order to treat the memory deficit associated with Alzheimer’s disease (AD), several clinical trials have tested the efficacy of DBS near the fornix. Early results from these studies indicated that patients that received fornix DBS experienced an improvement in memory and quality of life, yet the mechanisms behind this effect remain controversial. It is known that transmission between the medial limbic and corticolimbic circuits plays an integral role in declarative memory and dysfunction at the circuit level results in various forms of dementia, including AD. Here, we aimed to determine the potential underlying mechanism of fornix DBS by examining the functional circuitry and structures of the brain engaged by fornix DBS. A multimodal approach was employed to examine global and local temporal changes that occur in an anesthetized swine model of fornix DBS. Changes in global functional activity were measured by functional MRI (fMRI) and local neurochemical changes were monitored by fast scan cyclic voltammetry (FSCV) during electrical stimulation of the fornix. Additionally, intracranial microinfusions into the nucleus accumbens (NAc) were performed to investigate the global activity changes that occur with dopamine and glutamate receptor-specific antagonism. Hemodynamic responses in both medial limbic and corticolimbic circuits measured by fMRI were induced by fornix DBS. Additionally, fornix DBS resulted in increases in dopamine oxidation current (corresponding to dopamine efflux) monitored by FSCV in the NAc. Finally, fornix DBS-evoked hemodynamic responses in the amygdala and hippocampus decreased following dopamine and glutamate receptor antagonism in the NAc. The present findings suggest that fornix DBS modulates dopamine release on pre-synaptic dopaminergic terminals in the NAc, involving excitatory glutamatergic input and that the medial limbic and corticolimbic circuits interact in a functional loop.

OCD in animal models using quinpirole as dopaminergic inductor of preservative behavior

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In the reviewed articles, quinpirole is used as a dopamine D2 and D3 receptor agonist to induce persistent behavior in animal models. Dopamine has been related to preservative behavior also has been related with the perception of pain and relief. The preservative behavior was observed in an open field with objects of different shapes and sizes. The main structures studied with this methodology are the orbitofrontal cortex, striatum, thalamus, basolateral amygdala and nucleus accumbens. The animal models studied comply with the face, predictive and construct validity.