Hypothalamic regulation of the human hypothalamus-pituitary-thyroid(HPT)-axis

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TRH neurons of the paraventricular nucleus of the hypothalamus (PVN) are involved in the central regulation of the HPT-axis. Severe illness induces low T3 serum concentrations without a compensatory rise in TSH. This phenomenon is known as nonthyroidal illness (NTI). During NTI TRH mRNA expression in the PVN is positively correlated with serum T3, indicating a major setpoint change in the regulation of the HPT-axis.
To get more insight into the determinants of the decreased TRH mRNA found in NTI we study various molecular components of the HPT-axis in human post-mortem hypothalamus and pituitary, focussing on receptors and enzymes involved in thyroid hormone feedback regulation. MCT8 probably plays an important role in thyroid hormone metabolism in the CNS by providing neurons with thyroid hormone (Friesema et al., 2003).
Furthermore, thyroxine (T4) is converted locally into the biologically active thyroid hormone T3 by type II deiodinase (D2), while inactivation of T3 occurs through deiodination by type III deiodinase (D3). We have studied the distribution of MCT8, D2 and D3 in the human hypothalamus and pituitary for the first time using different techniques. D2 expression was predominantly found in the infundibular nucleus (IFN)/median eminence region and in the central lining of the third ventricle, while D3 was prominent in several hypothalamic nuclei including the PVN and IFN. MCT8 distribution showed overlap with both enzymes.
The distribution of thyroid hormone receptor (TR) α1, α2, β1 and β2 was investigated by means of immunocytochemistry both in the hypothalamus and in the anterior pituitary (AP). All four TR isoforms appeared to be present in the AP, with most abundant staining for TRα2. Hypothalamic staining was most prominent in the PVN and in the IFN. The functional implications of these findings for HPT axis feedback regulation and its changes during illness will be discussed.

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