ARC Journal of Neuroscience
Volume 3, Issue 1 2018, PP 5-8
ISSN 2456-057X
DOI: http://dx.doi.org/10.20431/2456-057X.0301002
www.arcjournals.org

Is there a Connection between Maternal Hypothyroidism and Developing Autism Spectrum Disorders?

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LETTER TO EDITOR

The activities of maternal thyroid hormones (THs) can induce important actions on the neural development, synaptogenesis, and normal brain development during the perinatal period (El-bakry et al., 2010; Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-u & 2018a-c; Ahmed et al., 2010, 2013a,b, 2014, 2015a,b & 2018a,b; Ahmed and Incerpi, 2013;Van Hercket al., 2013; Ahmed and El-Gareib, 2014,Incerpi et al., 2014; Candelotti et al., 2015; De Vito et al., 2015; El-Ghareeb et al., 2016; Ahmed and El-Gareib, 2017).Several authors mentioned that autism spectrum disorders (ASD)(group of neuropsychiatric disorders) is characterized by the alterations and impairments in the neuroanatomical, morphological, neuro chemical, movements, social, and language interactions in different brain regions such as the basal ganglia, corpus callosum, cerebellum, and limbic system (Rosenberg et al., 2009; Anney et al., 2010; Sajdel-Sulkowska et al., 2010). In addition, Roman (2007) and King (2011) observed that the maternal hypothyroidism during the gestation could disrupt the neural development and functions, and increase the risk of ASD. In addition, Ahmed et al. (2008) and Melancia et al. (2017) postulated that maternal thyroid hypothyroidism increased the risk of several neonatal neuro developmental disorders. These abnormalities may be probably due to the following: **(1)** the diminution in the activity of deiodinase 2 (D2) (reduced the conversion of thyroxine (T4) to 3,5,3'-triodothyronine (T3)) (Davis et al., 2008); and **(2)** the abnormal metabolism in the intra cerebellar TH due to the elevation in the activity of D3 in the cerebrospinal fluid (CSF) could increase the levels of reverse T3(rT3) and the ratio of rT3:T4 (Sampaolo et al., 2005).More interestingly, the levels of free rT3 and T4 in the CSF were augmented during the endogenous depression (Kirkegaard and Faber, 1991).On the other hand, hypothyroidism can alter the expression of genes in different brain regions (Van Hercket al., 2013). A systemic hypothyroidism in developing rat cerebellum can disrupt the migration of several cerebellar cells (granule and Purkinje cells) inducing several alterations in the gene expressions (Miyata et al., 2010). Reelin gene is regulated by the T3 in fetal brain, is responsible for the migration of neuronal cells, and is implicated in the developing ASD (Fatemi et al., 2005; Sampaolo et al., 2005; Verhoelst et al., 2005; Davis et al., 2008; Miyata et al., 2010). However, the associations between the maternal thyroid deficiency and the onset of neonatal ASD are still debated.

From the connection between the aforementioned explanations and the current view, it can be concluded that the developing autism due to the maternal hypothyroidism may be disrupted the activities of D2 and D3, the levels of T4 and T3, and the gene and thyroid receptors (TRs) expression resulting in a region specific T3 deficiency in the neonatal brain. These maternal disorders may impair the social, learning, and economic interactions for the neonates. Future studies are warranted to explore the developmental and molecular interactions of maternal thyroid dysfunction (thyroid stimulating hormone (TSH), T4 and T3) and autism development. Other studies are required to determine the activities of Ds and gene expression in ASD.

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Citation: *Ahmed R.G. Is there a Connection between Maternal Hypothyroidism and Developing Autism Spectrum Disorders?. ARC Journal of Neuroscience. 2018; 3(1):5-8. doi:dx.doi.org/10.20431/2456-057X.0301002.*