sive hepatic, but also with cardiometabolic diseases and NAFLD is thought to be involved in the pathogenesis of cardiometabolic diseases. Diagnosis of NAFLD by the gold standard method, liver biopsy, is invasive and, therefore, not feasible in routine practice. Consequently, there has been intense interest in blood markers that, alone or in combination with clinical parameters, would be able to identify patients with NAFLD. The most effective and safe treatment strategy to reduce liver fat content and improve hepatic inflammation and fibrosis in subjects with NAFLD is lifestyle intervention. However, a considerable amount of patients is not compliant with the respective recommendations or liver fat content and/or liver pathology does not improve, although weight loss can be achieved. In this respect novel studies have indicated that specific pharmacological treatment approaches may be effective and relatively safe to treat NAFLD.

https://doi.org/10.1016/j.orcp.2016.10.025

25

Glucose-sensing neurons of the mediobasal hypothalamus project to brown adipose tissue

Paul N. Mirabella*, Aneta Stefanidis, David C. Spanswick, Brian J. Oldfield

Monash University, Clayton, Victoria, Australia

It is well established that neural input to BAT remains a critical feature of its functional recruitment. In the case of postprandial thermogenesis, activation of BAT sympathetic nerve activity following peripheral or central glucose infusion suggests a central nutrient-sensing mechanism in the regulation of BAT activity. It is hypothesised that BAT-directed neurons in discrete hypothalamic brain regions alter their electrophysiological properties in response to increased extracellular glucose concentration.

Injection of the GFP-tagged, transsynaptic retrograde virus, pseudorabies virus (PRV), into the interscapular BAT of Sprague-Dawley rats allowed for identification of neurons with a known polysynaptic projection to BAT. Whole-cell patch clamp recordings were performed on GFP+ neurons from coronal sections of the arcuate nucleus (ARC) and retrochiasmatic area (RCh). Increasing the extracellular glucose concentration from 1 mM (''fasted'') to 5 mM (''fed'') revealed both glucose-excited (6.00 ± 0.84 mV; 0.63 ± 0.18 Hz; $n = 14$ (29%)) and glucose-inhibited (-5.34 ± 0.75 mV; -0.34 ± 0.07 Hz; $n = 18$ (37%)) BAT-directed neurons in the ARC. Similarly, there were also substantial numbers of glucose-excited (7.32 ± 2.20 mV; 0.75 ± 0.22 Hz; $n = 5$ (45%)) and glucose-inhibited (-3.12 ± 2.24 mV; -0.80 ± 0.44 Hz; $n = 4$ (36%)) neurons in the RCh that projected polysynaptically to BAT. Retrospective immunohistochemical analyses of biocytin-filled cells revealed both POMC+ ($n = 9$) and POMC− ($n = 5$) glucose-sensitive neurons in both regions.

Furthermore, in attempt to delineate the heterogeneity of glucose-sensitive neurons through their monosynaptic projections, Retrobeads (Rb) were injected into the paraventricular nucleus, lateral hypothalamus and spinal cord of rats, and the glucose sensitivity of ARC/RCh double-labelled (Rb+/PRV+) neurons was tested.

These data provide a basis for the postprandial regulation of BAT thermogenesis through glucose-sensing mechanisms in hypothalamic neurons. They also provide additional insights into the axonal trajectory of identified hypothalamic glucose-sensors, which may form the basis of the observed heterogeneity within these populations of glucose-responsive, BAT-directed neurons.

https://doi.org/10.1016/j.orcp.2016.10.026

26

Effect of glucocorticoid on brown adipose tissue function in humans — A randomised double-blind placebo controlled cross-over study

Moe Thuzar[1,2,3,*], W. Phillip Law[2,4], Jeyakantha Ratnasingam[1], Christina Jang[1,2], Ken K.Y. Ho[1,2]

[1] *Department of Endocrinology & Diabetes, Princess Alexandra Hospital, Brisbane, Queensland, Australia*
[2] *School of Medicine, University of Queensland, Brisbane, Queensland, Australia*
[3] *Princess Alexandra Hospital, Translational Research Institute, University of Queensland, Brisbane, QLD, Australia*
[4] *Department of Molecular Imaging, Princess Alexandra Hospital, Brisbane, Queensland, Australia*

Background: Glucocorticoid (GC) excess causes obesity. In animals, GC inhibits brown adipose tissue (BAT) function, leading to weight gain. The involvement of BAT in the development of obesity induced by GCs in humans is not known.