Melanocortin 4 receptor distribution in the human hypothalamus

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Research question and background

The melanocortin 4 receptor (MC4R) is an essential regulator of energy homeostasis and metabolism, and MC4R mutations represent the most prevalent monogenetic cause of obesity in humans known to date. Hypothalamic MC4Rs in rodents are well characterized in neuroanatomical and functional terms, but their expression pattern in the human hypothalamus is unknown.

Methods and tissues used

To determine the topographic distribution and identity of cells expressing MC4R mRNA in the human hypothalamus, locked nucleic acid in situ hybridization was performed on nine human postmortem hypothalami. In addition, co-expression of MC4R with glial fibrillary acidic protein (GFAP), vasopressin/oxytocin (AVP/OXT), corticotropin-releasing hormone (CRH), neuropeptide Y (NPY), agouti-related protein (AgRP), and α-melanocyte stimulating hormone (α-MSH) was examined.

Results and conclusions

Most intense MC4R mRNA expression was present in the paraventricular nucleus (PVN), the supraoptic nucleus (SON), and the nucleus basalis of Meynert. Most MC4R-positive cells in the SON also expressed AVP/OXT. Co-expression with AVP/OXT in the PVN was less abundant. We did not observe co-expression of MC4R mRNA and GFAP, CRH, NPY, AgRP, or α-MSH. However, fiber-like staining of NPY, AgRP, and α-MSH was found adjacent to MC4R-positive cells in the PVN. CONCLUSION: Expression of MC4R mRNA in the human hypothalamus is widespread and in close approximation to endogenous MC4R binding partners AgRP and α-MSH. PMID: 23211571 [PubMed - indexed for MEDLINE]