# Investigating the effect of histamine hypofunction on the development of the bed nucleus of the stria terminalis (BNST) and Tourette's syndrome (TS)

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Tourette's syndrome (TS) and obsessive-compulsive disorder (OCD) are neurodevelopmental disorders affecting approximately 0.6% of the population. While their exact causes remain unclear, severe cases have been linked to mutations in the Hdc gene, the enzyme responsible for histamine production and patients with this mutation are seen to exhibit lowered histamine levels. While generally seen as disorders of the basal ganglia, both TS and OCD show a strong social component where stress and anxiety can reduce the ability to suppress tics. A key brain region in regulating stress and anxiety is the bed nucleus of the stria terminalis (BNST), which receives strong histaminergic input (Marquez-Gomez et al. 2023). We hypothesize that the BNST is a critical hub in the emergence of TS and OCD symptoms and that its development is altered by reduced histamine levels. To investigate this, we are developing a novel pharmacological mouse model of histamine hypofunction, in which histamine levels are reduced transiently during critical windows in brain development. Preliminary data from our lab shows that reduced levels of histamine during embryonic development significantly alter cell-cycle kinetics in embryonic brain regions giving rise to both BNST and striatal neurons, suggesting that transiently lowered histamine levels may impact the formation of brain circuits.