Universität Basel

Research Project

Influence of glucocorticoids on human brown adipose tissue and cold induced thermogenesis

Third-party funded project

Project title Influence of glucocorticoids on human brown adipose tissue and cold induced thermogenesis
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Bereich Medizinische Fächer (Klinik) / Endokrinologie / Diabetologie
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Brown adipose tissue (BAT) is unique in its capability to convert chemical energy directly into heat. It is crucial to the survival of newborn infants and small mammals exposed to cold. The recent discovery of active BAT in human adults revealed exciting new aspects of human energy metabolism. Active BAT increases energy expenditure and can thereby counteract obesity and insulin resistance. BAT could thus serve as a potential therapeutic target to treat obesity and its associated diseases. Glucocorticoids (GCs) are frequently used in clinical therapy to suppress immune response in auto-immune, inflammatory and pulmonary diseases. However, their long-term use is associated with weight gain and insulin resistance. While the effects on GCs on glucose metabolism are quite well studied, data on energy expenditure in humans is scarce. Moreover, in vitro and animal data point towards an inhibiting effect of GCs on BAT function and development. This has hitherto not been investigated in humans.The aim of this project is to study both the acute and long-term effect of GCs on human BAT and cold induced thermogenesis (CIT) using a translational and multidisciplinary approach employing state-of-the-art imaging and molecular analysis. The project will be divided into three sub-projects: 1) The first projects aims to investigate the acute effect of one week of high-dose glucocorticoids on human BAT function and cold induced thermogenesis in an investigator-blinded, cross-over trial in healthy volunteers. Techniques used will comprise measurement of cold induced thermogenesis (CIT) by indirect calorimetry, functional and anatomic MRI, as well as molecular analysis of muscle and adipose tissue biopsies.2) The second project is designed as an observational study in patients requiring high-dose glucocorticoids for six weeks. It will comprise measurement of CIT, measurement of glucose uptake into cold stimulated BAT by 18F-FDG-PET/CT and measurement of novel biomarkers of BAT function.3) The third project will investigate the prevalence of retroperitoneal BAT in patients undergoing surgery for benign adrenal tumors and its relation to glucocorticoid secretion. We will analyze the tissue using real-time-PCR, Western-blotting and immunohistochemistry for classical markers of BAT and for recently described transcription factors that have been shown in rodents to be influenced by GC exposure.Together, these projects will allow us to develop a comprehensive overview of the consequences of GC excess on BAT and CIT.

Keywords temperature regulation; glucocorticoid excess; insulin resistance; glucocorticoid; Cushing's syndrome; brown adipose tissue; obesity; energy expenditure; diabetes; thermogenesis
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