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Severe Hypothyroxinemia, But No Behavioural or Auditory Effects in Rats, After Developmental Exposure to a Brominated Flame Retardant

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Abstract:
In all mammalian species, correct levels of thyroid hormones are important for proper brain development. In humans, a number of studies have shown that even mild maternal hypothyroxinemia during pregnancy is associated with impaired fetal brain development. Therefore exposure to chemicals that reduce human thyroid hormone levels could have detrimental consequences, both for the affected individuals and for society as a whole. In rats, developmental hypothyroidism induced by exposure to potent anti-thyroid drugs like propyl thiouracil (PTU), has been shown to causes adverse effects on brain development. Here we investigated whether exposure to a brominated flame retardant, known to act as a thyroid disrupter in rats, would also cause neurobehavioral changes. Time-mated Wistar rat dams (n=20) were dosed with a polybrominated diphenyl ether (PBDE) called DE-71. Exposure was from gestation day (GD) 7 through postnatal day (PND) 16 at doses of 0, 40, and 60 mg/kg/day. Serum thyroxine (T4), triiodothyronine (T3) and thyroid-stimulating hormone (TSH) were measured at various time points in dams and offspring, along with thyroid gland weights and histopathology. In the offspring, motor activity was determined on PND 21 and PND 79, cognition was assessed in a Morris water maze at 19 weeks of age, and hearing was assessed at 6 months of age by test of otoacoustic emission. In the dams, T4 and T3 levels were significantly decreased on GD 15 in both dose groups. Furthermore, the pups from both dose groups showed T4 reductions of ~70% on PND 16. However, postnatal body weights, TSH levels, thyroid gland weights and histopathology were unaffected by DE-71 treatment, as were motor activity levels, learning and hearing ability.This lack of effects in a validated battery of behavioral tests testing was surprising, because similar T4 reductions had previously caused significant effects on activity, learning and hearing ability in our PTU study. Further studies, investigating structural abnormalities in the brains of developmentally hypothyroid animals, could be used to elucidate why compounds showing T4 decreases of similar magnitudes cause such different effect on behavior. However, the present results indicate that the mode of action of a thyroid disrupting chemical is important with regards to its adverse effects on rodent brain development.