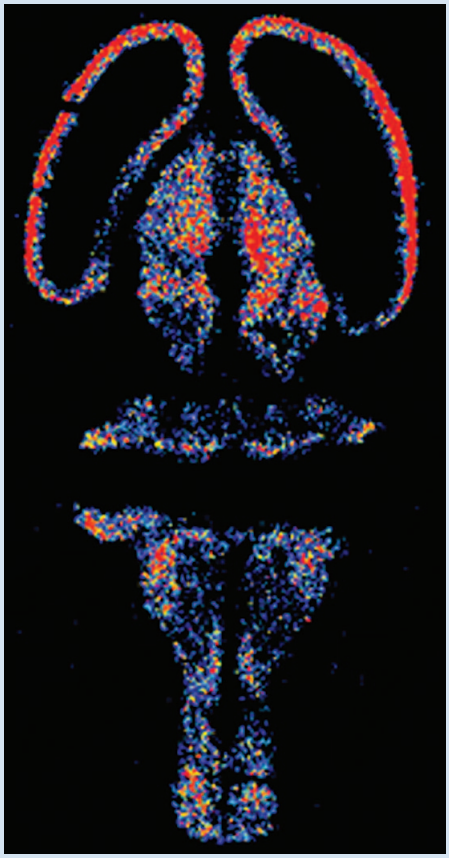
Thyroid Hormone and Brain Development Conference

Recently, the NIEHS/NIH/DHHS jointly cosponsored a conference titled "Thyroid Hormone and Brain Development: Translating Molecular Mechanisms to Population Risk" with the U.S. Environmental Protection Agency, the NIH Office of Rare Diseases, the Agency for Toxic Substances and Disease Registry, the American Chemistry Council, and the Center for Neuroendocrine Studies at the University of Massachusetts. This meeting, which included clinicians, endocrinologists, epidemiologists, toxicologists, and molecular biologists, as well as representatives of several advocacy groups, examined the current state of emerging multidisciplinary knowledge relevant to the role of thyroid hormone in brain development and the effects of environmental agents on this system. A summary of the science presented, a list of recommendations for future research directions, and research challenges are summarized here.



Pseudocolor autoradiogram of a fetal rat brain produced by *in situ* hybridization with a probe for the rat thyroid hormone receptor. The thyroid receptor is evident in the fetal cortex before the onset of fetal thyroid function.

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- Thyroid hormone effects on brain development are receptor-mediated and vary with the time of development. Furthermore, there are multiple types of thyroid receptors that play different roles in development, and the timing of thyroid insufficiency is associated with different neurological deficits. We need more laboratory-based studies to understand the relative sensitivity of various thyroid hormone–responsive end points in the developing brain to small changes in circulating levels of thyroid hormone, as well as to identify temporal windows of sensitivity to thyroid hormone.

- Certain environmental chemicals—some polychlorinated biphenyls, for example—can interfere with thyroid hormone action during brain development. Such chemicals likely can affect signaling through selective thyroid hormone receptors, thereby affecting brain development in a mosaic pattern. We need more information to understand the site and mechanism of action of these environmental chemicals during brain development. Thus, it is critical to improve animal models of thyroid disruption as well as advance our ability to extrapolate animal data to human risk.

- To improve our understanding of the basic biology of brain development, as well as the site and mechanism of action of environmental chemicals that target the thyroid system, we must increase the use of "-omics" technology (e.g., toxicogenomics), develop and use new imaging technologies, develop and use genetic models of thyroid hormone receptor defects or deficiency, and increase multidisciplinary and interdisciplinary research projects.

- It is clear that thyroid deficiency during pregnancy can result in neurological deficits in children. We also know that fetal thyroid receptors are present before the onset of fetal thyroid function, so fetal brain development is dependent on maternal thyroid hormone. Thus, it may be prudent to know that maternal thyroid status is normal before, as well as during, pregnancy to ensure that both mother and fetus are healthy.

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