Maternal hypothyroxinemia impairs spatial learning and synaptic nature and function in the offspring

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Abstract

Neurological deficits in the offspring caused by human maternal hypothyroxinemia are thought to be irreversible. To understand the mechanism responsible for these neurological alterations, we induced maternal hypothyroxinemia in pregnant rats. Behavior and synapse function were evaluated in the offspring of thyroid hormone-deficient rats. Our data indicate that, when compared with controls, hypothyroxinemic mothers bear litters that, in adulthood, show prolonged latencies during the learning process in the water maze test. Impaired learning capacity caused by hypothyroxinemia was consistent with cellular and molecular alterations, including: 1) lack of increase of phosphorylated c-fos on the second day of the water maze test; 2) impaired induction of long-term potentiation in response to theta-burst stimulation to the Schaffer collateral pathway in the area 1 of the hippocampus Ammon's horn stratum radiatum, despite normal responses for input/output experiments; 3) increase of postsynaptic density protein 95 (PSD-95), N-methyl-D-aspartic acid receptor subunit 1, and tyrosine receptor kinase B levels in brain extracts; and 4) significant increase of PSD-95 at the PSDs and failure of this molecule to colocalize with N-methyl-D-aspartic acid receptor subunit 1, as it was shown by control rats. Our findings suggest that maternal hypothyroxinemia is a harmful condition for the offspring that can affect key molecular components for synaptic function and spatial learning.