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Does PBDE (DE-71) induced developmental hypothyroxinemia correlate with behavioral effects in the rat?

Louise Ramhøj, Marta Axelstad*, Karen Riiber Mandrup, Sofie Christiansen, and Ulla Hass

*Division of Toxicology and Risk Assessment, National Food Institute, Technical University of Denmark, Mørkhøj Bygade 19, Dk-2860 Søborg, Denmark. *Contact: maap@food.dtu.dk*

Thyroid hormones are crucial during pre- and postnatal life for proper development of the brain. Developmental hypothyroxinemia results in hyperactivity and learning impairments in both rats and humans. For the anti-thyroid drug propylthiouracil (PTU) decreased maternal serum thyroxine (T4) levels in rat correlate with hyperactivity and learning impairments in the offspring. In the present study we pursued to establish the same correlation between decreased T4 and neurobehavioral changes for a class of environmental thyroid disrupting compounds; the polybrominated diphenyl ethers (PBDEs).

In an a large developmental toxicity study (n=20-21) time-mated Wistar rat dams were dosed with a technical penta-PBDE mixture (DE-71) from gestation day 7 through postnatal day (PND) 16 in doses of 0, 40, and 60 mg/kg/day. Serum T4, triiodothyronine (T3), and thyroid-stimulating hormone (TSH) were measured at various points in time in dams and offspring. The activity of the hypothalamic-pituitary axis was assessed by measuring thyroid gland weights and quantitative thyroid histology. In one male and one female per litter, motor activity levels were determined on PND 21 and PND 79, and cognition was assessed in the Morris water maze, at 19 weeks of age.

T4 and T3 levels were decreased dose-dependently in the dams on gestation day 15. The pups from all three dose groups were also markedly hypothyroxinemic during the entire postnatal period, with T4 reductions of ~70% at 2 weeks of age. However, the hypothalamic-pituitary-thyroid axis was not activated as TSH levels, thyroid weights and histopathology were unaffected. Activity and learning were likewise unaffected.

In conclusion, DE-71 induced profound hypothyroxinemia during development without causing behavioral changes in the rat offspring, despite a robust study design. The observed hypothyroxinemia was comparable to one induced by PTU and which caused behavioral effects correlating with serum T4 levels. Further studies are needed to elucidate the reasons for the dissimilar behavioral effects of DE-71 and PTU although similar effects on T4 are found.