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Letter to Editor

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Perinatal Hypothyroidism and Cytoskeleton Dysfunction

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Thyroid hormones (THs) are necessary for normal development particularly cytoskeletal system. Cytoskeletal system which consists of microtubules (Tubulin), microfilaments (Actin), and intermediate filaments, specific for neurons (Neurofilaments), glia (Glial Fibrillary Acidic Protein), or maturing cells (Vimentin, Nestin) can play important roles in neural cell shape and neuronal migration and outgrowth [1-40]. THs regulate and reorganize this system by non-genomic actions. Moreover, THs regulate the expression of extracellular matrix (ECM) and adhesion molecules that are important for neuronal migration and development, such as tenascin-C, neural cell adhesion molecule (N-CAM), reelin and dab1, laminin and fibronectin. Maternal THs controls the expression of neuronal migration and growth, branching of neurites, astrocytic cytoskeletal proteins, cell cycle regulators, neurotrophins and neurotrophin receptors and extracellular matrix proteins in the fetal brain [41-45].

In maternal hypothyroidism, there was reduction in the expression of GFAP protein in fetal brain in late gestation. In neonatal hypothyroid rats, the actin fibers are disorganized in brain (cerebellum). Also, the disruptions of laminin and developing cerebellum of hypothyroid rats were observed by Farwell et al. [40-45]. This alters the development of cellular cytoskeleton, synthesis of microtubule protein, axonal transport, neuronal outgrowth and neuronal behavior. These abnormalities might be attributed to the abnormalities in the development of cellular cytoskeleton (stabilization and composition of microtubule protein and in the delivery of cytoskeletal proteins to developing terminals via the slow component of axonal transport [40-48]. In parallel, the early postnatal hypothyroidism in rats raises both RNA and protein levels of tenascin-C in cerebellar Bergmann glia. On the other hand, Evans et al. [40] reported that maternal hyperthyroidism changes the expression of neuronal cytoskeletal proteins and accelerate the fetal neuronal differentiation. In agreement with this result, hypothyroidism reduced the matrix glia protein (MGP) mRNA levels while hyperthyroidism upregulated the MGP gene [34]. Moreover, the neurotrophins, in particular brain-derived neurotrophic factor (BDNF), are important in the course of development and are reduced in hypothyroidism [48-50] and increased in hyperthyroidism [30]. Also, T4 inhibits the activity of deiodinase 2 (D2) at the post-translational level including the microfilaments (Actin) [50]. The window of time for TH-dependent regulation of these processes is limited to pre- and perinatal life in rodents [42-45] neuronal cytoskeleton and neuronal growth either by affecting the developmental programs for expression of specific isoforms [50-59]. Thus, I may infer that thyroid disorders during the development can disrupt the cytoskeleton system, mitochondrial functions and gene expression. Further work is therefore required to determine whether normalization of circulatory THs levels can prevent the disturbance of fetal brain cytoskeletal protein expression.

Conflict of Interest

The author declares that no competing financial interests exist.

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