#17: Deletion of CTNNB1 in inhibitory circuitry contributes to autism-associated behavioral defects

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Mutations in Î²-catenin (CTNNB1) have been implicated in cancer and mental disorders. Recently, loss-of-function mutations of CTNNB1 were linked to intellectual disabilities (IDs), and rare mutations were identified in patients with autism spectrum disorders (ASD). As a key regulator of the canonical Wnt pathway, CTNNB1 has an essential role in neurodevelopment. However, the function of CTNNB1 in specific neuronal subtypes is unclear. To understand how CTNNB1 deficiency contributes to ASD, we generated CTNNB1 conditional knockout (cKO) mice in parvalbumin interneurons. cKO mice had increased anxiety, but had no overall change in motor function. Interestingly, CTNNB1 cKO in PV-interneurons significantly impaired object recognition and social interactions and elevated repetitive behaviors, which mimic the core symptoms of patients with ASD. Surprisingly, deleting CTNNB1 in parvalbumin-interneurons enhanced spatial memory. To determine the effect of CTNNB1 KO in overall neuronal activity, we found that c-fos was significantly reduced in the cortex, but not in the dentate gyrus and the amygdala. Our findings revealed a cell type specific role of CTNNB1 gene in regulation of cognitive and autistic-like behaviors. Thus, this study has important implications for development of therapies for ASDs carrying the CTNNB1 mutation or other ASDs that are associated with mutations in the Wnt pathway. In addition, our study contributes to a broader understanding of the regulation of the inhibitory circuitry.