Leptin

Leptin, an anorexigenic hormone in the hypothalamus, suppresses food intake and increases energy expenditure. Failing to respond to leptin will lead to obesity. Here, it is discovered that nuclear receptor Nur77 expression is lower in the hypothalamus of obese mice as compared to normal mice. Injection of leptin results in a significant reduction in body weight in wild-type mice, but in neither Nur77 knockout littermates nor mice with specific Nur77 knockdown in the hypothalamus. Hypothalamic Nur77 not only participates in leptin central control of food intake but also expands leptin's reach to the liver and adipose tissues to regulate lipid metabolism. Nur77 facilitates STAT3 acetylation by recruiting acetylase p300 and disassociating deacetylase HDAC1 to enhance the transcriptional activity of STAT3, consequently modulates the expression of downstream gene Pomc in the hypothalamus. Nur77 deficiency compromises response to leptin in high-fat diet mice. Under physiological conditions, severe leptin resistance in Nur77 knockout mice with increased appetite, lower energy expenditure, and hyperleptinemia contributes to aging-induced obesity. Together, our study opens a new avenue for regulating metabolism with Nur77 as the positive modulator in the leptin-driven anti-obesity in the hypothalamus [1].

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263 SAH patients were included of which leptin levels were assessed in 24 cases. BMI was recorded along disease severity documented by the Hunt and Hess and modified Fisher scales. The occurrence of clinical or functional DCI (neuromonitoring, CT Perfusion) was assessed. Long-term clinical outcome was documented after 12 months (extended Glasgow outcome scale). A total of 136 (51.7%) patients developed DCI of which 72 (27.4%) developed DCI-related cerebral infarctions. No association between BMI and DCI occurrence (P = .410) or better clinical outcome (P = .643) was identified. Early leptin concentration in serum (P = .258) and CSF (P = .159) showed no predictive value in identifying patients at risk of unfavorable outcomes. However, a significant increase of leptin levels in CSF occurred from 326.0 pg/ml IQR 171.9 prior to DCI development to 579.2 pg/ml IQR 211.9 during ongoing DCI (P = .049). No association between obesity and clinical outcome was detected. After DCI development, leptin levels in CSF increased either by an upsurge of active transport or disruption of the blood-CSF barrier. This trial has been registered at ClinicalTrials.gov (NCT02142166) as part of a larger-scale prospective data collection. BioSAB: https://clinicaltrials.gov/ct2/show/NCT02142166 [2].

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Chen Y, Wu R, Chen HZ, Xiao Q, Wang WJ, He JP, Li XX, Yu XW, Li L, Wang P, Wan XC, Tian XH, Li SJ, Yu X, Wu Q. Enhancement of hypothalamic STAT3 acetylation by nuclear receptor Nur77 dictates leptin sensitivity. Diabetes. 2015 Jan 9. pii: db141206. [Epub ahead of print] PubMed PMID: 25576055.
2)
Veldeman M, Weiss M, Simon TP, Hoellig A, Clusmann H, Albanna W. Body mass index and leptin levels in serum and cerebrospinal fluid in relation to delayed cerebral ischemia and outcome after aneurysmal subarachnoid hemorrhage. Neurosurg Rev. 2021 Apr 17. doi: 10.1007/s10143-021-01541-1. Epub ahead of print. PMID: 33866464.