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Editorial

Do PCBs Modify the Thyroid-Adipokine Axis during Development?

Ahmed RG*

Department of Zoology, Beni-Suef University, Egypt

***Corresponding author:** Ahmed RG, Department of Zoology, Division of Anatomy and Embryology, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt, Tel: 002-010-9147-1828; Email: r_g_a_ahmed@yahoo.com & ahmedragab08@gmail.com

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Editorial

Polychlorinated Biphenyls (PCBs) are widespread global contaminants and they are a class of industrial compounds (anthropogenic chemicals) consisting of paired phenyl rings with various degrees of chlorination [1-4]. In the United States, PCBs are manufactured as complex mixtures under the trade name Aroclor with a designation indicating the extent of chlorination [5]. Also, the U.S. Environmental Protection Agency recognizes PCBs as unavoidable toxins (2010 21CFR109.30.). They are highly lipophilic organochlorines, accumulated in the food chain and bioaccumulated in the biological tissues (adipose tissue) to levels that are associated with a variety of health effects in human and animals [6]. These potential effects are amplified during the development [7] and their elimination half lives are about 6 to 10 years [8].

PCBs may affect the growth and development by impairing thyroid function [9]. Interestingly, their interference mechanism with Thyroid Hormones (THs) metabolism in the mother, fetus and newborn may injure the developing brain [10], even at background environmental levels [11], via changing the availability of Thyroid Receptors (TRs) [12], deiodinases [13] and TH transporters [14], or altering GABA-mediated pathways [15], monoaminergic pathways and the activity of cholinesterases [10]. Also, these changes may mediate by Aryl Hydrocarbon Receptors (AhRs) [16]. In my recent work [17], I observed that the administration of 2,3,6-2',5'-Pentachlorinated Biphenyl (PCB 95) induced a reduction ($P<0.01$) in sera Thyroxine (T4), Triiodothyronine (T3) and Growth Hormone (GH) levels, and an increase ($P<0.01$) in serum Thyroid Stimulating Hormone (TSH) level at Postnatal Days (PNDs) 17 and 18. At PND 18, the administration of PCB 95 led to thyroid dysgenesis and the thyroid gland exhibited some histopathological changes, such as follicular destruction, luminal obliteration, edema, interfollicular fibroblast proliferation, hemorrhage, and hypertrophy with reduced colloidal contents. This dyshormonogenesis and dysgenesis may be attributed to the increase in the level of DNA-fragmentation at PNDs 17 and 18. These results imply that PCB 95 may act as disruptor for the developmental Hypothalamic–Pituitary–Thyroid Axis (HPTA). Obviously, exposure to PCB induced hypothyroidism in rats [18], in sledge dogs [19], in monkeys [20] and in children living near PCB-contaminated sites [21]. Also, a PCBs [7] and PCB metabolites [22] may act directly on TR to modulate its action or indirectly on an unknown TR-binding protein, which may then conformational changes in TR-DNA binding domain to dissociate TR from T3-Responsive Element (TRE). Indeed, the Persistent Organic Pollutants (POPs) show resistance to biological degradation and may exert a large variety of adverse health effects [23].

On the other hand, in animal and human studies, PCBs appear to disrupt the levels of adiponectin [23], leptin [24], tumor necrosis factor (TNF-α) [25], insulin [26], body weight and fat depots [27]. In my recent work [17], the hypothyroid state due to PCB 95 revealed a higher ($P<0.01$) levels of sera leptin, adiponectin and TNF-α, and a lower ($P<0.01$) levels of sera Insulin Growth Factor (IGF-I) and insulin in both PNDs with respect to control group. In particular, the administration of PCB 95 at PND 18 led to a maximal increase in the concentration of adiponectin and the highest drop in the concentrations of insulin and IGF1, respectively. This is probably due to the disturbance of the hormonal homeostatic mechanisms on this day. Interestingly, the body weight of the neonates in the PCB 95 group exhibited severe decreases throughout the experimental period in relation to that of the control group. The hypothyroidism by PCB 95 could impair the adipokines axis, fat metabolism and in general the postnatal development. Similarly, the full mixture of PCB, organochlorine pesticides and methylmercury also moderately increased (in an additive fashion) hypothalamic levels of the TNF-α and interleukins (IL6 or IL12) [28]. Also, Baker et al. [29] undertook that the dysfunction in the glucose homeostasis by PBCs could be AhR mediated. A previous laboratory experiments showing that a lower dose of Aroclor 1254 (200 μg/kg/day) [27] or a higher dose of bisphenol A (BPA) [30] induced a significantly decreased rat body weight, fat depots and a lower feeding efficiency. Generally, PCBs produce a wide spectrum of toxic effects in animals including body weight loss, toxicity, and teratogenicity [31]. However, a negative correlation was found between the level of adiponectin and PCB 153 [23], PCB 77 (3,3′,4,4′-tetrachlorobiphenyl) [25], 2,3,7,8-Tetrachlorodibenzo-P-Dioxin (TCDD) [32] and BPA [33]. More importantly, the changes in the level of serum adiponectin play a modest role in thyroid dysfunction in human [34].

From this point of view, the endocrine disrupting compounds can produce complex, mosaic effects during the life cycle [35]. Conclusively, loss of body weight may suggest a decline in the general health level of animals [36], which can be important in the interpretation of thyroid effects. However, these mechanisms associated with developing thyroid dysfunction are not fully understood.

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