Abstract

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Development of cholinergic neurons in rat brain regions: dose-dependent effects of propylthiouracil-induced hypothyroidism.

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OBJECTIVE AND METHODS: The effects of hypothyroidism on development of cholinergic system in brain regions (prefrontal cortex and hippocampus) were evaluated by measuring choline acetyltransferase (ChAT) activity and hemicholinium-3 binding to the high-affinity choline transporter.

RESULTS: Various degrees of thyroid deficiency were produced by perinatal exposure to propylthiouracil (PTU) in drinking water ranging from 5 ppm (mg/l) to 25 ppm beginning at gestational day 18 until postnatal day 21. ChAT, a marker for cholinergic nerve terminals, was reduced by PTU in a dose-dependent manner. Concomitant with the enzyme deficits, hemicholinium-3 binding was elevated, suggesting an increase in neuronal impulse activity. Although similar changes were seen in both brain regions examined, the magnitude and duration of these changes were more definitive in the prefrontal cortex. Nonetheless, these neurochemical alterations appeared to be recoverable when the rats returned to a euthyroid state, and no further changes were observed as the animals reached adulthood. In comparison, data reported in a succeeding article indicate that deficits in cognitive function were first seen in weanling hypothyroid rats, but that the behavioral impairments lasted well into adulthood when thyroid status and cholinergic parameters in the brain appeared to have recovered to normal.

CONCLUSION: These results suggest that alterations of cholinergic system caused by perinatal hypothyroidism are associated with neurobehavioral deficits at weaning, and these developmental deviations may cause permanent impairment of cognitive function despite recovery from the hormonal imbalance at adult ages.

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