



Effects of short-term exercise training on signs and symptoms of generalized anxiety disorder[☆]

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ABSTRACT

Background: No randomized controlled trial has investigated exercise training effects on signs and symptoms that characterize patients with Generalized Anxiety Disorder (GAD).

Objectives: To quantify and compare the effects of six weeks of resistance (RET) and aerobic exercise training (AET) on signs and symptoms associated with GAD.

Methods: Thirty sedentary women, aged 18–37 years, diagnosed by blinded clinicians with a primary DSM-IV diagnosis of GAD, who were not engaged in treatment other than pharmacotherapy, were randomized to six weeks of RET, AET, or wait list (WL). RET involved two weekly sessions of lower-body weightlifting. AET involved two weekly sessions of leg cycling matched with RET on body region, positive work, exercise time, and load progression. Outcomes included concentration difficulty, trait anxiety, symptoms of depression, tension, low vigor, fatigue and confusion, irritability, muscle tension, and pain location and intensity. Hedges' *d* effect sizes and 95% confidence intervals were calculated at weeks two, four, and six for each exercise condition compared to WL.

Results: RET significantly reduced feelings of anxiety-tension and the frequency and intensity of irritability. RET also resulted in six-week Hedges' *d* effect sizes ≥ 0.36 for trait anxiety, concentration, symptoms of depression, fatigue and vigor, and pain intensity. AET resulted in comparable improvements in trait anxiety, concentration, irritability, muscle tension, and symptoms of fatigue and vigor. Effects for 9 of 12 outcomes were non-significantly larger for RET compared to AET.

Conclusions: Short-term RET and AET provoke comparable improvements in signs and symptoms associated with GAD, particularly irritability, anxiety, low vigor and pain. Findings warrant further investigation.

Clinical trial registration: (ClinicalTrials.gov) Identifier: NCT00953654.

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1. Introduction

Findings from a recent randomized controlled trial indicated that short-term exercise training may be an effective adjuvant or augmentation treatment with minimal risk of adverse events to ameliorate worry symptoms, the hallmark symptoms of Generalized Anxiety Disorder (Herring, Jacob, Suveg, Dishman, & O'Connor, *in press*). In addition to pathological worry, patients with Generalized Anxiety Disorder (GAD) also are often characterized by an elevation in one or more associated signs and symptoms, including restlessness and feelings of anxiety, fatigue, difficulty concentrating, irritability, muscle tension (American Psychiatric Association, 2000),

pain (Beesdo, Jacobi, Hoyer, Low, & Hofler, 2010; Wittchen et al., 2002) and depression (Watson, 2009).

There has been limited success in treating the signs and symptoms associated with GAD. Although pharmacotherapy has shown some efficacy as a frequently employed first line treatment (Chessick, Allen, Thase, et al., 2006; Hackett, Haudiquet, & Salinas, 2003), there have been notable drawbacks including well-established negative side effects such as nausea and sexual dysfunction (Corona et al., 2009). Because GAD symptoms are heterogeneous, pharmacotherapy may well attenuate one symptom but exacerbate another. For example, selective serotonin reuptake inhibitors have shown efficacy for GAD symptom improvement (Chessick et al., 2006; Hackett et al., 2003), but they often exacerbate sleep disturbances (Schweitzer, 2005). Behavioral treatments also have demonstrated efficacy (Chambless et al., 1998), but there are logistical barriers associated with these treatments, including expense and the need for extensive specialized training among practitioners who provide

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therapy. Thus, there is a continued need to explore alternative or adjuvant treatments, including exercise training, for the associated signs and symptoms of GAD.

Exercise training has positive effects on multiple signs and symptoms that characterize patients with GAD, including poor concentration (Colcombe & Kramer, 2003), depression (Blumenthal et al. 1999), fatigue (Puetz, O'Connor, & Dishman, 2006), feelings of anxiety (Broocks et al., 1998), muscle tension (Smith, O'Connor, Crabbe, & Dishman, 2002), and pain (Busch, Schacter, Peloso, & Bombardier, 2002; Hayden, van Tulder, Malmivaara, & Koes, 2005). In addition, the relation between exercise and irritability is of potential interest in part because of associations between negative moods related to irritability, including anger and hostility, and the development and progression of heart disease (Chida & Steptoe, 2009; Kubzansky & Kawachi, 2000). No randomized controlled trial has investigated the effects of exercise training on the signs and symptoms that characterize patients with GAD.

There also is a need to compare the psychological consequences of resistance exercise training (RET) and aerobic exercise training (AET). Several lines of evidence suggest that RET can be as effective as AET for the improvement of anxiety and other signs and symptoms associated with GAD. This evidence includes: (1) compared to AET, RET has shown efficacy for attenuating symptoms of anxiety, depression, fatigue, and pain (O'Connor, Herring, & Carvalho, 2010); (2) compared to AET, RET has resulted in larger improvements in associated signs and symptoms of GAD among other samples, including fatigue among patients and healthy adults (Puetz et al., 2006; Puetz, Beaman, & O'Connor, 2008) and fatigue, quality of life, and depressive symptoms among cancer patients (Courneya et al., 2007); and, (3) given the high comorbidity of GAD and its overlapping etiology with major depressive disorder (MDD), compared to AET, RET has resulted in larger improvements in depressive symptoms and disturbed sleep among MDD patients (Singh et al., 2005).

Thus, the primary objective of this ancillary investigation was to quantify and compare the magnitude of the effects of six weeks of RET and AET, matched on body region, time actively engaged in exercise, positive work, and weekly load progression, on signs and symptoms that characterize GAD patients. We hypothesized that both exercise conditions would result in improvements in signs and symptoms, and that, because conditions were matched, the magnitude of the effect sizes would be similar between RET and AET.

2. Methods

The detailed methods and procedures of this investigation are reported elsewhere (Herring et al., *in press*). The study protocol for the trial was approved by an Institutional Review Board. All volunteers provided written informed consent. Thirty women living near Athens, Georgia were recruited. Inclusion criteria were: (1) age of 18–37 years; (2) no concurrent psychiatric or psychological therapy other than medication; and, (3) a primary DSM-IV diagnosis of GAD. Exclusion criteria were: (1) too few worry symptoms, defined by both a Psychiatric Diagnostic Screening Questionnaire GAD subscale score <6 (Zimmerman & Mattia, 2001) and a Penn State Worry Questionnaire score <45 (Meyer, Miller, Metzger, & Borkovec, 1990); (2) too high a level of physical activity, defined by a seven-day physical activity recall (7PAR) energy expenditure estimate >260 kilocalories per kilogram body weight per week (Blair et al., 1985) (3) pregnancy; and, (4) the presence of contraindications to moderate intensity exercise. Potential participants assigned an Anxiety Disorders Interview Schedule (ADIS-IV) clinician severity rating ≥ 4 were diagnosed with GAD (Brown, Di Nardo, & Barlow, 1994). Following ADIS-IV administration, eligible patients were enrolled in the trial within 1–15 days. Patients were block randomized to conditions in blocks

of three based on the three arms of the trial [RET, AET, and wait list (WL)] and stratified based on psychoactive medication use (no medication or medication use) to ensure three similar groups of equal size.

2.1. Baseline strength

Four-repetition maximum (4-RM) was obtained on leg press, leg curl, and leg extension using Cybex Eagle equipment. Predicted one-repetition maximums (1-RM) were calculated as: $1\text{-RM} = 4\text{-RM} \times 1.13$.

2.2. Intervention conditions

Because there is continued interest in knowing the minimum exercise stimulus necessary to elicit mental health benefits (Dunn, Trivedi, & O'Neal, 2001), both RET and AET involved two weekly sessions for six weeks. Sessions were conducted on Monday/Wednesday, Tuesday/Thursday, or Wednesday/Friday.

Recent meta-analytic findings of the anxiolytic effects of exercise among patients with a chronic illness revealed that significantly larger anxiety reductions resulted from exercise program lengths up to 12 weeks. However, less than 25% of the reviewed studies conducted exercise programs of less than eight weeks (Herring, O'Connor, & Dishman, 2010). Thus, because there is a need to examine whether shorter exercise program lengths can elicit positive mental health changes, the effects of six weeks of exercise training were investigated.

Since 1995, less than 20% of randomized controlled trials of exercise effects on anxiety among healthy adults and chronically-ill patients have examined the effects of exercise programs requiring participants to exercise less than three sessions per week, while approximately 60% have required exactly three sessions per week (Herring et al., 2010, unpublished data). Additionally, significantly better adherence has resulted from exercise programs requiring fewer sessions per week (Herring et al., 2010). Thus, we investigated the effects of two exercise training sessions per week.

2.3. Resistance exercise training

Each RET patient performed seven sets of 10 repetitions each of leg press, leg curl and leg extension exercises beginning at 50% of predicted one-repetition maximum (1-RM) during week one and progressing by five percent of predicted 1-RM weekly. A moderate intensity was selected because the largest mental health benefits of RET have resulted from progressive resistance exercise beginning at a moderate (i.e., 50%–60% 1-RM) intensity (O'Connor et al., 2010; Singh et al., 2005). Each exercise was preceded by a warm-up set of 10 repetitions beginning at 35% of predicted 1-RM during week one and progressing by five percent of predicted 1-RM each week. Heart rate and ratings of perceived exertion (RPE) were obtained following the completion of each exercise. Session RPE was obtained following the completion of the workout.

2.4. Aerobic exercise training

AET was matched to RET on (1) the time spent actively engaged in exercise, (2) the positive work completed (i.e., the work done against gravity), (3) a five percent progression in load (intensity) per week, and (4) body region exercised (legs). Each AET patient performed two sessions of 16 min of continuous, dynamic leg cycling exercise per week. Heart rate and RPE were obtained during the last 10 s of the 2nd, 7th and 15th minutes of each session. Session RPE was obtained following the completion of the workout.

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