

Adipose tissue as an active organ: blood flow regulation and tissue- specific glucocorticoid metabolism

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för
avläggande av medicine doktorsexamen framläggs till offentligt försvar i
Hörsal Betula, byggnad 6M,
fredagen den 11 nov, kl. 09:00.
Avhandlingen kommer att försvaras på svenska.

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Department of Public Health and Clinical Medicine, Medicine
Umeå University
Umeå 2011

Organization
Umeå University
Department of Public Health
and Clinical Medicine

Document type
Doctoral thesis

Date of publication
21 Oct 2011

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Title
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Abstract

Background: Despite advances in the treatment of atherosclerosis, cardiovascular disease is the leading cause of death worldwide. With the population getting older and more obese, the burden of cardiovascular disease may increase further. Premenopausal women are relatively protected against cardiovascular disease compared with men, but the reasons for this sex difference are partly unknown. Redistribution of body fat from peripheral to central depots may be a contributing factor. Central fat is associated with hyperlipidemia, hyperglycemia, hypertension, and insulin resistance. Two possible mediators of these metabolic disturbances are tissue-specific production of the stress hormone cortisol and adipose tissue blood flow (ATBF). The aim of this thesis was to determine the adipose tissue production of cortisol by the enzyme 11 β -hydroxysteroid dehydrogenase type 1 (11 β -HSD1) and to investigate the regulation of ATBF. **Materials and Methods:** Cortisol release was estimated by labeled cortisol infusions and tissue-specific catheterizations of subcutaneous and visceral adipose tissue in men. We investigated ATBF by ¹³³Xe-washout and its relation to autonomic activity, endothelial function, adipose tissue distribution, and adipokines in different groups of women. We further investigated the effect of two diets and weight loss on ATBF in women. **Results:** We demonstrated significant cortisol release from subcutaneous adipose tissue in humans. Splanchnic cortisol release was accounted for entirely by the liver. Cortisol release from visceral adipose tissue (to the portal vein) was not detected. ATBF decreased according to increasing weight and postmenopausal status, and the level of blood flow was associated with nitric oxide (NO) activity and autonomic activity. ATBF was also highly associated with leptin and both subcutaneous and visceral adipose tissue. After 6 months of diet and weight reduction, a significant difference in ATBF was observed between diet groups. **Conclusions:** Our data are the first demonstration of the contributions of cortisol generated from subcutaneous adipose tissue, visceral tissues, and liver by 11 β -HSD1. ATBF was linked to autonomic activity, NO activity, and the amount of adipose tissue (independent of fat depot). Postmenopausal overweight women exhibited loss of ATBF flexibility, which may contribute to the metabolic dysfunction seen in this group. Weight loss in a diet program could not increase the ATBF, although there were ATBF differences between diet groups. The results will increase understanding of adipose tissue biology and contribute to the development of treatment strategies targeting obesity and obesity-related disorders.

Key words

11 β -hydroxysteroid dehydrogenase type 1, adipose tissue, autonomic nervous system, blood flow, cortisol, nitric oxide, weight loss.

Language
English

ISBN
978-91-7459-280-1

ISSN
0346-6612

Number of pages
87 + 4 papers