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Research paper

Effects of additional exercise training on epicardial, intra-abdominal and subcutaneous adipose tissue in major depressive disorder: A randomized pilot study

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ABSTRACT

Objective: Major depressive disorder (MDD) is associated with increased amounts of intra-abdominal and epicardial adipose tissue, risk factors for the development of cardio-metabolic disorders. Exercise has been shown to reduce intra-abdominal fat in different conditions such as obesity and diabetes mellitus, thereby reducing cardio-metabolic risks. Therefore we examined the effects of exercise on adipose tissue compartments in patients with MDD.
Methods: Of thirty depressed patients included, twenty received supervised exercise training, and ten received no specific training. Volumes of subcutaneous, intra-abdominal and epicardial adipose tissue were measured using magnetic resonance imaging, and factors constituting the metabolic syndrome were determined.
Results: Significant effects of the training condition were observed on the amount of epicardial adipose tissue ($P=0.017$), subcutaneous adipose tissue ($P=0.023$), weight ($P=0.047$), body-mass index ($P=0.04$), high density lipoproteins ($P=0.021$) and the number of metabolic syndrome factors ($P=0.018$). The amount of intra-abdominal adipose tissue decreased slightly, although not significantly, in the exercise group.
Conclusion: Exercise training reduces the amount of visceral, in particular epicardial adipose tissue, in patients with MDD, and ameliorates factors constituting the metabolic syndrome. Given the high prevalence of cardio-metabolic disorders in major depression, exercise training may be recommended as an additional treatment component.

1. Introduction

The association between depression and cardio-metabolic disorders, in particular type-2 diabetes mellitus (T2DM) and ischemic heart disease is well documented, and several studies point to a bidirectional relationship (Anderson et al., 2001; Golden et al., 2008; Goldston and Baillie, 2008; Knol et al., 2006; Lett et al., 2004; Mezuk et al., 2008; Nouwen et al., 2010; Prince et al., 2007; Rugulies, 2002). The combination of depression with cardio-metabolic disorders remains a clinical challenge as the outcome of either condition is worsened by the presence of the other, leading to reduced quality of life, higher incidence of complications, and increased health care costs (Charlson et al., 2013; Egede et al., 2002; Holt and Katon, 2012; Rosengren et al., 2004).

Visceral obesity has been reported as a risk factor for the development of diabetes and cardiovascular disorders as early as 1956 (Vague, 1956). Since then, numerous studies repeated and confirmed the detrimental effect of visceral obesity. In particular, intra-abdominal adipose tissue (IAT) has been associated with the development of T2DM mellitus (Bjorntorp and Rosmond, 1999; Scheen and Van Gaal, 2014), and epicardial adipose tissue (EAT) has been associated with coronary artery disease (Iacobellis, 2015).

Several studies point to an association of major depressive disorder (MDD) with increased IAT (de Medeiros et al., 2008;

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Everson-Rose et al., 2009; Greggersen et al., 2011; Ludescher et al., 2008; Marijnissen et al., 2011; Murabito et al., 2013; Remigio-Baker et al., 2014; Vogelzangs and Penninx, 2011; Weber-Hamann et al., 2002; Weber-Hamann et al., 2006). In contrast, only one study was performed on cardiac adipose tissue in MDD. As with IAT, an increase of the amount of EAT was found in depressed patients compared to healthy participants (Kahl et al., 2014).

Exercise treatment is an integral part of obesity and diabetes management programs (American College of Cardiology/American Heart Association Task Force on Practice Guidelines, 2014; Inzucchi et al., 2012; Robertson et al., 2014; Umpierre et al., 2011), and has been shown to be effective in reducing IAT. A recent meta-analysis showed that aerobic and, although to a lesser extent, anaearobic (resistance) training is sufficient at reducing IAT (Ismail et al., 2012). The role for exercise treatment on the reduction of EAT is less clear. A study in twenty-four obese patients revealed a significant reduction of EAT after twelve weeks of aerobic training (Kim et al., 2009). A study in sixty post-menopausal women using a 16 weeks home-based treadmill intervention revealed a reduction of EAT and IAT (Fornieles Gonzalez et al., 2014). However, a recent meta-analysis showed effects of bariatric surgery and diet on EAT but no significant effect of exercise (Rabkin and Campbell, 2015).

2. Aims of the study

To the best of our knowledge no controlled study was performed on the effects of exercise on visceral adipose tissue compartments in depression. We therefore aimed at examining a structured, supervised exercise training comprising aerobic and anaerobic elements in depressed patients to test the hypothesis that exercise may affect IAT and EAT in these patients.

3. Methods

3.1. Participants

Study participants took part in a randomized pilot trial comparing the effects of adjunctive exercise on physiological and psychological parameters in depression (Kerling et al., 2015). The original sample consists of fourty-two depressed patients randomized to either additional exercise training (N=22) or to treatment as usual (N=20). The study protocol was approved by the local ethics committee, and all participants provided informed written consent prior to the beginning of the study. Due to financial restrictions, follow-up magnetic resonance imaging data (MRI) after six weeks were obtained from the first twenty patients in the intervention group (of twenty two patients in the original study), and the first ten patients in the treatment as usual group (of twenty patients in the original study).

All patients were treated in specialized psychotherapy wards and received cognitive behavioral therapy. The diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria and confirmed with standardized clinical interviews (SCID I/II; German version). At the time of the study, seventeen patients received antidepressant medication in the EXERCISE group, and nine 9 patients in the control group (CTRL, details are listed in Table 1). Two patients in the EXERCISE group received sedatives, and none in the CTRL group (Table 1).

Medical examination was performed according to the recommendations of the European Heart Association and gave no evidence for previous coronary artery disease, previous myocardial infarction and angioplasty in the group of depressed patients (Perk et al., 2012). None of the patients used ß-blockers or received other cardiologic treatments. Exclusion criteria were acute or chronic infectious disease, acute or lifetime immunological disorders, diabetes mellitus type 1 and type 2, lifetime or current cardiovascular disorders, pregnancy, schizophrenia, mental retardation, bipolar disorder, current substance abuse or dependency, and age younger than 18 years.

Table 1
Anthropometric and clinical data in the EXERCISE and the CTRL group at study entry (mean ± SD).

Measure	EXERCISE (N=20)		CTRL (N=10)		
	N	%	N	%	P
Female	8	40	4	40	n.s.
	Mean	SD	Mean	SD	P
Age	43.8	8.1	38.4	9.3	n.s.
Height (m)	1.74	0.09	1.72	0.09	n.s.
Weight (kg)	81.4	22.7	79.4	12.4	n.s.
BMI	26.3	5.0	26.5	3.3	n.s.
	N	%	N	%	P
Antidepressants	17	85	9	90	n.s.
SSRI	7	35	5	50	n.s.
SSNRI	4	20	3	30	n.s.
NDRI	4	20	0	0	n.s.
Agomelatine	4	20	3	30	n.s.
Sedatives	2	10	0	0	n.s.
Benzodiazepines	1	5	0	0	n.s.
Zolpidem	1	5	0	0	n.s.
	Mean	SD	Mean	SD	P
Smoking (pack-years)	5.2	7.6	3.1	8.5	n.s.
Physical activity before	2.7	1.6	3.1	1.8	n.s.
Drinking	5.2	7.6	0.8	0.9	n.s.
	Mean	SD	Mean	SD	P
BDI-2 sum score	30.5	10.6	30.0	8.5	n.s.
MADRS sum score	23.4	8.1	23.8	9.8	n.s.

Legend: Anthropometric and clinical data. We observed no significant differences of anthropometric data, behavioral habits and medication between the groups at study entry. SSRI: selective serotonin reuptake inhibitor; SNRI: selective serotonine and noradrenalin reuptake inhibitor; NDRI: noradrenalin and dopamin reuptake inhibitor.

3.2. Behavioral assessments

Depression severity was assessed using the German versions of the 10-item, clinician-rated Montgomery-Åsberg Depression Rating Scale (MADRS) and the self-reported, 21-item Beck Depression Inventory. Physical activity prior to study entry was assessed using a 6-point Likert scale with descriptors ranging from "never" (1) to "very often" (Cuppett and Latin, 2002). Smoking habits were measured in pack-years (the number of cigarettes smoked per day x years of smoking/20), and alcohol consumption was measured in drinks consumed per week.

3.3. Magnetic Resonance Imaging (MRI)

Epicardial adipose tissue (EAT), intra-abdominal adipose tissue (IAT) and subcutaneous adipose tissue (SAT) were examined using a 1.5 T MRI scanner (Avanto, Siemens Healthcare). EAT is defined as the cardiac fat internal to the fibrous layer of the parietal pericardium (Sacks and Fain, 2007; Talman et al., 2014). To quantify EAT, ECG-gated T1-weighted dark-blood turbo spin-echo sequences were acquired in short- and long-axis views at the following specifications: TR/TE=750/37 ms, flip angle=180°, matrix=384 × 187, field of view=380 mm, and slice thickness=10 mm. EAT was quantified between the atrioventricular plane and the apex by manual segmentation using QMass 7.1 software (Medis, Leiden, The Netherlands) as described previously (Kahl et al., 2014). To quantify IAT and SAT, the T1-weighted 3D Volume Interpolated Breathold Examination (VIBE)