Demonstrating a Potential Causative Link Between Dendritic Degeneration and Hydrocephalus Using Par3 Conditional Knockout Mouse Models

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Hydrocephalus is a neurological condition characterized by a buildup of cerebrospinal fluid (CSF) within the ventricles of the brain. This CSF accumulation results in the dilation of cerebral ventricles and increased intracranial pressure, causing deficits in memory, information processing, and executive function. Dendritic spines are the main postsynaptic target of excitatory synaptic inputs. Spine dysfunction has been implicated to be a common substrate among disorders associated with cognitive impairment. However, its relation to hydrocephalus has rarely been examined. Thus, this study aims to evaluate the effects of hydrocephalus on dendritic morphology of hippocampal pyramidal neurons. We found neonatal Par3 Nestin-Cre conditional knockout (cKO) mice developed severe hydrocephalus. To determine if dendritic alterations were caused by hydrocephalus or by the loss of Par3 in neurons, a Par3 CaMK2a-Cre cKO mouse model was first utilized. Brain tissue blocks of CaMK2a-Cre mice were impregnated using Golgi staining to determine morphology. Spine densities were calculated using ImageJ analysis software. Compared to age-matched controls, Par3 CaMK2a-Cre mice revealed a statistically significant reduction in mean spine density (129.65±5.66 spines/100μm vs. 100.65±3.89 spines/100μm). These hippocampal changes indicate that neuronal Par3 loss contributes to dendritic degeneration. To fully identify the role of hydrocephalus, an inducible Nestin-Cre line is needed in the future. A causative link between dendritic degeneration and hydrocephalus would suggest that changes in dendritic morphology may be the structural basis behind the neurobehavioral deficits of hydrocephalus. Such knowledge can lead to more targeted therapeutics for disorders related to synaptic malformation.

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