**Effects of prolactin on metabolism**
– changes induced by hyperprolactinemia

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Avhandlingen baseras på följande delarbeten:

Ling C, Svensson L, Odén B, Weijdegård B, Edén B, Edén S, Billig H.

II Prolactin suppresses malonyl-CoA concentration in human adipose tissue.
Nilsson L, Roepstorff C, Kiens B, Billig H, Ling C.
*Submitted*

III Prolactin and growth hormone regulate adiponectin secretion and receptor expression in adipose tissue.

IV Suppressed lipid oxidation in women with pathological hyperprolactinemia.
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Effects of prolactin on metabolism
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ABSTRACT

High prolactin levels during breast-feeding, is recognized to influence metabolism in order to supply glucose and fat for milk production. Pathologic overproduction of prolactin, hyperprolactinemia, is a condition primarily associated with reproductive disorders; however, the metabolic impact of elevated prolactin indicates that these parameters might be considered in clinical management of the condition. Prolactin receptors have previously not been demonstrated in human adipose tissue, and prolactin-related effects in adipose tissue, therefore, were regarded as indirect. This thesis focuses on the demonstration of prolactin receptors in human adipose tissue, and the metabolic function of prolactin stimulation in vitro and in vivo.

We have demonstrated the expression of four prolactin receptor isoforms in human adipose tissue, the L-, I-, s1a- and s1b-prolactin receptors. Prolactin stimulation of cultured human adipose tissue in vitro was found to reduce lipoprotein lipase activity, and thereby likely diminishes the ability for fat uptake. Furthermore, lipogenic parameters such as glucose transporter 4 expression and malonyl-CoA concentration in the cultured adipose tissue were also found to be suppressed by prolactin. The insulin-sensitizing hormone adiponectin is secreted from adipose tissue, and prolactin stimulation during culture suppressed adiponectin secretion. These results were confirmed in female prolactin transgenic mice, which were observed to have suppressed adiponectin serum levels. The effects of prolactin were further investigated in an initiated study of hyperprolactinemic women in vivo. By using indirect calorimetry, these women were demonstrated to have a decreased fat oxidation.

Based on the results of this thesis and other studies, there are indications that prolactin could be a potent and specific regulator of several metabolic processes. The regulation of nutrient flux is important to maintain a balanced metabolism. The metabolic effects in hyperprolactinemia are often overlooked in clinical practice, but we find further investigations motivated in order to clarify the magnitude of metabolic effects in hyperprolactinemia.

Keywords: prolactin, prolactin receptor, hyperprolactinemia, adipose tissue, lipoprotein lipase, malonyl-CoA, glucose transporter 4, retinol-binding protein 4, adiponectin, lipid oxidation