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Adrenal gland volume, intra-abdominal and pericardial adipose tissue in major depressive disorder

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Summary Major depressive disorder (MDD) is associated with an increased risk for the development of cardio-metabolic diseases. Increased intra-abdominal (IAT) and pericardial adipose tissue (PAT) have been found in depression, and are discussed as potential mediating factors. IAT and PAT are thought to be the result of a dysregulation of the hypothalamus—pituitary—adrenal axis (HPAA) with subsequent hypercortisolism. Therefore we examined adrenal gland volume as proxy marker for HPAA activation, and IAT and PAT in depressed patients. Twenty-seven depressed patients and 19 comparison subjects were included in this case-control study. Adrenal gland volume, pericardial, intraabdominal and subcutaneous adipose tissue were measured by magnetic resonance imaging. Further parameters included factors of the metabolic syndrome, fasting cortisol, fasting insulin, and proinflammatory cytokines. Adrenal gland and pericardial adipose tissue volumes, serum concentrations of cortisol and insulin, and serum concentrations tumor—necrosis factor-α were increased in depressed patients. Adrenal gland volume was positively correlated with intra-abdominal and pericardial adipose tissue, but not with subcutaneous adipose tissue. Our findings point to the role of HPAA dysregulation and hypercortisolism

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as potential mediators of IAT and PAT enlargement. Further studies are warranted to examine whether certain subtypes of depression are more prone to cardio-metabolic diseases.

1. Introduction

Unipolar depression is one of the most common disorders worldwide with a lifetime prevalence of 17% in Western societies, and is expected to be among the three leading causes of burden of disease in 2030, together with HIV/AIDS and ischemic heart disease (CVD) (Murray et al., 2010). The comorbidity of MDD with type 2 diabetes mellitus and ischemic heart disease is common, and the conditions are considered to have a bidirectional relationship (Rugulies, 2002; Surtees et al., 2008; Mezuk et al., 2008). Potential factors for an increased cardio-metabolic morbidity and mortality in patients with depression include lifestyle factors such as inactivity and smoking (Mitchell et al., 2015), increased rates of metabolic disturbances (higher fasting glucose) and the metabolic syndrome (Kahl et al., 2012; Vancampfort et al., 2013; Scharnholz et al., 2014), a dysregulation of pro- and anti-inflammatory cytokines (Dowlati et al., 2010; Valkanova et al., 2013), a dysregulation of the hypothalamus—pituitary—adrenal axis (HPAA) with subsequent hypercortisolism (Stetler and Miller, 2011), and body composition changes with increased intra-abdominal (IAT) and pericardial adipose tissue (PAT) (Kahl et al., 2014; Greggersen et al., 2011).

In particular, hypercortisolism as a result of HPAA dysregulation has been discussed to contribute to insulin resistance, glucose intolerance, hypertension, and produces central obesity (Wajchenberg, 2000). Hypercortisolism associated insulin resistance is thought to be an important regulator of intra-abdominal adipose tissue accumulation (Rebuffé-Scrive et al., 1992). Cortisol and insulin stimulate lipid uptake by activating lipoprotein lipase, an effect that is facilitated by high concentrations of the cortisol activating enzyme 11-ß-hydroxysteroiddehydrogenase type 1 and glucocorticoid receptors in intra-abdominal fat (Rebuffé-Scrive et al., 1990). Visceral obesity independently predicts future myocardial infarction and is strongly and positively associated with an increased mortality risk (Kuk et al., 2006; Nicklas et al., 2004).

Several studies have examined components of the HPAA such as adrenal gland volume, and single fat compartments such as IAT and PAT in depression. In detail, enlarged adrenal gland volume has been found in three case-control studies (Kessing et al., 2011), and most although not all cross-sectional studies have reported increased volumes of intra-abdominal adipose tissue in patients with major depression using imaging technology (Eskandari et al., 2005; Everson-Rose et al., 2009; Greggersen et al., 2011; Kim et al., 2011a,b; Krishnamurthy et al., 2008; Ludescher et al., 2008; Weber-Hamann et al., 2002; Williams et al., 2009). One study reported increased PAT in depression so far (Kahl et al., 2014).

However, studies examining both visceral fat compartments and measures of the HPAA had divergent results. Ludescher et al. (2008) studied 10 patients with MDD using MRI and found increased volumes of IAT in depression, and a correlation with adrenal volume. In a study with 22 postmenopausal women with major depressive disorder (MDD) using MRI Weber-Hamann et al. (2002) found elevated volumes of IAT only in the hypercortisolemic subgroup. In the follow-up hyper- and normocortisolemic depressed patients showed a larger accumulation of intra-abdominal fat mass over time compared to controls (Weber-Hamann et al., 2006). Kahl et al. (2005) studied 18 premenopausal women with MDD and 18 women comorbid with MDD and borderline personality disorder using MRI and found increased IAT in bothgroups, but no significant correlations between morning cortisol concentrations and IAT. Scharnholz et al. (2014) using MRI described volumes of IAT similar to a comparison group in patients with absent evidence for activation of the HPAA (non-suppressors to 1 mg dexamethasone).

Whether increases of IAT and PAT in depression are the result of HPAA dysregulation and relative hypercortisolism is a matter of debate. In patients with adrenal incidentalomas, accumulation of IAT and epicardial adipose tissue has recently been reported (Debono et al., 2013; Iacobellis et al., 2013). Therefore we examined IAT, PAT and adrenal gland volume and aimed at testing the following hypotheses: (1) adrenal gland volume is increased in depressed patients, (2) IAT and PAT are increased in depressed patients, and (3) IAT and PAT correlate with adrenal gland volume.

2. Methods and materials

2.1. Subjects

Twenty-seven inpatients with MDD (12 women, 15 men) treated at the Department of Psychiatry at the Hannover Medical School were included. The diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria and confirmed using standardized clinical interviews (SCID I/II; German version). At the time of the study, twelve patients were treated with selective serotonin reuptake inhibitors, 5 with selective serotonin and noradrenaline reuptake inhibitors, 3 with agomelatine, 1 with a dopamine and noradrenaline reuptake inhibitor, 2 with quetiapine, 2 with mirtazapine, 1 with noradrenaline reuptake inhibitors, and 1 with a tricyclic antidepressant. An exhaustive medical examination gave no evidence for previous coronary artery disease, previous myocardial infarction and angioplasty in the group of depressed patients. Nineteen healthy subjects who were recruited through announcements on university bulletin boards served as the comparison group (CG). A standardized psychiatric interview was used to confirm the absence of any current or lifetime history of major psychiatric disorder for every subject in this group. None of the CG subjects suffered from an acute or chronic infectious disease, had a lifetime autoimmune disorder, or had received