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Abstract

Pitt-Hopkins Syndrome (PTHS), a rare neurodevelopmental disorder resulting from TCF4 gene haploinsufficiency, leads to profound cognitive challenges, including intellectual disability and learning and memory deficits. Understanding the neural basis of these cognitive impairments is essential for advancing therapies. Dendritic spines, minute protrusions on neurons, are key players in synaptic connections and memory formation, making their morphology a vital focus. Changes in spine characteristics are linked to various neurological disorders, including autism spectrum disorder. This research explores how TCF4 haploinsufficiency in PTHS may affect dendritic spine morphology, specifically in the hippocampus, but also in the cortex, and its role in learning and memory deficits. By comparing dendritic spine characteristics between a novel PTHS mouse model, which exhibits TCF4 haploinsufficiency, and wildtype mice, we aim to test the hypothesis that TCF4 haploinsufficiency leads to a reduction in spine number and concurrent alterations in their size and shape. Through Golgi staining, widefield microscopy, and future image analysis, this investigation lays the groundwork to elucidate the intricate relationship between dendritic spine structure and cognitive function in PTHS, potentially paving the way for therapeutic advancements and improved quality of life for affected individuals.