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Physical activity, exercise, depression and anxiety disorders

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Abstract There is a general belief that physical activity and exercise have positive effects on mood and anxiety and a great number of studies describe an association of physical activity and general well-being, mood and anxiety. In line, intervention studies describe an anxiolytic and antidepressive activity of exercise in healthy subjects and patients. However, the majority of published studies have substantial methodological shortcomings. The aim of this paper is to critically review the currently available literature with respect to (1) the association of physical activity, exercise and the prevalence and incidence of depression and anxiety disorders and (2) the potential therapeutic activity of exercise training in patients with depression or anxiety disorders. Although the association of physical activity and the prevalence of mental disorders, including depression and anxiety disorders have been repeatedly described, only few studies examined the association of physical activity and mental disorders prospectively. Reduced incidence rates of depression and (some) anxiety disorders in exercising subjects raise the question whether exercise may be used in the prevention of some mental disorders. Besides case series and small uncontrolled studies, recent well controlled studies suggest that exercise training may be clinically effective, at least in major depression and panic disorder. Although, the evidence for positive effects of exercise and exercise training on depression and anxiety is growing, the clinical use, at least as an adjunct to established treatment approaches like psychotherapy or pharmacotherapy, is still at the beginning. Further studies on the clinical effects of exercise, interaction with standard treatment approaches and details on the optimal type, intensity, frequency and duration may further support the clinical administration in patients. Furthermore, there is a lack of knowledge on how to best deal with depression and anxiety related symptoms which hinder patients to participate and benefit from exercise training.

Keywords Depression · Anxiety · Anxiety disorder · Physical activity · Exercise

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Introduction

"On order for man to succeed in life, god provided him with two means, education and physical activity. Not separately, one for the soul and the other for the body but for the two together. With these two means, men can attain perfection" (Plato, fourth century BC).

Physical activity is associated with a range of health benefits, and its absence can have harmful effects on health and well being, increasing the risk for coronary heart disease, diabetes, certain cancers, obesity, hypertension and all cause mortality (CDC 1996). Physical inactivity may also be associated with the development of mental disorders: some clinical and epidemiological studies have shown associations between physical activity and symptoms of depression and anxiety in cross-sectional and prospective-longitudinal studies (Abu-Omar et al. 2004a, b; Bhui and Fletcher 2000; Farmer et al. 1988; Dunn et al. 2001; Goodwin 2003; Haarasilta et al. 2004; Lampinen et al. 2000; Motl et al. 2004). Moreover, exercise is an integral part in the treatment and rehabilitation of many medical conditions. Improving physical

well being may also lead to improved psychological well being and is generally accepted that physical activity may have positive effects on mood and anxiety. What is the empirical evidence for this belief: what do we not know about the association of physical activity and depression or anxiety (disorders) and can/should exercise (training) be used in the treatment of depression or anxiety disorders?

The recommendations for physical activity have shifted in the last decade: in the 1990s the focus of public health recommendations was on 3–5 exercise bouts per week (American College of Sports Medicine 1978, 1990). Since 1995, (Pate et al. 1995) physical activity of moderate intensity for at least 30 min on most if not every day during the week is recommended, and besides "classical" exercise training, everyday physical activity such as brisk walking, gardening or window washing is regarded as health enhancing physical activity. Following this shift in public health recommendations, standardized instruments for the assessment of physical activity independent of the context (sports, at home, for transportation, at work) have been developed. One of this instruments is the international physical activity questionnaire (IPAQ) (Craig et al. 2003), which allows to calculate metabolic equivalents during the last week and first studies have been published using such instruments, broadening the focus of research from the effects of exercise (training) to physical activity and (mental) health and disease.

Physical activity, exercise and the prevalence and incidence of depression and anxiety disorders

Cross-sectional studies have consistently associated high self-reported levels of habitual physical activity with better mental health and a correlation of habitual exercise level with low depression (but not anxiety) has been described in adolescents (Morris et al. 1992) and elderly subjects (Ruuskanen and Ruoppila 1995). Controlling for social class and health status, Steptoe and Butler (1996) showed in a large cohort ($n = 5{,}061$) that vigorous exercise participation was related to lower emotional distress. In line, Steptoe et al. (1997) reported that after controlling for age and sex, exercise correlated with lower depression in 16,483 undergraduates. In upper Bavaria, Germany ($n = 1{,}536$) (Weyerer 1992) and in separate samples from the United States and Canada totaling 55,000 subjects (Stephens 1988), self-reported level of recreational physical activity correlated with better mental health, including fewer symptoms of both anxiety and depression (after controlling for confounding variables including age, sex, sociodemographic status and physical illness). In the European Union, physical activity (in everyday life) as measured with the IPAQ was associated with self-rated health in general (Abu-Omar et al. 2004b) and also with self-rated mental health (Abu-Omar et al. 2004a). A total of 16,230 respondents, age 15 years and above, were studied; in some of the 15 nations, evidence for a dose-response relationship between physical activity and mental health was found. On a diagnostic level, Goodwin (2003) analyzed the data of the US National Comorbidity Survey ($n = 5{,}877$): the association of regular physical activity and lower prevalence of current major depression, social phobia, specific phobia, and agoraphobia was significant and persisted after controlling for sociodemographic characteristics, self-reported physical disorders and comorbid mental disorders.

In most studies, fitness was not directly assessed and Thirlaway and Benton (1992) found that fitness interacted with exercise habits such that highly fit subjects who do not exercise had poorer mental health status than all others; fit nonexercisers may have been temporarily prevented from exercising, which may worsen the mood and increase anxiety (Morris et al. 1990).

Simultaneously, measuring exercise habits and mood or anxiety (disorders) in cross-sectional survey is inherently ambiguous about cause and effect. Therefore, prospective longitudinal studies are necessary to further characterize the association of physical activity and mental disorders. Until now, these studies are rare and at least in part, prospective longitudinal studies support results and hypothesis derived from cross-sectional studies: Paffenbarger et al. (1994) found that physical activity negatively correlated with depression approximately 25 years later in a sample of 10,201 men. In a sample of 4,848 subjects, Camacho et al. (1991) reported that the absence of exercise habits was linked to later depression across two 9-year periods. However, this study did not control for depression at study entry. In 2,084 elderly people, stratified into low and high depression, daily walking predicted improved depression in both the groups after 3 years (Mobily et al. 1996). In older adults, Strawbridge et al. (2002) reported a protective effect of physical activity on the development of depression. Studying 1,900 subjects for 8 years, Farmer et al. (1988) reported that regular exercise reduced the risk to develop a depression. In line, Motl et al. (2004) reported that naturally occurring changes in physical activity are inversely related to depressive symptoms during early adolescence. In a sample of 2,548 adolescents and young adults, we recently described that subjects with regular physical activity had substantially lower overall incidence of any and comorbid mental disorders after 4 years and a lower incidence of somatoform-, dysthymic- and some anxiety disorders (Ströhle et al. 2007).

Exercise (training) in the treatment of depression and anxiety disorders

The early literature on exercise as a treatment for depression and anxiety disorders was positive. However, these studies suffered from a variety of methodological flaws (Lawlor and Hopker 2001) and may have dampened the enthusiasm towards implementing exercise training in the routine care and treatment. In the past decade, however, controlled clinical trials have been performed, examining the administration of exercise training in the treatment of depression and some anxiety disorders.

Depression

A great number of studies suggest that exercise training may reduce depressive symptoms in nonclinical and clinical populations (Blumenthal et al. 1989; DiLorenzo et al. 1999; Roth and Holmes 1987; King et al. 1993) and in patients with major depression (Blumenthal et al. 1999; Dunn et al. 2005; Singh et al. 2005; Martinsen et al. 1985; Klein et al. 1985; Veale et al. 1992; McNeil et al. 1991; Singh et al. 2001; Dimeo et al. 2001). In addition to meta-analytic results, selected studies on different aspects of exercise treatment of major depression are presented.

Meta-analytic studies provide one means of summarizing the growing body of primary research and identifying variables that may moderate the effects of exercise on depression. North et al. (1990) analyzed 80 studies and reported an effect size (ES) of −0.53, indicating that exercise training reduced depression scores by approximately one half a standard deviation as compared to the comparison groups; an even larger effect size (−0.94) was reported in clinical populations (e.g., substance abusers, post-myocardial infarction or hemodialysis patients). Including only studies with patients diagnosed with major depression (not due to a general medical condition, $n = 30$), Craft and Landers (1998) reported an effect size of −0.72, showing that only the length of the exercise program was a significant moderator of the clinical effects, with programs of at least 9 weeks being associated with larger reductions in depression. Patient characteristics (age, gender, severity of depression) were not significant moderators and when compared with standard treatment of depression (pharmacotherapy, psychotherapy), exercise training has comparable beneficial effects. Limiting the analyses to randomized controlled trials ($n = 14$), Lawlor and Hopkins reported an effects size of −1.1, when exercise training was compared to no-treatment control groups. In addition, exercise training was as effective as cognitive therapy, with a nonsignificant effects size of −0.3. Craft and Perna (2004) converted the overall effect sizes of these meta-analyses to a binomial effect size, allowing to examine the practical clinical significance: exercise training increased the success rate to 67–74%. Because in a wide range of medical settings, a 50% reduction of symptoms is considered a treatment response, these success rates are quite remarkable. In a more recent quantitative and qualitative review of studies in patients diagnosed with major depression ($n = 11$), Stathopoulou et al. (2006) reported an effect size of −1.42 for the advantage of exercise training over control conditions.

A possible dose response relationship of exercise in the treatment of major depression was studied by Dunn et al. (2005): a dose consistent with public health recommendations (17.5 kcal/kg per week) (Pate et al. 1995) was an effective treatment for mild to moderate major depression and a lower dose was comparable to placebo with no differences between 3 and 5 weekly sessions.

Although no control group was involved, a study of Dimeo et al. (2001) suggests that in treatment-resistant patients with major depression, 30 min of treadmill walking for ten consecutive days may be sufficient to produce a clinically relevant and statistically significant reduction in depression, as measured with the Hamilton Depression rating Scale. These findings are substantiated by a more recent study involving a placebo exercise group (low-intensity stretching and relaxation exercises) in patients receiving a standard antidepressant treatment: the reduction of depression scores and the response rates were larger in the exercise training group Knubben et al. (2006).

Some studies (Dunn et al. 1998; Kodis et al. 2001), but not all (King et al. 1991) have reported that supervised exercise training results in larger improvements in functional capacity compared with home-based exercise, and that greater energy expenditure is associated with larger reductions in depressive symptoms (Dunn et al. 2005). However, this issue needs further well controlled studies in patients with major depression.

While most studies employed walking or jogging programs, the efficacy of nonaerobic exercise has also been studied. In depressed elderly, a resistance training program was more effective than the control condition (Singh et al. 1997). Comparing random assignment to running or weight lifting, Doyne et al. (1987) reported that both the activities reduced depressive symptoms, and that there were no statistically significant differences at the end of the active treatment phase or at follow-up after 1 year. Similarly, Martinsen et al. (1989) could not find differences between aerobic (jogging or brisk walking) and nonaerobic (strength training, coordination and flexibility training) exercise training.

Blumenthal et al. (1999) could show that 16 weeks of group exercise training in older patients with major depression was as effective as antidepressant treatment with sertraline. Most remarkable is that, the 10-month

relapse rate was significantly lower in the exercise group (8%), when compared to the sertraline (38%) or the combination group (31%) (Babyak et al. 2000). In a recent study, Blumenthal et al. (2007) reported that also in adults with major depression, the efficacy of exercise seems generally comparable to antidepressant medication and both tend to be better than placebo. Additionally, it seems that exercise compares quite favorably with standard psychotherapy of major depression: in the few studies that have evaluated their relative efficacy, running was just as effective as psychotherapy (Greist et al. 1979), cognitive therapy or a combination of cognitive therapy and running (Fremont and Craighead 1987).

Anxiety disorders

Compared to the wide range of research on the positive effects of exercise in major depression, anxiety disorders have been less frequently studied. In addition, the clinical diversity of anxiety disorders does not allow to generalize from studies in one specific anxiety disorder to other disorders. Changes in the diagnostic criteria further complicate the interpretation of early studies. However, there is no doubt on the possible anxiolytic effects of aerobic exercise training on healthy volunteers (Long and Satvel 1995). In addition, studies on healthy subjects and two case reports (Orwin 1974; Muller and Armstrong 1975) suggest that an acute bout of exercise is anxiolytic as well. In contrast, exercise may induce acute panic attacks (Broocks et al. 1998; Barlow and Craske 1994) or increase subjective anxiety in patients with panic disorder more than in other people. However, there is preliminary evidence that an acute bout of exercise has an antipanic activity in healthy subjects (Ströhle et al. 2005) and in patients with panic disorder (Esquivel et al. 2002), and that patients with panic disorder are more vulnerable to experience somatic symptoms after exercise.

Numerous meta analyses have been published on the effect of exercise on anxiety (Petruzzello et al. 1991; Long and van Stavel 1995; Guszkowska 2004). However, only two have examined the effects of exercise in subjects with increased anxiety levels. In one meta-analysis, 11 studies have been analyzed reporting trait anxiety for subjects being identified as highly anxious: the mean effect size was 0.47, indicating that relative to control, exercise training resulted in a moderate reduction in anxiety (Petruzzello et al. 1991). The second meta analysis studied the effects of aerobic and anaerobic exercise on depression and anxiety symptomatology in subjects with anxiety scores above the 50th percentile. Eleven randomized studies compared the effects of an exercise training with a wait-list control and analyses revealed an effect size of 0.94. Within these comparisons, the effect size of studies with formal anxiety disorders ($n = 7$) was 0.99 (Stich 1998).

In patients with high trait anxiety or generalized anxiety disorder, aerobic exercise training was superior to strength and mobility exercises (Steptoe et al. 1989) or no treatment and comparable effective as cognitive behavior therapy (McEntee and Halgin 1999). In a mixed patient sample (panic disorder, generalized anxiety disorder or social phobia), a home-based walking program improved the clinical efficacy of a group cognitive behavioral therapy as compared to educational sessions with a focus on healthy eating (Merom et al. 2007).

Case reports (Dractu 2001) and two published clinical studies suggest that exercise training may be used therapeutically in patients with anxiety neurosis (Sexton et al. 1989) and panic disorder (Broocks et al. 1998); Broocks and coworkers compared clomipramine, exercise training and placebo in patients with panic disorder and demonstrated that although clomipramine had a more rapid onset of action, both the active treatments were significantly better than (pill) placebo. In the most recent study of this group, exercise training was not superior to relaxation in panic disorder patients treated with paroxetine or placebo (Wedekind et al. submitted). Preliminary evidence exists, that panic disorder responds to both aerobic and nonaerobic interventions (Martinsen et al. 1989).

Posttraumatic stress disorder may also respond to exercise training (Manger 2000; Manger and Motta 2005). However, comparable to the situation in agoraphobia, social phobia and specific phobia adequately sized randomized controlled clinical trials are necessary to conclude that exercise training is an effective treatment for patients with specific anxiety disorders. At the moment, we have the best evidence for the effectiveness of exercise training in patients with panic disorder, although replication of these results is still missing.

Conclusions

Developmental, neurobiological and psychological factors (Cotman and Berchtold 2002; Cohen and Rodriguez 1995) might underlie, mediate and/or moderate the association of physical activity and some mental disorders in a very dynamic way. Thus, the effects of physical activity might stimulate a complex system and trigger a cascade of events, which, for example, result in higher resilience against (stress-associated) mental disorders (Cotman and Berchtold 2002; Cohen and Rodriguez 1995; Charney 2004). Further characterization and randomized intervention studies are needed before concluding that exercising sports is a promising target preventing the onset of specific mental disorders. Such a preventive effect may be especially relevant for individuals at high risk for these disorders either encoded genetically, acquired during premorbid life, or as a

scar imprinted by previous disease episodes or traumatic events (Ströhle and Holsboer 2003). This highly relevant public health topic must be addressed with controlled intervention studies based on public funding.

Studies have been presented giving evidence that physical activity and exercise can be also used in the treatment of depression and anxiety disorders. The mechanisms responsible for exercise-related improvements in depression and anxiety disorders are not all known, and it is most likely to be a complex interaction of psychological and neurobiological mechanisms underlying, mediating and/or moderating these effects. At the moment we are far away from a conclusive model explaining the antidepressant and anxiolytic activity of exercise. In brief, some of the currently discussed mechanisms are highlighted: although some studies suggest that social support is not necessarily critical to the therapeutic effects of exercise training, a number of psychological factors have been proposed: increased self-efficacy, a sense of mastery, distraction, and changes of self-concept seem to be involved in the therapeutic efficacy of exercise training. In panic disorder, exercise training may also be regarded as an exposure therapy (Marks 1999). In addition, biological pathways are also suggested, including increased central norepinephrine neurotransmission (Sothman and Ismail 1984, 1985), changes in the hypothalamic adrenocortical system (Droste et al. 2003; Ströhle and Holsboer 2003), and increased secretion of atrial natriuretic peptide (Ströhle et al. 2006), amine metabolites, as well as serotonin synthesis and metabolism (Dishman et al. 1997; Ransford 1982) and β-endorphins. Further discerning the different mechanisms of the antidepressive and anxiolytic activity of help might further improve the clinical effectiveness of exercise treatment of depression and anxiety disorders.

There is a lack of systematic studies on how to best deal with depression and anxiety related symptoms which hinder patients to participate and benefit from exercise training. At the moment, strategies to change physical activity, which have been successful in healthy subjects, can be adapted for those with depression or anxiety disorders. Medical clearance is necessary for subjects with risk factors for cardiovascular disease. The physical activity readiness questionnaire (PAR-Q) (Thomas et al. 1992) is a simple screening instrument commonly used in preparticipation screening for moderate intensity physical activity programs. After the choice for the intended mode of exercise training, exercise testing should be performed accordingly and exercise prescription ends with the initiation and monitoring of a training program. Especially in patients, an initial over demand must be avoided. For longer training programs, prescription adjustment should be performed according to an increased fitness level, and a posttraining exercise testing has been emphasized as a basis for feedback to training participants.

Unfortunately, no general concept for the therapeutic administration of physical activity for patients with depression and anxiety disorders) has been developed so far (Meyer and Broocks 2000). Usually, 3–4 training sessions/week should be performed with a duration of at least 20–30 min. Most studies have an overall program duration of 8–14 weeks. An activity diary is recommended and daily life physical activity should also be recorded. Moderate intensity activities such as walking are more successful than vigorous physical activity programs (Dishman and Buckwort 1996) and interventions that target specific groups or are tailored to the individual are more effective than more generic interventions (Marcus et al. 1998; Marcus and Forsyth 1998; Strecher et al. 2002; Segar et al. 2002). Exercise prescription or motivational messages in printed form or by computer seem to be also more effective than face-to-face counseling alone (Dishman et al. 1997; Smith et al. 2000; Swinburn et al. 1998). For patients with depression or anxiety disorders, disorder-specific information on exercise (training) should be given to the patients. For example, patients with major depression with diurnal changes should exercise later in the day; patients with panic disorders or panic attacks, should be informed that in rare cases exercise-associated bodily sensations may trigger panic attacks, despite an anxiolytic activity of acute (Ströhle et al. 2005) and long-term exercise (Broocks et al. 1998), and that this increase of symptoms may be regarded as a form of exposure. The activity diary should include measurements for depression and anxiety symptom severity and it is hypothesized such a direct feedback on the association of exercise and well-being may enhance adherence to exercise programs in patients. Strategies used with cognitive behavioral therapy may be applied to exercise (training): situational analysis, goal setting, self monitoring, homework activities, and supportive follow-up may support compliance and help achieve and maintain a new behavior (Otto et al. 2007). In some patients with the most severe forms of major depression, participation in an exercise program needs prior improvement of symptoms by other treatment approaches. Other patients, e.g., partial responders, or subjects with barriers to traditional medical or psychological treatment approaches, like, for example, minority women may especially benefit from exercise training (Otto et al. 2007). Implementation and further optimization of exercise training programs for patients with depression or anxiety disorders need a multidisciplinary approach involving scientists and practitioners in psychiatry, psychology, sport medicine and health care providers as well as public funding.

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