

Multidirectional Imprinting of Maternofetal Thyroid Hormones

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The regular activities of thyroid hormones (THs) are essential for the fetal and neonatal development (El-bakry et al., 2010; Ahmed, 2011, 2012a,b, 2013, 2014, 2015a-c, 2016a-d, 2017a-o; Ahmed et al., 2008, 2010, 2012, 2013a,b, 2014; 2015a,b; Ahmed and Ahmed, 2012; Ahmed and Incerpi, 2013; Van Herck et 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; Endendijk et al., 2017; Gigena et al., 2017). The hypothyroidism during the gestation can cause several irreversible damages in the central nervous system (CNS) (Ahmed et al., 2008; Forhead and Fowden, 2014; ATA, 2015; Opazo et al., 2017). The neural damages include the following:

- Variation in developing CNS (Iskaros et al., 2000; Zhang and Lazar, 2000; Collazos et al., 2003; Pop et al., 2003; Ausó et al., 2004; Bianco and Larsen, 2005; Buimer et al., 2005; Cuevas et al., 2005; Klecha, 2006; Cheng et al., 2010; Raymond and LaFranchi, 2010; Negro et al., 2011; Moleti et al., 2011; Patel et al., 2011; Stagnaro-Green et al., 2011; Gessl et al., 2012; Parkes et al., 2012; Ramprasad and Bhattacharyya, 2012; Bernal and Morte, 2013; Chang and Pearce, 2013; Pascual and Aranda, 2013; Forhead and Fowden, 2014; Schroeder and Privalsky, 2014; Somberg and Molnar, 2016);
- Distortion the cellular migration and outgrowth (Martinez-Galan et al., 1997; Ausó et al., 2004; Cuevas et al., 2005; Ahmed et al., 2008; Cheng et al., 2010); disturbance in the neurotransmitter system (Wu et al., 2010; Cattani et al., 2013; Koromilas et al., 2014; pazo et al., 2017);

- Decrease the regulation of Myelin Basic Protein (MBP) (O'Shea and Williams, 2002; Bernal et al., 2003; Calza et al., 2005);
- Increased the apoptosis and the cellular death (Koromilas et al., 2010; pazo et al., 2017);
- Distortion in the neurite growth and axon of hippocampal regions (CA1-3) (Ahmed et al., 2008; Opazo et al., 2008; Koromilas et al., 2010);
- Disturbance in the spatial learning related to c-Fos and c-Jun genes (Opazo et al., 2008); and
- Reduction in the formation of myelinated axons (O'Shea and Williams, 2002; pazo et al., 2017).

On the other hand, the gestational hypothyroidism can alter the immune system.

- Diminish the leukocytes and the cellular number of B cells and T cells in thymus and spleen (Rooney et al., 2003);
- Decrease the weight of thymus and spleen (Erf, 1993; pazo et al., 2017);
- Elevate the number of lymphocytes (Albornoz et al., 2013) and inflammatory cells (Nieto et al., 2016; pazo et al., 2017); and
- Disturb the ratio of CD8+ and CD4+ T cells (Erf, 1993).

On the basis of these data, it can be decided that the THs are significant for the maturation of CNS and immune system though the mechanisms triggered in immune cells are uncommon. Also, the gestational THs insufficiency may distort the maternofetal immune response. However, the mechanism of this disturbance remains still indefinite.

Additional studies are necessary to improve the quality of our life.

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REFERENCES

- [1] Ahmed, O.M., Abd El-Tawab, S.M., Ahmed, R.G., 2010. Effects of experimentally induced maternal hypothyroidism and hyperthyroidism on the development of rat offspring: I- The development of the thyroid hormones-neurotransmitters and adenosinergic system interactions. *Int. J. Dev. Neurosci.* 28, 437-454.
- [2] Ahmed, O.M., Ahmed, R.G., 2012. Hypothyroidism. In *A New Look At Hypothyroidism*. Dr. D. Springer (Ed.), ISBN: 978-953-51-0020-1), In Tech Open Access Publisher, Chapter 1, pp. 1-20.
- [3] Ahmed, O.M., Ahmed, R.G., El-Gareib, A.W., El-Bakry, A.M., Abd El-Tawaba, S.M., 2012. Effects of experimentally induced maternal hypothyroidism and hyperthyroidism on the development of rat offspring: II-The developmental pattern of neurons in relation to oxidative stress and antioxidant defense system. *Int. J. Dev. Neurosci.* 30, 517-537.
- [4] Ahmed, O.M., El-Gareib, A.W., El-bakry, A.M., Abd El-Tawab, S.M., Ahmed, R.G., 2008. Thyroid hormones states and brain development interactions. *Int. J. Dev. Neurosci.* 26(2), 147-209. Review.
- [5] Ahmed, R.G., 2011. Perinatal 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin exposure alters developmental neuroendocrine system. *Food Chem. Toxicology*, 49, 1276-1284.
- [6] Ahmed, R.G., 2012a. Maternal-newborn thyroid dysfunction. In the *Developmental Neuroendocrinology*, pp. 1-369. Ed R.G. Ahmed. Germany: LAP LAMBERT Academic Publishing GmbH & Co KG.
- [7] Ahmed, R.G., 2012b. Maternal-fetal thyroid interactions, *Thyroid Hormone*, Dr. N.K. Agrawal (Ed.), ISBN: 978-953-51-0678-4, In Tech Open Access Publisher, Chapter 5, pp. 125-156.
- [8] Ahmed, R.G., 2013. Early weaning PCB 95 exposure alters the neonatal endocrine system: thyroid adipokine dysfunction. *J. Endocrinol.* 219 (3), 205-215.
- [9] Ahmed, R.G., 2014. Editorial: Do PCBs modify the thyroid-adipokine axis during development? *Annals Thyroid Res.* 1(1), 11-12.
- [10] Ahmed, R.G., 2015a. Chapter 1: Hypothyroidism and brain development. In *Advances in hypothyroidism treatment*. Avid Science Borsigstr. 9, 10115 Berlin, Berlin, Germany. Avid Science Publications level 6, Melange Towers, Wing a, Hitec City, Hyderabad, Telangana, India. pp. 1-40.
- [11] Ahmed, R.G., 2015b. Hypothyroidism and brain developmental players. *Thyroid Research J.* 8(2), 1-12.
- [12] Ahmed, R.G., 2015c. Editorials and Commentary: Maternofetal thyroid action and brain development. *J. of Advances in Biology;* 7(1), 1207-1213.
- [13] Ahmed, R.G., 2015d. Developmental adipokines and maternal obesity interactions. *J. of Advances in Biology;* 7(1), 1189-1206.
- [14] Ahmed, R.G., 2016a. Maternal bisphenol A alters fetal endocrine system: Thyroid adipokine dysfunction. *Food Chem. Toxicology*, 95, 168-174.
- [15] Ahmed, R.G., 2016b. Gestational dexamethasone alters fetal neuroendocrine axis. *Toxicology Letters*, 258, 46-54.
- [16] Ahmed, R.G., 2016c. Maternal iodine deficiency and brain disorders. *Endocrinol. Metab. Syndr.* 5, 223. <http://dx.doi.org/10.4172/2161-1017.1000223>.
- [17] Ahmed, R.G., 2016d. Neonatal polychlorinated biphenyls-induced endocrine dysfunction. *Ann. Thyroid. Res.* 2 (1), 34-35.
- [18] Ahmed, R.G., 2017a. Developmental thyroid diseases and GABAergic dysfunction. *EC Neurology* 8.1, 02-04.
- [19] Ahmed, R.G., 2017b. Hyperthyroidism and developmental dysfunction. *Arch Med.* 9, 4.
- [20] Ahmed, R.G., 2017c. Anti-thyroid drugs may be at higher risk for perinatal thyroid disease. *EC Pharmacology and Toxicology* 4.4, 140-142.
- [21] Ahmed, R.G., 2017d. Perinatal hypothyroidism and cytoskeleton dysfunction. *Endocrinol Metab Syndr* 6, 271. doi:10.4172/2161-1017.1000271
- [22] Ahmed, R.G., 2017e. Developmental thyroid diseases and monoaminergic dysfunction. *Advances in Applied Science Research* 8(3), 01-10.
- [23] Ahmed, R.G., 2017f. Hypothyroidism and brain development. *J. Anim Res Nutr.* 2(2), 13.
- [24] Ahmed, R.G., 2017g. Antiepileptic drugs and developmental neuroendocrine dysfunction: Every why has A Wherefore. *Arch Med* 9(6), 2.
- [25] Ahmed, R.G., 2017h. Gestational prooxidant-antioxidant imbalance may be at higher risk for postpartum thyroid disease. *Endocrinol Metab Syndr* 6, 279. doi:10.4172/2161-1017.1000279.
- [26] Ahmed, R.G., 2017i. Synergistic actions of thyroid-adipokines axis during development. *Endocrinol Metab Syndr* 6, 280. doi:10.4172/2161-1017.1000280.
- [27] Ahmed, R.G., 2017j. Thyroid-insulin dysfunction during development. *International*

- Journal of Research Studies in Zoology 3(4), 73-75. DOI: <http://dx.doi.org/10.20431/2454-941X.0304010>.
- [28] Ahmed, R.G., 2017k. Developmental thyroid diseases and cholinergic imbalance. *International Journal of Research Studies in Zoology* 3(4), 70-72. DOI: <http://dx.doi.org/10.20431/2454-941X.0304009>.
- [29] Ahmed, R.G., 2017l. Thyroid diseases and developmental adenosinergic imbalance. *Int J Clin Endocrinol* 1(2), 053-055.
- [30] Ahmed, R.G., 2017m. Maternal anticancer drugs and fetal neuroendocrine dysfunction in experimental animals. *Endocrinol Metab Syndr* 6, 281. doi:10.4172/2161-1017.1000281.
- [31] Ahmed, R.G., 2017n. Letter: Gestational dexamethasone may be at higher risk for thyroid disease developing peripartum. *Open Journal Of Biomedical & Life Sciences (Ojbili)* 3(2), 01-06.
- [32] Ahmed, R.G., 2017o. Deiodinases and developmental hypothyroidism. *EC Nutrition* 11.5, 183-185.
- [33] Ahmed, R.G., Abdel-Latif, M., Ahmed F., 2015b. Protective effects of GM-CSF in experimental neonatal hypothyroidism. *International Immunopharmacology* 29, 538–543.
- [34] Ahmed, R.G., Abdel-Latif, M., Mahdi, E., El-Nesr, K., 2015a. Immune stimulation improves endocrine and neural fetal outcomes in a model of maternofetal thyrotoxicosis. *Int. Immunopharmacol.* 29, 714-721.
- [35] Ahmed, R.G., Davis, P.J., Davis, F.B., De Vito, P., Farias, R.N., Luly, P., Pedersen, J.Z., Incerpi, S., 2013b. Nongenomic actions of thyroid hormones: from basic research to clinical applications. An update. *Immunology, Endocrine & Metabolic Agents in Medicinal Chemistry*, 13(1), 46-59.
- [36] Ahmed, R.G., El-Gareib, A.W. 2014. Lactating PTU exposure: I- Alters thyroid-neural axis in neonatal cerebellum. *Eur. J. of Biol. and Medical Sci. Res.* 2(1), 1-16.
- [37] Ahmed, R.G., El-Gareib, A.W., 2017. Maternal carbamazepine alters fetal neuroendocrine-cytokines axis. *Toxicology* 382, 59–66.
- [38] Ahmed, R.G., El-Gareib, A.W., Incerpi, S., 2014. Lactating PTU exposure: II- Alters thyroid-axis and prooxidant-antioxidant balance in neonatal cerebellum. *Int. Res. J. of Natural Sciences* 2(1), 1-20.
- [39] Ahmed, R.G., Incerpi, S., 2013. Gestational doxorubicin alters fetal thyroid–brain axis. *Int. J. Devl. Neuroscience* 31, 96–104.
- [40] Ahmed, R.G., Incerpi, S., Ahmed, F., Gaber, A., 2013a. The developmental and physiological interactions between free radicals and antioxidant: Effect of environmental pollutants. *J. of Natural Sci. Res.* 3(13), 74-110.
- [41] Albornoz, E.A., Carreó, L.J., Cortés, C., et al., 2013. Gestational hypothyroidism increases the severity of experimental autoimmune encephalomyelitis in adult offspring. *Thyroid* 23, 1627–1637.
- [42] ATA, 2015. American Thyroid Association.
- [43] Ausó, E., Lavado-Autric, R., Cuevas, E., et al., 2004. A moderate and transient deficiency of maternal thyroid function at the beginning of fetal neocortico-genesis alters neuronal migration. *Endocrinology* 145, 4037–4047.
- [44] Bernal, J., Guadano-Ferraz, A., Morte, B., 2003. Perspectives in the study of thyroid hormone action on brain development and function. *Thyroid* 13, 1005–1012.
- [45] Bernal, J., Morte, B., 2013. Thyroid hormone receptor activity in the absence of ligand: physiological and developmental implications. *Biochim Biophys Acta* 1830, 3893–3899.
- [46] Bianco, A.C., Larsen, P.R., 2005. Cellular and structural biology of the deiodinases. *Thyroid* 15, 777–786.
- [47] Buimer, M., van Wassenaer, A.G., Ganzevoort, W., et al., 2005. Transient hypothyroxinemia in severe hypertensive disorders of pregnancy. *Obstet Gynecol* 106, 973–979.
- [48] Calza, L., Fernandez, M., Giuliani, A., et al., 2005. Thyroid hormone and remyelination in adult central nervous system: a lesson from an inflammatory-demyelinating disease. *Brain Res Brain Res Rev.* 48, 339–346.
- [49] Candelotti, E., De Vito, P., Ahmed, R.G., Luly, P., Davis, P.J., Pedersen, J.Z., Lin, H-Y., Incerpi, I., 2015. Thyroid hormones crosstalk with growth factors: Old facts and new hypotheses. *Immun., Endoc. & Metab. Agents in Med. Chem.*, 15, 71-85.
- [50] Cattani, D., Goulart, P.B., de Liz Oliveira Cavalli, V.L., et al., 2013. Congenital hypothyroidism alters the oxidative status, enzyme activities and morphological parameters in the hippocampus of developing rats. *Mol Cell Endocrinol.* 375, 14–26.
- [51] Chang, D.L.F., Pearce, E.N., 2013. Screening for maternal thyroid dysfunction in pregnancy: a review of the clinical evidence and current guidelines. *J Thyroid Res* 851326.
- [52] Cheng, S-Y., Leonard, J.L., Davis, P.J., 2010. Molecular aspects of thyroid hormone actions. *Endocr Rev.* 31, 139–170.
- [53] Collazos, J., Ibarra, S., Mayo, J., 2003. Thyroid hormones in HIV infected patients in the highly active antiretroviral therapy era: evidence of an interrelation between the thyroid axis and the immune system. *Aids* 17, 763–765.

- [54] Cuevas, E., Auso, E., Telefont, M., et al., 2005. Transient maternal hypothyroxinemia at onset of corticogenesis alters tangential migration of medial ganglionic eminence derived neurons. *Eur J Neurosci.* 22, 541–551.
- [55] De Vito, P., Candelotti, E., Ahmed, R.G., Luly, P., Davis, P.J., Incerpi, S., Pedersen, J.Z., 2015. Role of thyroid hormones in insulin resistance and diabetes. *Immun., Endoc. & Metab. Agents in Med. Chem.*, 15, 86-93.
- [56] El-bakry, A.M., El-Ghareeb, A.W., Ahmed, R.G., 2010. Comparative study of the effects of experimentally-induced hypothyroidism and hyperthyroidism in some brain regions in albino rats. *Int. J. Dev. Neurosci.* 28, 371-389.
- [57] El-Ghareeb, A.A., El-Bakry, A.M., Ahmed, R.G., Gaber, A., 2016. Effects of zinc supplementation in neonatal hypothyroidism and cerebellar distortion induced by maternal carbimazole. *Asian Journal of Applied Sciences* 4(04), 1030-1040.
- [58] Endendijk, J.J., Wijnen, H.A.A., Pop, V.J.M., van Baar, A.L., 2017. Maternal thyroid hormone trajectories during pregnancy and child behavioral problems. *Hormones & Behav.* 94, 84–92.
- [59] Erf, G.F., 1993. Immune development in young-adult C.RF-hyt mice is affected by congenital and maternal hypothyroidism. *Proc Soc Exp Biol Med* 204, 40–48.
- [60] Forhead, A.J., Fowden, A.L., 2014. Thyroid hormones in fetal growth and parturition maturation. *J Endocrinol.* 221, R87–R103.
- [61] Gessl, A., Lemmens-Gruber, R., Kautzky-Willer, A., 2012. Thyroid disorders. *Handb Exp Pharmacol.* 361–386.
- [62] Gigena, N., Alamino, V.A., Montesinos, M.M., Nazar, M., Louzada, R.A., Wajner, S.M., Maia, A.L., Masini-Repiso, A.M., Carvalho, D.P., Cremaschi G.A., Pellizas, C.G., 2017. Dissecting thyroid hormone transport and metabolism in dendritic cells. *J. Endocrinology* 232, 337–350.
- [63] Incerpi, S., Hsieh, M-T., Lin, H-Y., Cheng, G-Y., De Vito, P., Fiore, A.M., Ahmed, R.G., Salvia, R., Candelotti, E., Leone, S., Luly, P., Pedersen, J.Z., Davis, F.B., Davis, P.J., 2014. Thyroid hormone inhibition in L6 myoblasts of IGF-I-mediated glucose uptake and proliferation: new roles for integrin $\alpha\beta3$. *Am. J. Physiol. Cell Physiol.* 307, C150–C161.
- [64] Iskaros, J., Pickard, M., Evans, I., Sinha, A., 2000. Thyroid hormone receptor gene expression in first trimester human fetal brain. *J Clin Endocrinol Metab.* 85, 2620–2623.
- [65] Klecha, A.J., 2006. Integrative study of hypothalamus-pituitary thyroid-immune system interaction: thyroid hormone mediated modulation of lymphocyte activity through the protein kinase C signaling pathway. *J Endocrinol* 189, 45–55.
- [66] Koromilas, C., Liapi, C., Schulpis, K.H., et al., 2010. Structural and functional alterations in the hippocampus due to hypothyroidism. *Metab Brain Dis.* 25, 339–354.
- [67] Koromilas, C., Liapi, C., Zarros, A., Stolakis, V., 2014. Effects of experimentally-induced maternal hypothyroidism on crucial offspring rat brain enzyme activities. *Int J Dev Neurosci.* 1–6.
- [68] Martinez-Galan, J.R., Pedraza, P., Santacana, M., et al., 1997. Early effects of iodine deficiency on radial glial cells of the hippocampus of the rat fetus. A model of neurological cretinism. *J Clin Invest.* 99, 2701–2709.
- [69] Moleti, M., Trimarchi, F., Vermiglio, F., 2011. Doubts and concerns about isolated maternal hypothyroxinemia. *J Thyroid Res* 1–7.
- [70] Negro, R., Soldin, O.P., Obregon, M-J., Stagnaro-Green, A., 2011. Hypothyroxinemia and pregnancy. *Endocr Prac: Off J Am Coll Endocrinol Am Assoc Clin Endocrinologists* 17, 422–429.
- [71] Nieto, P.A., Penalzoa, H.F., Salazar-Echegarai, F.J., et al., 2016. Gestational hypothyroidism improves the ability of the female offspring to clear *Streptococcus pneumoniae* infection and to recover from pneumococcal pneumonia. *Endocrinology* en20151957.
- [72] O’Shea, P.J., Williams, G.R., 2002. Insight into the physiological actions of thyroid hormone receptors from genetically modified mice. *J Endocrinol.* 175, 553–570.
- [73] Opazo, M.C., Gianini, A., Pancetti, F., et al., 2008. Maternal hypothyroxinemia impairs spatial learning and synaptic nature and function in the offspring. *Endocrinology* 149, 5097–5106.
- [74] Opazo, M.C., Haensgen, H., Bohmwald, K., Venegas, L.F., Boudin, H., Elorza, A.A., Simon, F., Fardella, C., Bueno, S.M., Kalergis, A.M., Riedel, C.A., 2017. Imprinting of maternal thyroid hormones in the offspring. *International Reviews of Immunology*, DOI: 10.1080/08830185.2016.1277216.
- [75] Parkes, I.L., Schenker, J.G., Shufaro, Y., 2012. Thyroid disorders during pregnancy. *Gynecol Endocrinol.* 28, 993–998.
- [76] Pascual, A., Aranda, A., 2013. Thyroid hormone receptors, cell growth and differentiation. *Biochim Biophys Acta* 1830, 3908–3916.
- [77] Patel, J., Landers, K., Li, H., et al., 2011. Thyroid hormones and fetal neurological development. *J Endocrinol* 209, 1–8.
- [78] Pop, V.J., Brouwers, E.P., Vader, H.L., et al., 2003. Maternal hypothyroxinaemia during early

- pregnancy and subsequent child development: a 3-source follow-up study. *Clin Endocrinol (Oxf)* 59, 282-288.
- [79] Ramprasad, M., Bhattacharyya, S.S., Bhattacharyya, A., 2012. Thyroid disorders in pregnancy. *Indian J Endocr Metab.* 16, S167–S170.
- [80] Raymond, J., LaFranchi, S.H., 2010. Fetal and neonatal thyroid function: review and summary of significant new findings. *Curr Opin Endocrinol, Diabetes, Obes.* 17, 1–7.
- [81] Rooney, A.A., Fournier, M., Bernier, J., Cyr, D.G., 2003. Neonatal exposure to propylthiouracil induces a shift in lymphoid cell sub-populations in the developing postnatal male rat spleen and thymus. *Cell. Immunol.* 91–102.
- [82] Schroeder, A.C., Privalsky, M.L., 2014. Thyroid hormones, T3 and T4, in the brain. *Front. Endocrinol.* 5, 40.
- [83] Somberg, J., Molnar, J., 2016. Adverse reactions of amiodarone on the thyroid. *Cardiology* 134, 364–365.
- [84] Stagnaro-Green, A., Abalovich, M., Alexander, E., et al., 2011. Guidelines of the American thyroid association for the diagnosis and management of thyroid disease during pregnancy and postpartum. *Thyroid* 21, 1081–1125.
- [85] Van Herck, S.L.J., Geysens, S., Bald, E., Chwatko, G., Delezie, E., Dianati, E., Ahmed, R.G., Darras, V.M., 2013. Maternal transfer of methimazole and effects on thyroid hormone availability in embryonic tissues. *Endocrinol.* 218, 105-115.
- [86] Wu, P-C., Fann, M-J., Kao, L-S., 2010. Characterization of Ca²⁺ signaling pathways in mouse adrenal medullary chromaffin cells. *J Neurochem.* 112, 1210–1222.
- [87] Zhang, J., Lazar, M.A., 2000. The mechanism of action of thyroid hormones. *Annu Rev Physiol* 62, 439–466.

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