Regulation of local thyroid hormone bioactivity in the developing brain by deiodinases

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A strict regulation of thyroid hormone levels is required for normal human brain development. The iodothyronine deiodinases D1 and D2 catalyze the conversion of T4 to T3; D3 catalyzes the degradation of T3, and the conversion of T4 to reverse T3. To determine the role of deiodinases in the regulation of intracellular thyroid hormone levels in the developing human brain, we determined the D2 and D3 activity and T3, T4 and rT3 levels in different fetal and post-natal brain regions at 13-42 weeks post-menstrual age. D1 activity was undetectable.

The developmental changes in the concentrations of the iodothyronines, and of D2 and D3 activities, showed spatial and temporal specificity. Considerable D2 activity was found in the cortex, which correlated positively with T4 (r=0.65). Cortex D3 activity was very low, as was D3 activity in germinal eminence and choroid plexus. Highest D3 activities were found in the cerebellum (64 fmol/min/mg); D3 activities decreased with age. Cerebellar T3 was very low, increasing with age. Other regions with high D3 activities (midbrain, basal ganglia, brain stem, spinal cord, hippocampus) also had low T3, until D3 started decreasing after midgestation. D3 was correlated with T3 (r=-0.682) and with rT3/T3 (r=0.812) and rT3/T4 (r=0.889).

These data suggest that D2 is important for the local production of T3 in the cortex. Because of the high D3 activities in the different brain areas and the good correlations between D3 activities and thyroid hormone ratios, D3 may protect the developing brain from excessive T3 until differentiation is required.

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