

Short Communication

Maternal Hypothyroidism and Multiple Sclerosis: Disruption the Developing Neuroendocrine System

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Maternal thyroid hormones (THs; 3,5,3'-triiodothyronine (T3) and thyroxin (T4)) have dynamic trophic actions during the perinatal development [1-76], in particular the developing brain and myelination process [5,66,77-81]. It is widely known that the appropriate myelinated growth, at postnatal day 25 in the rat, is responsible for protection and insulation of axons and is vital for the function of Central Nervous System (CNS), in particular the learning and memory function [82-84]. Alternatively, there is a link between the hypothyroidism and the vulnerability of the CNS to inflammatory diseases by the thymus or spleen (cells of the immune system). In maternal hypothyroidism, the dysfunction in the thymic selection increases the accumulation of autoimmune T cells and the risk of autoimmune-inflammatory disorders in the offspring [85], such as multiple sclerosis [86]. Multiple sclerosis is a long-lasting, neuroinflammatory demyelinating dysfunction of the CNS that mostly disturbs young adults [87,88]. The etiology of multiple sclerosis might be due to a disturbance in the genetic process, immunological (autoimmune disorders), infectious, or environmental factors [89]. Symptoms of multiple sclerosis during pregnancy are urinary insistence, fatigue, lower extremities paresthesias and gait difficulties [90,91].

On the other hand, deficiency in the levels of maternal THs during the gestation can decrease the growth and differentiation of myelinated axons [86,92], and cause permanent defects in the developing CNS including a mental retardation and cognitive disturbances [5,84,93,94]. In mild-moderate iodine insufficiency, maternal and neonatal hypothyroxinemia, a low circulating free T4 with no change in free T3 or thyroid stimulating hormone (TSH), can disrupt the levels of nuclear Myelin Binding Protein (MBP) and increase the apoptosis causing a reduction in the cellular survival [95]. More importantly, Wei et al. [94] reported that hypothyroxinemia due to the maternal mild iodine decreases the expression of myelin-related proteins and delays the growth of neonatal myelination. Notably, a reduction in the levels of gestational THs can increase the severity of multiple sclerosis [86,96].

From the preceding results, the present overview presumed that any disorders in the activity of maternal thyroid gland during the gestation may increase the demyelination (hypomyelination) and

decrease the thickness of the myelin sheath. These disruptions may increase the vulnerability of the CNS to multiple sclerosis and several inflammatory-immune impairments.

As well, the gestational hypothyroidism associated with the multiple sclerosis may cause the following:

- (1) Perturb the neural organization and synaptogenesis,
- (2) Delay the development and progress of the fetal and neonatal neuroendocrine system (thyroid-brain axis),
- (3) increase the teratogenic consequences;
- (4) increase the risk of developing brain disorders (mental retardation or cognitive disorders); and
- (5) Delay the fetal and neonatal development generally.

Thus, both diseases may be a major avoidable health problem worldwide. These conditions may be depending on the severity, distribution and time of both diseases. Though, their molecular mechanisms are obscure. To date, it is not obvious whether the described effects of both diseases on the fetal or neonatal neuroendocrine system in experimental animal models might be fitted to human health. These observations strongly recommend assessing maternal THs and treating hypothyroidism before or during the gestation to avoid the vulnerability to any inflammatory diseases, in particular, multiple sclerosis in the fetal or neonatal CNS. Further experiments are influential to examine the impact of maternal hypothyroidism and multiple sclerosis on the fetal and neonatal neuroendocrine system (thyroid-brain axis). Moreover, the molecular and immunological variation due to both diseases during the gestation and lactation periods should be addressed. This could assist to understand the pathogenesis of both diseases and planning new therapeutic approaches.

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