Impact of vAChT Knockdown on Compulsive Grooming in a SAPAP3-KO Mouse Model of OCD

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Ranked as the fourth most common neurological disorder, obsessive-compulsive disorder (OCD) is characterized by symptoms including excessive or repetitive behaviors, otherwise known as compulsions. It is theorized that these compulsions are induced when the striatum, a brain region in the basal ganglia responsible for guiding decision-making and movement, is hyperactive. Knocking out the SAPAP3 gene, which encodes a postsynaptic scaffolding protein, causes the development of OCD-like symptoms in mice, including compulsive self-grooming. Recent reports demonstrated that the striatal dysfunction in the SAPAP3 knockout mice is associated with elevated striatal acetylcholine (ACh) release. In this project, mice that received experimental reductions of striatal ACh release via shRNA knockdown of the vesicular acetylcholine transporter (vAChT), a transporter that packages ACh into synaptic vesicles in SAPAP3 knockout mice, were analyzed. SAPAP3 knockout mice that received the vAChT knockdown treatment had reduced compulsive grooming compared to control mice that received a scrambled control treatment. These findings demonstrate that the striatal cholinergic system is a potential therapeutic target for modulating acetylcholine and treating OCD symptoms.

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