

# OFFICIAL ABSTRACT and CERTIFICATION

## Enhanced Cholinergic Interneuron Striatal Density Demonstrated in a SAPAP3 Knockout: An Indirect Quantification of Elevated Acetylcholine Levels in an OCD Mouse Model

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Obsessive Compulsive Disorder (OCD) is characterized by obsessive thoughts leading to compulsive behaviors. The cortico-striato-thalamo-cortical feedback loop is known to be implicated in OCD as an action selection pathway where the striatum decides between a "go pathway" or a "no-go pathway" for any specific action. 95% of striatal cells are spiny projection neurons (SPNs), comprised of direct SPNs (dSPNs) and indirect SPNs (iSPNs) which promote and inhibit action respectively. Preliminary data from our lab suggests that dSPNs are preferentially more excited and iSPNs are preferentially less excited in SAPAP3 KO OCD mouse models. Cholinergic interneurons (ChIs), the main source of striatal acetylcholine (ACh), have never been directly observed for participating in OCD's circuitry, but previous studies have altered ACh levels by directly manipulating ChIs which caused these mice to exhibit OCD-like behaviors of increased grooming and anxiety regardless of a rise or fall in ACh levels. Likewise, past papers have identified a rise in ACh binding to iSPNs' M1 (muscarinic) receptors to increase their excitability, and conversely decrease dSPNs' excitability when binded to their M4 receptors. Consequently, we hypothesized ChIs would participate in OCD's circuitry and modulated SPN excitability would be due to a decline in ACh. To investigate, we performed immunohistochemistry on SAPAP3 KO and WT mice for ChIs as an indirect quantification of ACh. Our results show a rise in ChI density in KO mice which demonstrates that ChIs are implicated in the circuitry and lowers the probability that ACh directly modulates SPN excitability in OCD mouse models.

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