Streszczenie w języku angielskim

Despite the legal regulations on the production and use of polychlorinated biphenyls (PCBs), these compounds, due to their long half-life, are still present in the environment, posing a real threat to human and animal organisms. Moreover, they are the most common persistent organic pollutants in the world. In spite of extensive knowledge on the influence of PCBs (especially of planar structure) on many biological processes, the literature still lacks data on the influence of their hydroxylated metabolites (OH-PCB; which concentration in the environment increases) on the synthesis and secretion of thyroid hormones [TH: thyroxine (T_4) and triiodothyronine (T_3)] and the processes responsible for maintaining the appropriate concentration of T_3 in the blood (e.g. deiodination). In addition, the molecular mechanism of action of these compounds in thyroid and liver cells has not yet been elucidated. Therefore, the aim of the study was to determine the influence of PCB and OH-PCB on TH secretion, T_4 to T_3 conversion, concentration of iodothyronine deiodinases (DIO1, DIO2, DIO3), mRNA expression of genes involved in TH synthesis (*TSHR, NIS, TPO, TG*), metabolism (*DIO1, DIO2, DIO3*), transport (*OATP1C1, MCT8, MCT10, LAT1*) and TH receptors involved in gene transcription (*TRα* and *THRB*). Chicken thyroid and liver explants were incubated in Eagle's medium supplemented with thyroid stimulating hormone (TSH; 250 mU / ml; for thyroid explants) or dexamethasone (DEX; 250 mU / ml; for liver explants), PCB118, PCB153, 4-OH- PCB107 and 3-OH-PCB153 (0.5×10^{-8}M) and TSH / DEX combination with the above PCB and OH-PCB. The results of *in vitro* experiments showed that in respect to thyroid explants all applied PCBs and OH-PCBs (except for 4-OH-PCB107) inhibited basal and TSH-stimulated T_4 secretion. Moreover, they increased basal and reduced TSH-stimulated T_3 secretion. In addition, PCBs and OH-PCBs decreased the TSH-stimulated *TSHR* expression. Following PCB and OH-PCB exposure, significant changes in mRNA expression of *NIS, TPO,* and *TG* were observed. Tested compounds affected *DIO1* and *DIO3* transcript levels and protein abundances of each DIO. Furthermore, PCB-dependent effects on *OATP1C1, MCT8,* and *MCT10* mRNA expression were found. For liver explants, it has been shown that the tested PCBs and OH-PCBs interacted with and/or abolished the inhibitory effects of DEX on T_3 secretion and T_4 to T_3 conversion. These compounds, affected basal and DEX-modified mRNA expression and protein concentration of all three deiodinases. PCBs and OH-PCBs did not change *MCT8* gene expression; however, PCB118 and 4-OH-PCB107 reduced *MCT10* mRNA levels with a concomitant increase in basal and DEX-stimulated *LAT1* mRNA expression. PCB153 and

3-OH-PCB153 did not influence *MCT10* expression, but they elevated basal and reduced DEX-stimulated *LAT1* mRNA levels. Only 4-OH-PCB decreased *TRβ0* mRNA expression. In conclusion, both PCB118 and PCB153 and their OH-PCBs affected TH secretion and the conversion of T_4 to T_3. Moreover, these compounds influenced the processes of synthesis and deiodination of iodothyronines as well as their transport across the chicken thyroid and liver cell membranes. Moreover, the influence of PCBs and OH-PCBs depended mainly on the type of PCB congener and the exposure time. These results indicate that in the laying hen not only the parental PCBs, but also the OH-PCBs are potent disruptors of the thyroid gland and liver function. These results reveal that not only parent PCBs, but also their hydroxylated derivatives, may affect cell metabolism regulated, inter alia, by iodothyronine in two ways: (i) directly by disturbing the synthesis and secretion of iodothyronines as well as (ii) indirectly by changing the availability of TH in the organism.