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The effects of exercise on transdiagnostic treatment targets: A meta-analytic review

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ABSTRACT

Background: The present study meta-analytically reviewed the effects of exercise on four transdiagnostic treatment targets: anxiety sensitivity (AS), distress tolerance (DT), stress reactivity (SR), and general self-efficacy (GSE).

Methods: We conducted systematic searches of peer-reviewed studies in bibliographical databases (Cochrane Library, psychINFO, PubMed) before April 1, 2018. Only randomized controlled trials (RCT) evaluating the effect of exercise on AS, DT, SR, or GSE using at least one validated outcome instrument in a sample of adolescents (≥13 years old) or adults were selected. We employed a meta-analysis of effects using random-effects pooling modeling for each treatment target.

Results: The systematic search yielded 28 RCTs meeting eligibility criteria. Exercise interventions had a large effect on reducing AS (six studies, Hedges's $g = 0.72$, $p = .001$), a medium effect on increasing GSE (eight studies, Hedges's $g = 0.59$, $p < .001$), and a small effect on reducing SR (ten studies, Hedges's $g = 0.32$, $p < .001$). Evidence from four studies suggested that exercise interventions had a small but non-significant effect on increasing DT (Hedges's $g = 0.21$, $p = .26$).

Conclusions: This meta-analysis provides preliminary evidence exercise can engage certain transdiagnostic targets. Further research is required to optimize exercise intervention parameters to achieve the strongest effects on these important mechanistic variables.

1. Introduction

Psychiatric comorbidity is common in clinical settings and an important concern for mental healthcare professionals. Nearly half of those with a psychiatric disorder meet criteria for more than one disorder in a 12-month period (Kessler, Chiu, Demler, & Walters, 2005). Anxiety and mood disorders are by far the most common disorders, with approximately one in four respondents meeting criteria for at least one anxiety or mood disorder in a national sample (Kessler et al., 2005). For example, among those with Posttramatic Stress Disorder (PTSD) the odds of also meeting diagnostic criteria for an anxiety or mood disorder after adjusting for sociodemographic variables are 4.3 and 4.9, respectively, compared to individuals without PTSD (Pietrzak, Goldstein, Southwick, & Grant, 2011). Similar elevations in odds of meeting for an anxiety or mood disorders (2.7 and 3.4 respectively) were seen among individuals experiencing partial PTSD (i.e. not meeting full diagnostic criteria; Pietrzak et al., 2011). Not surprisingly, comorbidity has been strongly associated with greater severity of symptoms and impairment (Kessler et al., 2005). Until relatively recently, comorbidity has complicated treatment decisions, as most empirically supported interventions are conceptualized and designed for a single disorder. Efforts to research, define, and treat underlying commonalities of mental health distress has been garnering interest in recent years (Craske, 2012).

Transdiagnostic treatment approaches targeting underlying causes and maintaining factors common to many mental health disorders have emerged with promising results (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015). Initial tests of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (Ellard, Fairholme, Boisseau, Farchione, & Barlow, 2010), for example, that targets maintaining factors applicable to all anxiety and unipolar mood disorders have been encouraging (Barlow et al., 2017; Farchione et al., 2012; Steele et al., 2018). Likewise, False Safety Behavior Elimination Therapy (Riccardi, Korte, & Schmidt, 2017; Schmidt et al., 2012), group based transdiagnostic CBT (Norton, Hayes, & Springer, 2008), and mindfulness- and acceptance-based transdiagnostic treatments (Arch et al., 2013; Khoury et al., 2013) have been found efficacious in reducing anxiety symptoms

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among a heterogenous mix of anxiety disorders. Additionally, comparisons of CBT-based transdiagnostic treatment approaches to active treatment-as-usual conditions have shown positive effects (Andersen, Toner, Bland, & McMillan, 2016; Reinholt & Krogh, 2014). Transdiagnostic approaches have also shown success when disseminated and implemented at community clinics and Veteran Affair Medical Centers (Creed et al., 2016; Gros, Szafranski, & Shead, 2017). Current evidence suggests transdiagnostic treatments may be effective because they engage important mediators of change and underlying vulnerabilities such as tolerance for uncertainty, positive and negative affect (Talkovsky & Norton, 2018), anger (Cassiello-Robbins et al., 2018), hope, neuroticism (Gallagher, 2017), and rumination (Heeren & Philippot, 2011).

Attending to patient preferences requires making available a wide range of strategies that can be implemented to engage therapeutic targets. In the current study, we sought to address the question whether exercise can be a tool in the arsenal of a clinician who seeks to intervene on key mechanisms underlying the maintenance and amelioration of anxiety and depressed mood. Hence, complementing descriptive, experimental, and meta-analytic studies documenting the anxiolytic and antidepressant effects of exercise (Schuch et al., 2016; Stathopoulou, Powers, Berry, Smits, & Otto, 2006; Stonerock, Hoffman, Smith, & Blumenthal, 2015; Stubbs et al., 2017), the current study aimed to meta-analytically review the efficacy of exercise for engaging four putative transdiagnostic treatment targets, namely anxiety sensitivity (AS), distress tolerance (DT), stress reactivity (SR), and general self-efficacy (GSE). Recognizing that by limiting the focus to four outcomes, we may inadvertently underestimate the potential of exercise as a transdiagnostic treatment tool, we will provide a rationale for selecting these four for the current analyses.

1.1. Maintenance factors in anxiety and depressed mood

1.1.1. Anxiety sensitivity

Elevated anxiety sensitivity (AS), or fear of arousal-related bodily sensations, amplifies anxiety, resulting in an increased distress response to anxiety symptoms and general stress (Otto et al., 2016; Otto & Smits, 2018; Smits, Otto, Powers, & Baird, 2018). Heightened AS has been found to be a key factor in the etiology and maintenance of anxiety disorders (Olatunji & Wolitzky-Taylor, 2009; Taylor, 1999), mood disorders (Naragon-Gainey, 2010; Otto, Pollack, Fava, Uccello, & Rosenbaum, 1995), trauma- and stressor-related disorders (Marshall, Miles, & Stewart, 2010), as well as alcohol and substance use disorders (Howell, Leyro, Hogan, Buckner, & Zvolensky, 2010; Lejuez, Paulson, Daughters, Bornovalova, & Zvolensky, 2006; Schmidt, Zvolensky, & Maner, 2006). Evidence suggests reductions in AS during treatment are related to improvement in anxiety (e.g., reduced posttraumatic stress and panic attack frequency; Gallagher et al., 2013; Smits, Powers, Cho, & Telch, 2004; Vujanovic, Bernstein, Berenz, & Zvolensky, 2012), depression symptoms (Mitchell, Capron, Raines, & Schmidt, 2014), smoking cessation (Assayag, Bernstein, Zvolensky, Steeves, & Stewart, 2012; Zvolensky, Rosenfield et al., 2018; Zvolensky, Garey et al., 2018), and reduced problem drinking (Watt, Stewart, Birch, & Bernier, 2006; Wolitzky-Taylor et al., 2015). Thus, targeting AS is prudent when intervening transdiagnostically.

1.1.2. Distress tolerance

Distress tolerance (DT) reflects the perceived or actual ability to experience and withstand negative emotional or aversive states (Leyro, Zvolensky, & Bernstein, 2010; Simons & Gaher, 2005). Individuals low in DT tend to minimize exposure to distressing states by restricting their expression of emotion (Leyro et al., 2010) or by engaging in avoidant and escape behaviors (McHugh & Otto, 2011). Low DT has been related to a range of psychopathology, including anxiety, trauma, mood, substance use, and personality disorders (Anestis, Gratz, Bagge, & Tull, 2012; Buckner, Keough, & Schmidt, 2007; Laposa, Collimore, Hawley, & Rector, 2015; Vujanovic, Bonn-Miller, Potter, Marshall, & Zvolensky, 2011). While DT is considered theoretically similar to AS, it differs conceptually in that DT encompasses maladaptive responding to a wide range of emotions beyond anxiety, such as pain and sadness (Leyro et al., 2010), as well as a wider range of maladaptive reactions (e.g., cognitive reactions, behavioral reactions; Wolitzky-Taylor et al., 2015). Treatments that enhance tolerance to distress have found that increases in DT are associated with improvements in symptom severity across anxiety and mood disorders (Banducci, Connolly, Vujanovic, Alvarez, & Bonn-Miller, 2017; Williams, Steinberg, Griffiths, & Cooperman, 2013), PTSD (Boffa, Short, Gibby, Stentz, & Schmidt, 2018), borderline personality disorder (Linehan, 1993), and substance use disorders (Bornovalova, Gratz, Daughters, Hunt, & Lejuez, 2012; Brown et al., 2008; Wolitzky-Taylor et al., 2015).

1.1.3. Stress reactivity

Stress reactivity (SR) refers to an individual's physiological, behavioral, cognitive, and subjective-emotional response to environmental stressors more broadly (Wolitzky-Taylor et al., 2015). Research indicates that higher SR may contribute to vulnerability for development of psychopathology, including psychosis, depression, and anxiety disorders (Schlotz, 2013) as well as the recurrence of mood and anxiety episodes (Morris, Rao, & Garber, 2012). In addition to major life stressors, the way in which an individual perceives and responds to daily environmental stressors, such as minor interpersonal conflict or increased work demands, has been implicated as a risk factor for internalizing symptoms (Wiegner, Hange, Björkelund, & Ahlborg, 2015). For example, an individual who responds to a stressful situation with greater arousal or negative affect may become quickly overwhelmed by minor inconveniences (e.g. being late due to traffic, co-worker asking to cover a shift), contributing to low mood, fatigue, and anxiety. This "spillover" effect of negative affect has been shown to predict treatment outcomes in cognitive therapy for depression (Cohen et al., 2008). Similarly, the cumulative psychological effect of daily stressors or hassles among college students predicted subsequent depression and anxiety symptoms (D'Angelo & Wierzbicki, 2003) and routine work stressors among police officers, such as dissatisfaction with organizational support or uneven workload, predicted PTSD symptoms (Liberman et al., 2002; Maguen et al., 2009). Given its role in conferring risk for a broad of a range of psychopathology, SR has been suggested as an important transdiagnostic treatment target (Conway, Starr, Espejo, Brennan, & Hammen, 2016).

SR has been shown to be sensitive to change through treatments such as stress management interventions (Limm et al., 2010) and cognitive reappraisal interventions (Jamieson, Mendes, Blackstock, & Schmader, 2010; Jamieson, Peters, Greenwood, & Altose, 2016; Moore, Vine, Wilson, & Freeman, 2015). Mindfulness-Based Stress Reduction (MBSR) interventions have been associated with decreased SR as well as symptom improvement in generalized anxiety disorder (Hoge et al., 2013) and major depression (Britton, Shahar, Szepsenwol, & Jacobs, 2012). Collectively, these findings suggest that improving SR may contribute to better treatment outcomes and improved psychological well-being in a broad array of psychological conditions including mood and anxiety disorders.

1.1.4. General self-efficacy

General self-efficacy (GSE) reflects the generalized belief in one's ability to cope with adversity or complete difficult or novel tasks (Bandura, 2010; Schwarzer & Jerusalem, 1995). Improving one's perceived ability to cope with challenging situations is an important goal of therapy. Indeed, GSE has been shown to be a protective factor, with higher self-efficacy mediating the relationship between daily stress and positive mental health outcomes such as well-being (Schönfeld, Brailovskaia, Bieda, Zhang, & Margraf, 2016). In contrast, low self-efficacy has been shown to mediate the relationship between stressful life events and depression (Maciejewski, Prigerson, & Mazure, 2000). Moreover, domain-specific self-efficacy, the belief in one's ability to

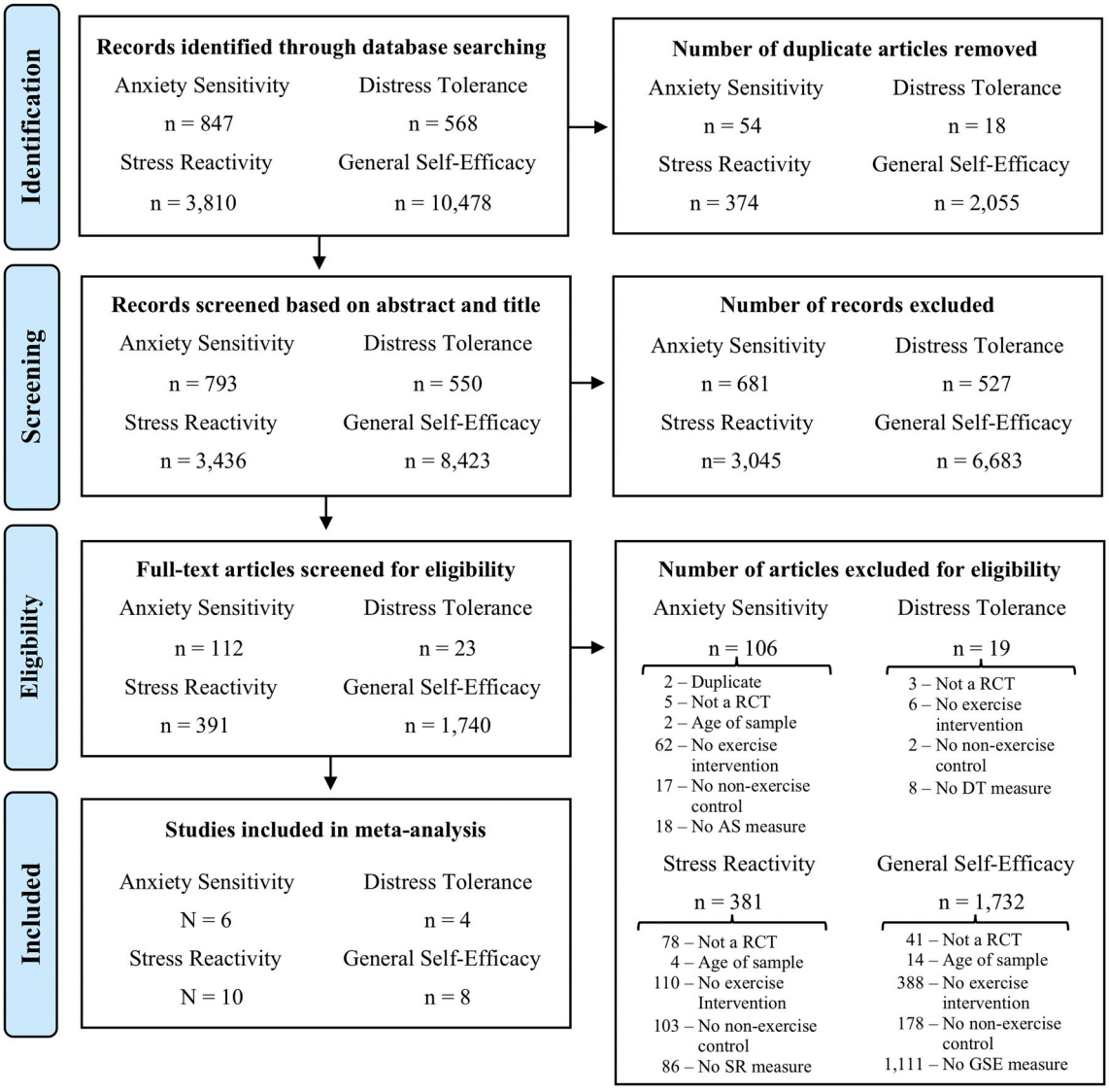

Fig. 1. Flow diagram of the study selection process. The articles not eligible for inclusion in this analysis often violated more than one eligibility criteria; however, for simplicity, each excluded article is only counted once and listed under the broadest criteria it violated (i.e. 'not an RCT' to 'didn't use a validated measure assessing a construct of interest'). RCT = randomized controlled trial, AS = anxiety sensitivity, DT = distress tolerance, SR = stress reactivity, GSE = general self-efficacy.

cope with challenges in a very specific domain of tasks (e.g. self-efficacy specific to engaging in exercise, utilizing a specific skill taught in therapy, or handling a panic attack), has emerged as a mediator of treatment outcome (Gallagher et al., 2013; Goldin et al., 2012; May, Hunter, Ferrari, Noel, & Jason, 2015). Collectively, these findings support the hypothesis that enhancing self-efficacy during intervention will improve treatment outcome for anxiety, mood, and related disorders.

1.2. Malleable with exercise

There are several features of exercise that can promote improvements in AS, DT, SR, and GSE. For example, exercise provides exposure to distressing or aversive physiological states and therefore can be used to help patients reestablish a sense of safety around bodily sensations (i.e. fear extinction), a relevant process for patients with elevated AS (Smits, Powers, Berry, & Otto, 2007). By persisting with exercise, patients can also practice building tolerance to a range of negative emotions and aversive states beyond anxiety sensations (e.g., body pain, fatigue), which is useful for those with low DT. These experiences with exposure and persistence may also facilitate reappraisal of arousal and stressors, such that exercise may buffer the effects of stressors (Deboer et al., 2012; Medina, Jacquart, & Smits, 2015; Smits et al., 2016; Smits, Meuret, Zvolensky, Rosenfield, & Seidel, 2009; Zschucke, Renneberg, Dimeo, Wüstenberg, & Ströhle, 2015), improve resilience to stress (Salmon, 2001) and thus reduce SR (e.g., Benvenutti et al., 2017; Ebbesen, Prkachin, Mills, & Green, 1992; von Haaren, Haertel, Stumpp, Hey, & Ebner-Priemer, 2015).

Exercise—as a systematic and planned physical activity—also provides opportunities to overcome physical and mental challenges to complete difficult and novel tasks, providing a pathway to achieve mastery experiences and develop a sense of self-efficacy. A sense of self-efficacy for specific exercise tasks is likely to develop with repeated exercise sessions (Sobol et al., 2016). However, exercise may also improve one's overall view of their capacity to overcome physical and mental challenges broadly. It is this GSE that may assist in the efforts to reverse the negative and vulnerable self-evaluations characteristic of mood and anxiety disorders. Prescribing an exercise intervention to individuals who have low GSE or DT or elevated AS or SR may produce a variety of mental health benefits. Exercise is an appealing alternative or complementary intervention for targeting these transdiagnostic therapeutic outcomes. The present study aimed to review and analyze

Table 1a
Sample characteristics for articles included in the meta-analysis examining the effect of exercise on anxiety sensitivity.

Study	Description of Sample	Recruitment Source	N	Age mean (SD)	% Female	% Race
Broman-Fulks and Storey (2008)	• ≥18 years of age • Elevated AS (ASI-R > 26) • In good physical health (assessed with the PAR-Q) • No current psychotherapy or psychiatric medications • Not currently involved in aerobic exercise programs	• Undergraduate psychology students	24	19.0 (1.9)	79.2%	91.7% White 4.2% African-American 4.2% Asian
Smits et al. (2008)	• Elevated AS (ASI ≥ 25) • In good physical health (assessed with the PAR-Q) • Body mass index < 35 • No more than one aerobic exercise session per week • No current psychotherapy and stabilized on any psychiatric medications	• Undergraduate psychology students • Community members	60	20.7 (5.8)	75%	71% White 9% African American 7% Asian 7% Hispanic 4% American Indian 2% listed as "other"
Broman-Fulks, Kelso, and Zawilinski (2015)	• In good physical health (assessed with the PAR-Q) • Exercising no more than one time per week	Not reported	77	19.7[a]	60%	84.4% White 9.1% African American 1.3% Hispanic/Latino 3.9% "other"
LeBouthillier and Asmundson (2015)	• 18–65 years old • In good physical health (assessed with the PAR-Q or medical clearance) • 6 weeks stabilized on any psychiatric medications • Not currently taking benzodiazepines or antipsychotic medication	• Undergraduate students • Community members	40	33.3 (12.6)	60%	80% White 5% African-Canadian 7.5% First Nations 2.5% Pacific Islander 5% Asian
Sabourin, Watt, Krigolson, and Stewart (2016)	• Female • High AS (ASI > 27) • In good physical health for physical activity	• Undergraduate students	40	*Not reported*	100%	90% White
LeBouthillier and Asmundson (2017)	• 18–65 years old • Reside in Regina, Saskatchewan area • < 150 min of moderate to vigorous exercise weekly • In good physical health (assessed with the PAR-Q) • Diagnosed with an anxiety-related disorder using the SCID-5-RV • No current psychotherapy • 6 weeks stabilized on any psychiatric medications • Not currently taking benzodiazepines or antipsychotic medication • No symptoms of psychosis • Low risk for suicide • Not involved in litigation	• Community members	48	32.6[a]	76.8%	89.3% White 1.8% Black/African Canadian 1.8% Asian 3.6% Indian 1.8% Multiracial 1.8% "other"

Notes: SD = standard deviation, AS = anxiety sensitivity, ASI-R = Anxiety Sensitivity Index-Revised, PAR-Q = Physical Activity Readiness Questionnaire, ASI = Anxiety Sensitivity Index, SCID-5-RV = Structured Clinical Interview for DSM-5, Research Version.

[a] When mean age for entire samples were not reported in the original article they were calculated by taking the average of the subgroup means; it is not possible to calculate the entire sample SD in the same way.

randomized controlled trials (RCTs) of exercise to provide a controlled effect-size of exercise for improving 1) AS, 2) DT, 3) SR, and 4) GSE—variables thought to affect the course of anxiety and related disorders, unipolar depression, and overall treatment progress.

2. Methods

2.1. Search strategy

The databases Cochrane Library, psychINFO, and PubMed were searched for relevant studies published in English before 01 April 2018 using the following search terms: "exercis*", "physical", "activit"*, "yoga", "tai chi", "qi gong", "qigong", "resistance*" AND "anxiety sensitivity", "distress tolerance", "self-efficacy", "stress respon*", "stress react*". Search parameters were set to limit results to peer-reviewed studies examining human subjects. We adhered to the PRISMA guidelines for conducting systematic and meta-analytical reviews (Liberati et al., 2009; Moher, Liberati, Tetzlaff, & Altman, 2009).

2.2. Study selection

The resulting studies' titles and abstracts were examined by four authors (JJ, CD, MD, and SF) to remove duplicate studies and obviously irrelevant or ineligible reports. Investigators then examined full-text studies to determine compliance with inclusion criteria. Two authors (JJ, CD) independently confirmed the studies identified met the inclusion criteria and discussed any discrepancies to reach a final consensus. A study was deemed eligible if it reported on an RCT evaluating the effect of exercise compared to a non-exercise control (e.g. waitlist, treatment as usual, attention control, or extremely light exercise or stretching) on an outcome of interest, using at least one validated outcome instrument measured after the exercise intervention, and included a sample with a mean age of ≥13 years. The outcomes of interest were AS, DT, SR, and GSE.

Table 1b
Intervention characteristics for articles included in the meta-analysis examining the effect of exercise on anxiety sensitivity.

Study	Exercise Intervention (E)		Control Group (C)		N	N by Group	Outcome Measure	Assessment Timepoints Used for Comparison
Broman-Fulks and Storey (2008)	L = 2 weeks F = 6x; 2-4x/week D = 20 min	Supervised treadmill walking/jogging at 60–90% of HR_{max}	L = 2 weeks F = 6x; 2-4x/week D = NA	Waitlist control group; matched on appointment frequency	24	E = 12 C = 12	ASI-R	• Pre-intervention • Post-intervention, immediately after 6th session
Smits et al. (2008)	L = 2 weeks F = 3x/week D = 20 min	E = supervised treadmill running at 70% of HR_{max} E+ = supervised treadmill running at 70% of HR_{max} with cognitive restructuring	L = 2 weeks F = NA D = NA	Waitlist control group; matched on assessment frequency	60	E = 19 E+ = 21 C = 20	ASI	• Pre-intervention • 1-week post-intervention
Broman-Fulks et al. (2015)	L = 1 day F = 1x D = 20 min	E-A = Aerobic exercise; supervised treadmill running at 65–75% of HR_{max} E-R = Resistance training; supervised squats, bench press, & lat pulldowns to exhaustion with at least 10 repetitions per set for 2 sets	L = 1 day F = 1x D = 20 min	Rest control group; sat quietly in chair	77	E-A = 25 E-R = 26 C = 26	ASI-3	• Pre-intervention, same day as intervention • Post-intervention, same day as intervention
LeBouthillier and Asmundson (2015)	L = 1 day F = 1x D = 30 min	Cycling at 60–80% of HRR with increasing resistance each min for 5 min followed by decreasing resistance each min for 5 min followed by a 10-min sprint	L = 1 day F = 1x D = 30 min	Placebo control group; 36 stretches held for 45 s each	40	E = 21 C = 19	ASI-3	• Pre-intervention during recruitment • Seven days post-intervention
Sabourin et al. (2016)	Part 1: L = 3 days F = 3x D = 60 min Part 2: L = 10 weeks F = 3x/week D = 10 min	Part 1: psychoeducation on anxiety disorders and AS, cognitive restructuring, and group exercise with therapist-led discussion Part 2: unsupervised running	Part 1: L = 3 days F = 3x D = 60 min Part 2: L = 10 weeks F = NA D = NA	Part 1: Attention control group; health education on exercise, nutrition, and sleep on optimal health with therapist-led discussion in groups Part 2: assessment only pre/post	40	E = 18 C = 22	ASI	• Pre-intervention • Post-intervention
LeBouthillier and Asmundson (2017)	L = 4 weeks F = 3x/week D = 40 min	E-A = Aerobic exercise; supervised stationary cycling at 60–80% of HRR E-R = Resistance training; 2–3 supervised sets of 10–12 reps of machine leg press, machine chest press, machine hamstring curl, dumbbell single arm row, machine shoulder press, machine triceps extension, and machine bicep curl	L = 4 weeks F = 1x/week D = NA	Waitlist control group; online questionnaires from home	48	E-A = 23[a] E-R = 18[a] C = 15	ASI-3	• Pre-intervention • 1-week post-intervention

Notes: Anxiety Sensitivity Index (ASI) is a 16-item questionnaire in which respondents indicate the degree to which anxiety symptoms are distressing and the concern about negative consequences of anxiety symptoms (Reiss, Peterson, Gursky, & McNally, 1986). The ASI has high internal consistency, favorable retest reliability and good construct validity (Schmidt, Lerew, & Jackson, 1999; Taylor, Koch, & McNally, 1992). The Anxiety Sensitivity Index–Revised (ASI-R) is a revised and expanded version of the original 16-item ASI and has adequate construct validity (Taylor & Cox, 1998) and internal consistency (Deacon et al., 2003). Anxiety Sensitivity Index-3 (ASI-3) is a revised, 18-item version of the ASI with sound psychometric properties including good convergent, discriminant, and criterion-related validity (Taylor et al., 2007). L = length of intervention, F = frequency of intervention sessions, D = duration of intervention exercise bouts/sessions, min = minutes, HR = heart rate, NA = not applicable, HRR = heart rate reserve, AS = anxiety sensitivity.

[a] Sample sizes for E-A and E-R include the eight participants from the waitlist control who completed the re-randomization process.

Table 2a
Sample characteristics for articles included in the meta-analysis examining the effect of exercise on distress tolerance.

Study	Description of Sample	Recruitment Source	N	Age mean (SD)	% Female	% Race
Broman-Fulks et al. (2015)	• In good physical health (assessed with the PAR-Q) • Exercising no more than one time per week	*Not reported*	77	19.7[a]	60%	84.4% White 9.1% African American 1.3% Hispanic/Latino 3.9% "other"
LeBouthillier and Asmundson (2015)	•18–65 years old •In good physical health (assessed with the PAR-Q or medical clearance) •6 weeks stabilized on any psychiatric medications •Not currently taking benzodiazepines or antipsychotic medication	•Undergraduate students •Community members	40	33.3 (12.6)	60%	80% White 5% African-Canadian 7.5% First Nations 2.5% Pacific Islander 5% Asian
Medina, Hopkins, et al. (2015)	• ≥18 years of age • Female • Elevated emotional eating (≥2.06 on the emotional eating subscale of the Dutch Eating Behavior Questionnaire) • Elevated dietary restraint (≥15 on the Dietary Restraint Scale) • Elevated perceived stress (≥0.50 SD above the community mean on the Perceived Stress Questionnaire) • Written physician medical clearance to participate in yoga • Doesn't engage in mind-body practices (yoga, tai chi, meditation, etc.) > 1x/week in the last year • No significant change in physical activity pattern in the previous 3 months • No current severe depression or substance dependence • No life-time history of anorexia nervosa or severe mental illness or inpatient psychiatric hospitalization within the past year • Body mass index ≤ 40 • No current psychotherapy or psychiatric medications	• Community members	52	33.6 (6.4)	100%	75% White, non-Hispanic 19.2% Hispanic/Latina
LeBouthillier and Asmundson (2017)	• 18–65 years old • Reside in Regina, Saskatchewan area • < 150 min of moderate to vigorous exercise weekly • In good physical health (assessed with the PAR-Q) • Diagnosed with an anxiety-related disorder using the SCID-5-RV • No current psychotherapy • 6 weeks stabilized on any psychiatric medications • Not currently taking benzodiazepines or antipsychotic medication • No symptoms of psychosis • Low risk for suicide • Not involved in litigation	• Community members	48	32.6[a]	76.8%	89.3% White 1.8% Black/African Canadian 1.8% Asian 3.6% Indian 1.8% Multiracial 1.8% "other"

Notes: SD = standard deviation, PAR-Q = Physical Activity Readiness Questionnaire, SCID-5-RV = Structured Clinical Interview for DSM-5, Research Version.
[a] When mean age for entire samples were not reported in the original article they were calculated by taking the average of the subgroup means; it is not possible to calculate the entire sample SD in the same way.

Table 2b
Intervention characteristics for articles included in the meta-analysis examining the effect of exercise on distress tolerance.

Study	Exercise Intervention (E)		Control Group (C)	N	N by Group	Outcome Measure	Assessment Timepoints Used for Comparison
Broman-Fulks et al. (2015)	L = 1 day F = 1x D = 20 min	E-A = Aerobic exercise; supervised treadmill running at 65–75% of HR_{max} E-R = Resistance training; supervised squats, bench press, & lat pulldowns to exhaustion with at least 10 repetitions per set for 2 sets	Rest control group; sat quietly in chair	77	E-A = 25 E-R = 26 C = 26	DTS	● Pre-intervention, same day as intervention ● Post-intervention, same day as intervention
LeBouthillier and Asmundson (2015)	L = 1 day F = 1x D = 30 min	Cycling at 60–80% of HRR with increasing resistance each min for 5 min followed by decreasing resistance each min for 5 min followed by a 10-min sprint	Placebo control group; 36 stretches held for 45 s each	40	E = 21 C = 19	DTS	● Pre-intervention, during recruitment ● 1-week post-intervention
Medina, Hopkins, et al. (2015)	L = 8 weeks F = 2x/week D = 90 min	Bikram Yoga; series of 26 poses, two breathing exercises, and two resting postures at a local yoga studio in a room heated to 104 °F	Waitlist control group; online questionnaires from home	52	E = 27 C = 25	DTS	● Pre-intervention ● 1-week post-intervention
LeBouthillier and Asmundson (2017)	L = 4 weeks F = 3x/week D = 40 min	E-A = Aerobic exercise; supervised stationary cycling at 60–80% of HRR E-R = Resistance training; 2–3 supervised sets of 10–12 reps of machine leg press, machine chest press, machine hamstring curl, dumbbell single arm row, machine shoulder press, machine triceps extension, and machine bicep curl	Waitlist control group; online questionnaires from home	48	E-A = 23[a] E-R = 18[a] C = 15	DTS	● Pre-intervention ● 1-week post-intervention

Notes: Distress Tolerance Scale (DTS) is a 15-item self-report scale measuring four facets involved in the expectation of, evaluation of, and reaction to distressing states (Simons & Gaher, 2005). The DTS has temporal stability over a 6-month period, adequate construct validity, and high internal consistency (Bernstein, Zvolensky, Vujanovic, & Moos, 2009; Medina, Hopkins, Powers, Baird, & Smits, 2015; Simons & Gaher, 2005). L = length of intervention, F = frequency of intervention sessions, D = duration of intervention exercise bouts/sessions, min = minute, HR = heart rate, HRR = heart rate reserve, min = minutes.
[a] Sample sizes for E-A and E-R include the eight participants from the waitlist control who completed the re-randomization process.

Studies describing data from case studies, reviews, conference abstracts, protocols, or letters to the editors were not included. Exercise interventions were defined as systematic physical activity interventions that included planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness (American College for Sports Medicine, 2013). We included several yoga practices (e.g. Hatha, Iyengar, Ashtanga, Vinyasa, power, hot, Bikram, Kundalini, ariel, acro, and Baptize yoga), Tai Chi, and qigong as they are grounded in physical movement and consistent with this definition of exercise.

We restricted inclusion of studies to those that employed psychometrically sound self-report and behavioral outcome measures. Specifically, studies testing the effects of exercise on AS were included if they used the Anxiety Sensitivity Index 1, 2, or 3 (Deacon, Abramowitz, Woods, & Tolin, 2003; Osman et al., 2010; Peterson & Heilbronner, 1987). Studies were included if they assessed DT using any self-report Distress Tolerance Scale (Simons & Gaher, 2005) or behavioral tasks including but not limited to the Mirror-Tracing Persistence Task (Strong et al., 2003) and the Paced Auditory Serial Addition Task (Lejuez, Kahler, & Brown, 2003). We limited the inclusion of studies testing the effects of exercise on SR to those that measured an individual's emotional reactivity in response to a stressor using a visual analog or single item scale self-reporting current feelings of stress (Lesage, Berjot, & Deschamps, 2012), measures of arousal (e.g., the Profile of Mood States; Shacham, 1983), measures of negative affect (e.g., the Positive Affect-Negative Affect Schedule; Watson, Clark, & Tellegen, 1988), or measures of state anxiety (e.g., the State-Trait Anxiety Inventory; Spielberger, 2007). If the stressor occurred on the same day as the exercise intervention, we required the inclusion of a post-exercise and pre-stressor assessment. Finally, studies testing the effects of exercise on GSE were included if they employed the General Self-Efficacy Scale (Schwarzer & Jerusalem, 1995) or a similar measure of GSE.

Only a post-intervention assessment point was required for inclusion. While using baseline measurements in a repeated measures analysis reduces problems associated with between-subject variability in baseline scores, the presence of baseline measurement is not essential for judging the efficacy of an intervention in an RCT (Sedgwick, 2014). Therefore, we did not require both a measure before and after the intervention.

2.3. Data extraction

Two authors (JJ, CD) independently extracted outcome data from original studies, entered the data into Comprehensive Meta-Analysis (CMA) software (Borenstein, Hedges, Higgins, & Rothstein, 2013), and compared the data extracted for discrepancies. Means and standard deviations were extracted for all measures. Authors of eligible studies were contacted when necessary with requests for additional information missing from reports.

2.4. Quality assessment

Two authors (JJ, CD) independently assessed the risk of bias of included studies using the Cochrane Collaboration's Risk of Bias tool (Higgins et al., 2011), with any disagreements resolved by discussion to reach consensus. The Cochrane Collaboration's Risk of Bias tool specifies different domains which may predispose studies to bias: random sequence generation; allocation sequence concealment; blinding (participants, personnel); blinding (outcome assessment); completeness of outcome data, and selective outcome reporting. Blinding is considered separately for different outcomes where appropriate (e.g. blinding may have the potential to differently affect subjective versus objective outcome measures). Each item is judged as being at high, low, or unclear risk of bias as set out in the criteria provided by Higgins et al., (2011). Studies were deemed to be at the highest risk of bias if they are scored as high or unclear risk of bias for either the sequence generation or

Table 3a
Sample characteristics for articles included in the meta-analysis examining the effect of exercise on stress reactivity.

Study	Description of Sample	Recruitment Source	N	Age mean (SD)	% Female	% Race
Hobson and Rejeski (1993)	• Female • Low to moderately fit	• University students in a required health/fitness class	80	18.3 (0.9)	100%	*Not reported*
Kubitz and Landers (1993)	• 18–35 years old • In good physical health • Not involved in regular exercise program for the past 3-months	• Undergraduate students • Community members	27	23.0 (3.6)	63%	*Not reported*
Anshel (1996)	• Male • Aerobically inactive and unfit based on aerobic fitness pretest (below average Aerobic Power Index score) • No previous experience with stress management or relaxation training • No previous experience with the stressor	• Undergraduate students	30	21.9 *(SD not reported)*	0%	*Not reported*
Calvo, Szabo, and Capafons (1996)	Not reported	• Undergraduates students in a psychology course	89	21.3[a]	65%	*Not reported*
Throne, Bartholomew, Craig, and Farrar (2000)	• Healthy • Currently active firefighters	• Six fire stations	41	35.7 (7.3)	7%	*Not reported*
Neumann, Brown, Waldstein, and Katzel (2006)	• Diagnosed with silent myocardial ischemia as part of an ongoing study • Not currently smoking and no heavy alcohol consumption • At least a high school education • No history or current symptomatic coronary artery disease, major ST-segment abnormalities, left-bundle-branch block, complex arrhythmias, poorly controlled hypertension, severe hypertension requiring 3+ medications, stroke, peripheral arterial disease, poorly controlled hyperlipidemia, diabetes mellitus, dementia • No history of psychiatric disorders	• Community members • Retirement Community members	25	69 (8)	32%	*Not reported*
Taylor and Katomeri (2007)	• In good physical health (assessed with the PAR-Q) • Smoked at least 10 cigarettes daily for the past 3 years	• Community members	60	28.6[a]	57%	*Not reported*
Robert-McComb, Chyu, Tacón, and Norman (2015)	• Male • 18–45 years old • In good physical health (assessed with the PAR-Q) • No prior mind-body exercise or meditation practice • Not taking any medications that may affect heart rate	• Undergraduate students	20	22.4[a]	0%	*Not reported*
von Haaren et al., (2015)	• Male • ≤1x moderately active for 60 min/week	• Electrical engineering students	60	21.4 (1.6)	0%	*Not reported*
Zschucke et al. (2015)	• Male • 20–30 years old • Right-handed • Exercising either < 1x/week or intensively training in an endurance sport ≥ 3x/week (e.g. running, cycling, swimming, rowing) • Non-smoker • Body mass index between 19 and 25 • Not taking any medications • No history of neurological or mental illness (assessed with the MINI)	• University students • Members of an elite sport training center	36	24.4[a]	0%	*Not reported*

Notes: SD = standard deviation, PAR-Q = Physical Activity Readiness Questionnaire, MINI = Mini International Neuropsychiatric Interview.
[a] When mean age for entire samples were not reported in the original article they were calculated by taking the average of the subgroup means; it is not possible to calculate the entire sample SD in the same way.

allocation concealment domains, based on growing empirical evidence that these factors are particularly important potential sources of bias (Higgins et al., 2011). Because trials assessing the effect of behavioral interventions are rarely able to mask the allocation assignment, there was not an expectation that participants and intervention providers would be completely masked to the allocations.

2.5. Data synthesis and analysis

We used CMA software (Borenstein et al., 2013) to estimate controlled effect sizes using Hedges's *g*, which corrects for parameter bias due to small sample size (Hedges & Olkin, 1985). To compute Hedges's *g*, we extracted means, standard deviations, and information from significance tests (e.g., *t, F, p;* Hedges & Olkin, 1985). Pooled effect sizes were estimated for AS, DT, SR, and GSE separately using random effects models, which assume significant heterogeneity of the included studies. For studies with multiple intervention groups, all relevant independent intervention groups were included and used in a pairwise comparison with the control group. Multiple measures for a single outcome from an individual study were included where appropriate and pooled for analysis. No prioritization was given to one assessment measure over another. We report the I^2 statistic, which is a measure of heterogeneity in percentages such that an I^2 of 0% would indicate zero observed heterogeneity, 25% would be low heterogeneity, 50% moderate, and 75% high (Higgins, Thompson, Deeks, & Altman, 2003). The I^2 statistic tends to have substantial bias when the number of studies is small, therefore I^2 should be interpreted cautiously in these cases and 95% confidence intervals are reported to supplement the I^2 point estimate (von Hippel, 2015). We also report the *Q* statistic, which is a significance test that rejects the null hypothesis if the variability among the effect sizes is greater than what would be likely from only sampling error. Publication bias was assessed by visual inspection of a funnel plot (Egger, Smith, Schneider, & Minder, 1997) and if publication bias appears plausible Duval's and Tweedie's trim and fill procedure was conducted (Duval & Tweedie, 2000).

Table 3b
Intervention characteristics for articles included in the meta-analysis examining the effect of exercise on stress reactivity.

Study	Exercise Intervention (E)		Control Group (C)		N	N by Group	Outcome Measure	Stressor	Assessment Timepoints Used for Comparison
Hobson and Rejeski (1993)	L = 1 day F = 1x E10 = 10 min D E25 = 25 min E40 = 40 min	E10 = supervised stationary cycling at 70% of HRR E25 = supervised stationary cycling at 70% of HRR E40 = supervised stationary cycling at 70% of HHR	L = 1 day F = 1x D = 10 min	Attention control; seated upright on stationary bicycle	80	E10 = 20 E25 = 20 E40 = 20 C = 20	• PANAS-Negative Affect Items	• Stroop color-word task	• Post-intervention[a], pre-stressor • Post-intervention[a], post-stressor
Kubitz and Landers (1993)	L = 8 weeks F = 3x/week D = 40 min	Supervised stationary cycling with at 60–85% HRR	L = 8 weeks F = NA D = NA	Waitlist control group; matched on assessment frequency	27	E = 14 C = 13	• STAI-State Items	• Stroop color-word task • Mental arithmetic tasks	• Post-intervention, pre-stressor • Post-intervention, post-stressor
Anshel (1996)	L = 10 weeks F = 3x/week D = 30 min	Supervised stationary cycling at 50 rpm for 3 m at 300, 600, & 900 kpm and an HR of 170 bpm	L = 10 weeks F = 3x/week D = 30 min	Placebo control; group discussions and videotapes on health-related topics	30	E = 15 C = 15	• POMS	• Criterion motor/visual tracking task	• Post-intervention, pre- to post-stressor change
Calvo et al. (1996)	L = 12 weeks F = 3x/week D = 60 min	Guided group exercise; consisting of aerobic and resistance components with increasing levels of difficulty, performed at 75% of HRR	L = 12 weeks F = 3x/week D = 60 min	Education control group; seminars on practical issues of psychological research	89	E = 44 C = 45	• CSAQ	• Mental arithmetic tasks • Fine motor task • Speech	• Post-intervention, post-stressor
Throne et al. (2000)	L = 16 weeks F = 4x/week D = 40 min	Combination of low-to-moderate and high-intensity rowing	L = 16 weeks F = NA D = NA	Non-rowing control; continued lifestyle as normal, match on assessment frequency	41	E = 21 C = 20	• PANAS • STAI-State Items	• Strategy & tactics drill	• Post-intervention, pre- to post-stressor change
Neumann et al. (2006)	L = 24 weeks F = 3x/week D = 40 min	Guided individual treadmill walking program at 70% HRR or at ischemic threshold	L = 24 weeks F = NA D = NA	Waitlist control group; match on assessment frequency	25	E = 14 C = 11	• STAI-State	• Anger-recall task • Anger role-play • Mental arithmetic tasks	• Post-intervention, post-stressor
Taylor and Katomeri (2007)	L = 1 day F = 1x D = 15 min	Supervised brisk treadmill walking	L = 1 day F = 1x D = 15 min	Passive rest; sitting quietly in exercise facility	60	E = 31 C = 29	• MPSS-Stress Item	• Stroop word color task • Speech • Cigarette challenge	• Post-intervention[a], pre-stressor • Post-intervention[a], post-stressor
Robert-McComb et al. (2015)	L = 8 weeks F = 2x/week D = 60 min	Tai Chi Chuan; group classes led by an experienced instructor, included breathing techniques	L = 8 weeks F = NA D = NA	Waitlist control group; matched on assessment frequency	20	E = 9 C = 11	• STAI	• WAIS-R block design or stimulus/response task • Timed math or anagram task • Speech Stressors were counter balanced from pre- to post-intervention	• Post-intervention, pre-stressor •Post-intervention, post-stressor Instructed not to exercise on day of test
von Haaren et al., (2015)	L = 20 weeks F = 2x/week D = 30–90 min	Guided group (7–8) running program; increasing intensity and duration (3 min/week) to reach individual HR requirements	L = 20 weeks F = NA D = NA	Waitlist control group; match on assessment frequency	60 36	E = 30 C = 30	• PS Single Item • MDMQ-Calmness Item • NAS	• Real life stressor (school exams)	• Post-intervention, post-stressor

(*continued on next page*)

Table 3b (*continued*)

Study	Exercise Intervention (E)		Control Group (C)		N	N by Group	Outcome Measure	Stressor	Assessment Timepoints Used for Comparison
Zschucke et al. (2015)	L = 1 day F = 1x D = 30 min	Supervised treadmill running at 60–70% of individual VO_2max	L = 1 day F = 1x D = 30 min	Placebo control group; light stretching and light gymnastic exercises (e.g. rotating ankle) that did not induce significant cardiovascular activation		E = 18 C = 18		• Montreal Imaging Stress Task	• Post-intervention[a], pre-stressor • Post-intervention[a], post-stressor

Notes: The Positive Affect-Negative Affect Schedule (PANAS) has 10-items assessing state negative affect and 10-items assessing state positive affect which are uncorrelated with one another (Watson et al., 1988). The PANAS has adequate internal consistency (Watson, Wiese, Vaidya, & Tellegen, 1999). The State-Trait Anxiety Inventory (STAI) is a self-report measure with subscales assessing either state or trait levels of anxiety and has good reliability and validity (Spielberger, 1989; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The Profile of Mood States (POMS) measures five dimensions of participants' state affect and has good reliability and validity (Grove & Prapavessis, 1992). The Cognitive-Somatic Anxiety Questionnaire (CSAQ) has 10-items assessing state cognitive anxiety and 10-items assessing state somatic anxiety with good internal consistency (Calvo, Alamo, & Ramos, 1990). The Mood and Physical Symptoms Scale (MPSS) has several single items assessing withdrawal symptoms including stress (e.g. "How stressed do you feel right now?") and has good sensitivity to change (West & Hajek, 2004). Perceived stress (PS) is a single item assessing perceived control over a situation (Fahrenberg, Brügner, Foerster, & Käppler, 1999; Rau, Georgiades, Fredrikson, Lemne, & de Faire, 2001). Multidimensional Mood Questionnaire (MDMQ) measures several dimensions at a state level, one of which is calmness, and has been validated and shows good reliability (Steyer, Schwenkmezger, & Eid, 1997; Wilhelm & Schoebi, 2007). The numerical analogous scale (NAS) evaluates how stressed a participant feels in the moment using a single item scale (Lesage et al., 2012). L = length of intervention, F = frequency of intervention sessions, D = duration of intervention exercise bouts/sessions, min = minutes, HRR = heart rate reserve, NA = not applicable, m = meters, kpm = kilograms per meter, HR = heart rate, bmp = beats per minute, WAIS-R = Wechsler Adult Intelligence Scale-Revised.

[a] Assessments were conducted on the same day as the intervention.

3. Results

3.1. Search results and trial characteristics

The search yielded 15,703 studies, which were reviewed for eligibility in the meta-analyses. As illustrated in the PRISMA flowchart (Fig. 1), we identified six eligible studies examining the effect of exercise on AS. Most studies targeted individuals with elevated levels of AS or anxiety disorders and the majority of participants were females. Four studies employed some form of high-intensity aerobic exercise while two included a resistance training intervention. These interventions ranged from a single bout of exercise in some studies to 4-week exercise interventions in others. Descriptions of sample and intervention characteristics are reported in Tables 1a and 1b respectively.

Four eligible studies examining the effect of exercise on DT were identified. These studies included a mix of both healthy and clinical populations, and the majority of participants across the four studies were female. Of the studies included in our analysis, one employed a yoga intervention, three used aerobic exercise, and two also included a resistance training intervention. Two studies used a single bout of exercise, one used a 4-week exercise intervention and another an 8-week intervention. Descriptions of sample and intervention characteristics are reported in Tables 2a and 2b respectively.

We identified 16 eligible studies examining the effect of exercise on SR. However, six did not respond to requests for additional data required for the trial to be included in the meta-analysis, resulting in the inclusion of ten studies. In terms of their target population, studies included for SR surveyed a diverse sample of healthy and clinical populations in the domains of both mental and physical health. The majority of participants were female; however, four studies used an all-male sample. The types of stressors administered for these studies ranged from combinations of word and mental arithmetic tasks to motor and speech tasks. While a large majority of the interventions included for SR involved some form of aerobic exercise, a study utilizing a combination of aerobic and resistance exercises, a study with a moderate-intensity walking intervention, and a study with a Tai Chi intervention were included. Exercise interventions ranged from 1-week to 24-weeks in length. Descriptions of sample and intervention characteristics are reported in Tables 3a and 3b respectively.

Eight eligible studies examining the effect of exercise on GSE were identified. The studies targeted a variety of populations including college students, older adults, individuals with depressive symptoms, and individuals with high-stress levels. The majority of participants included in these studies were also female. These studies included a variety of exercise interventions including alpine skiing, different forms of yoga and qigong. Exercise interventions ranged in length from 6 to 16 weeks. Description of sample and intervention characteristics are reported in Tables 4a and 4b respectively.

3.2. Bias risk assessment

3.2.1. Anxiety sensitivity

Among the studies examining anxiety sensitivity (AS), sequence generation was adequate in 2/6 (33%) studies and allocation concealment was adequate in 1/6 (17%) trials. Blinding of participants and trial personnel was adequate in 2/6 (33%) studies; however, it is important to note the barriers that arise to blinding participants and personnel to behavioral interventions. Blinded outcome assessment for self-report data was adequate in 1/6 (17%) studies as self-report measures were administered via automated questionnaires; 4/6 (67%) studies did not describe who conducted the self-report outcome assessments, and 1/6 (17%) had the person who delivered the intervention administer the questionnaires and therefore has a high risk for bias. Low risk of bias in the 'incomplete outcome data' domain was found in 5/6 (83%) trials and all six had adequate ratings for the selective outcome reporting domain (Fig. 2).

Table 4a
Sample characteristics for articles included in the meta-analysis examining the effect of exercise on general self-efficacy.

Study	Description of Sample	Recruitment Source	N	Age mean (SD)	% Female	% Race
Tsang, Fung, Chan, Lee, and Chan (2006)	• ≥65 years old • Diagnosed with depression or having features of depression (assessed with the GDS) • Chronic medical illness • No changes in medication or dosage in the previous four weeks	• Non-government care and attention home residents	82	82.4[a]	80.5%	*Not reported*
Finkenzeller, Müller, Würth, and Amesberger (2011)	• 60–75 years old • Intermediate level skiers • ≥2–3 h of moderate activity per week • No serious health problems	• Community members	22	67.4[a]	48.8%	*Not reported*
Tsang et al. (2013)	• ≥65 years old • Chronic medical illness • Diagnostic record of major depressive disorder based on DSM-IV or ≥ 8 on the GDS • No changes in medication or dosage in the previous four weeks • No prior experience practicing qigong • < 20 on the MMSE	• Psychogeriatric day clinic patients • Geriatric day care center patients • Care and attention home residents	38	80.2[a]	68.4%	*Not reported*
Bonura and Tenenbaum (2014)	• 18–65 years old • In good physical health (assessed with a health history) • No prior yoga experience	• Community activities facility members • Senior living community residents	98	77.0 (7.3)	69.8%	*Not collected*
de Vries, van Hooff, Geurts, and Kompier (2016)	• High levels of study-related fatigue (defined as ≥ 2.2 on the Emotional Exhaustion Scale of the Utrecht Burnout Scale for Students and ≥22 on the Fatigue Assessment Scale) • Exercise ≤ 1 h a week • Not currently receiving psychological or pharmacological treatment for fatigue • Did not reported a medical cause of their fatigue • No current drug addiction • Physically able to run	• University students	99	20.8[a]	80.8%	*Not reported*
Koopman et al. (2016)	• 18–75 years old • Diagnosis of postpolio syndrome • Severe perceived fatigue (assessed with the subscale fatigue severity of the Checklist Individual Strength ≥ 35) • No life-threatening comorbidity • Ability to walk indoors with or without a walking aid • Ability to cycle on an ergometer against a load of at least 25 W • In good physical health for exercise (assessed with the PAR-Q)	• Hospital and rehabilitation center patients	44	58.4[a]	54.5%	84.1% White
Prathikanti et al. (2017)	• Met diagnostic criteria for mild-to-moderate depression (assessed with the MINI and scores of 14–28 on the Beck Depression Inventory-II). • No current psychotherapy, antidepressant pharmacotherapy, or herbal or nutraceutical mood remedies • Did not currently engage in mind-body practices • No substance use disorders in the last 3 months and no comorbid Axis I diagnosis (assessed with the MINI) • No history of suicide attempts or suicidal ideation • Not currently pregnant • No history of seizure disorder, uncontrolled hypertension, or carotid artery stenosis	• Community members	38	43.4 (14.8)	68%	58% European descent 16% Asian descent 11% Latino descent 8% African descent 8% Multiracial/ ethnic
Hewett, Pumpa, Smith, Fahey, and Cheema (2018)	• ≥18 years old • < 150 min of moderate-intensity exercise per week for more than 6 months • At least mild stress (defined as score > 14 on the stress component of the Depression, Anxiety and Stress Scale • No self-reported diagnosis of chronic diseases • Able to safely practice Bikram yoga • No participation in Bikram yoga in the past six months	• Community members	63	37.2 (10.8)	79%	*Not reported*

Notes: SD = standard deviation, GDS = Geriatric Depression Scale, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders-V, MMSE = Mini-Mental State Examination, PAR-Q = Physical Activity Readiness Questionnaire, MINI = Mini International Neuropsychiatric Interview.

[a] When mean age for entire samples were not reported in the original article, they were calculated by taking the average of the subgroup means; it is not possible to calculate the entire sample SD in the same way.

Table 4b
Intervention characteristics for articles included in the meta-analysis examining the effect of exercise on general self-efficacy.

Study	Exercise Intervention (E)		Control Group (C)		N	N by Group	Outcome Measure	Assessment Timepoints Used for Comparison
Tsang et al. (2006)	L = 16 weeks F = 3x/week D = 30–45 min	Qigong (Baduanjin—the most common form of Chinese qigong used as exercise); group training under supervision of trained qigong practitioner	L = 16 weeks F = 3x/week D = 30–45 min	Attention control; newspaper reading group run by a qualified therapist, provided as rehabilitation activity	82	E = 34 C = 48	CGSS	• Pre-intervention • Post-intervention
Finkenzeller et al. (2011)	L = 12 weeks F = 2-3x/week D = 3.5 h	Guided group alpine skiing based on assessed skill level	L = 12 weeks F = NA D = NA	Non-skiing, life as usual control; matched on assessment frequency	22	E = 13 C = 9	GSES	• Pre-intervention • Post-intervention
Tsang et al. (2013)	L = 12 weeks F = 3x/week D = 45 min	Health qigong exercise provided in group format, led by qualified qigong instructors using the eight-section brocades protocol	L = 12 weeks F = 3x/week D = 45 min	Attention control; newspaper reading and discussion group led by a research assistant, provided as rehabilitation activity	38	E = 21 C = 17	CGSS	• Pre-intervention • Post-intervention
Bonura and Tenenbaum (2014)	L = 6 weeks F = 1x/week D = 45 min	E = Guided chair exercise with paralleled physical movement of the asanas in groups E-Y = Guided Hatha chair yoga: pranayama, asana, & meditation in groups	L = 6 weeks F = NA D = NA	Waitlist control; matched on assessment frequency	98	E = 33 E-Y = 33 C = 32	GSES	• Pre-intervention • Post-intervention (after last session)
de Vries et al. (2016)	L = 6 weeks F = 3x/week D = 90 min	Moderate-intensity group running: 2 unsupervised runs and 1 supervised run per week in a group of 10	L = 6 weeks F = NA D = NA	Waitlist control; matched on assessment frequency	99	E = 50 C = 49	GSES	• Pre-intervention • Post-intervention
Koopman et al. (2016)	L = 16 weeks F = 4x/week D = 28–60 min	Home-based stationary cycling 3x/week for 28–38 min at 60%–70% HRR; a guided group-training program 1x/week for 60 min with muscle strengthening/functional exercises in specific muscle groups	L = 16 weeks F = varied D = varied	Usual care control; consisting of assistive devices, orthoses, and physical therapy	44	E = 22 C = 22	ALCOS	• Pre-intervention • Post-intervention
Prathikanti et al. (2017)	L = 8 weeks F = 2x/week D = 90 min	Guided group Hatha yoga using a well-defined set of yoga postures in sequences	L = 8 weeks F = 2x/week D = 90 min	Attention control; instructor led modules on yoga history & philosophy	38	E = 20 C = 18	GSES	• Pre-intervention • Post-intervention (after last session)
Hewett et al. (2018)	L = 16 weeks F = 3-5x/week D = 90 min	Bikram Yoga; series of 26 poses, two breathing exercises, and two resting postures at a local yoga studio in a room heated to 104 °F	L = 16 weeks F = NA D = NA	Lifestyle as normal; matched on assessment frequency	63	E = 29 C = 34	GSES	• Pre-intervention • 1-Week Post-intervention

Notes: General Self-Efficacy Scale (GSES) is a 10-item scale assessing a general sense of perceived ability to cope with a variety of stressors and has good internal consistency (Nilsson, Hagell, & Iwarsson, 2015; R; Schwarzer & Jerusalem, 1995; R; Schwarzer, Mueller, & Greenglass, 1999). The Chinese General Self-efficacy Scale (CGSS) is a Chinese adaptation of the GSES and has good internal consistency and test-retest reliability (Chiu & Tsang, 2004; Zhang & Schwarzer, 1995). Algemene Competentie Schaal (ALCOS) is a validated Dutch Version of the General Self Efficacy Scale (Bosscher, Smit, & Kempen, 1997). L = length of intervention, F = frequency of intervention sessions, D = duration of intervention exercise bouts/sessions, min = minutes, NA = not applicable, HRR = heart rate reserve.

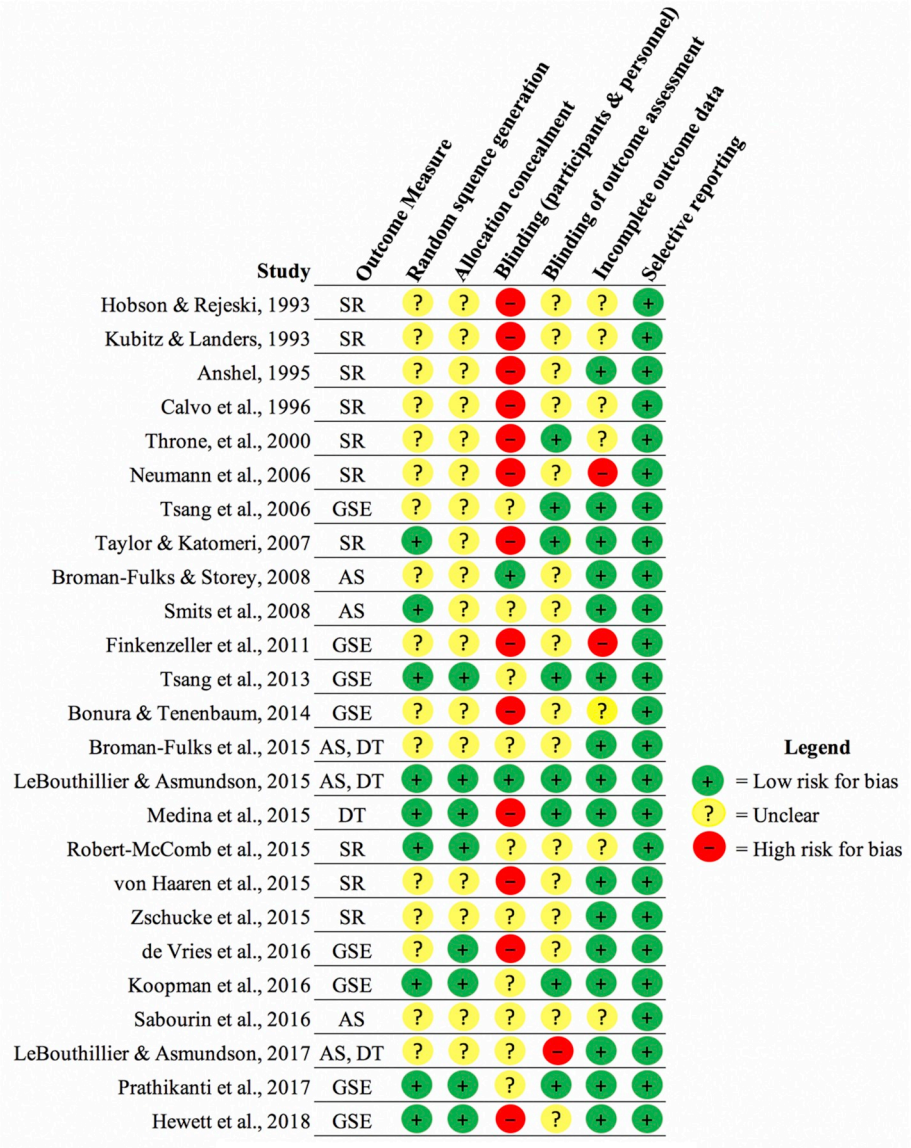

Fig. 2. Risk bias assessment. AS = anxiety sensitivity, DT = distress tolerance, SR = stress reactivity, GSE = general self-efficacy.

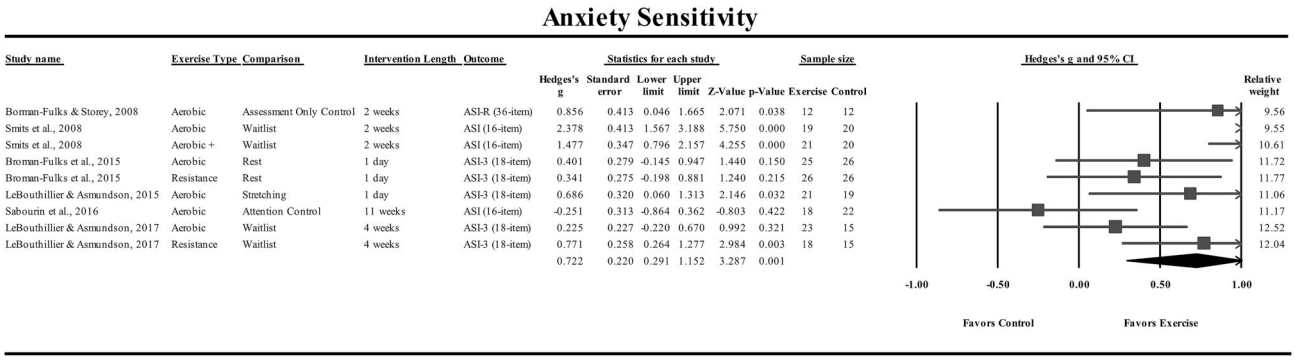

Fig. 3. Effect size estimates (Hedges's *g*) and 95% confidence intervals (CI) for the efficacy of exercise relative to control comparison groups on anxiety sensitivity. ASI = Anxiety Sensitivity Index, ASI-R = Anxiety Sensitivity Index-Revised.

3.2.2. Distress tolerance

Among the studies examining distress tolerance (DT), sequence generation and allocation concealment were adequate in 2/4 (50%) studies. Blinding of participants and trial personnel was adequate in 1/4 (25%) studies while 1/4 (25%) studies were judged to be at high risk of bias in this domain. Blinded outcome for self-report data was adequate in 2/4 (50%) studies as self-report measures were administered via automated questionnaires; 1/4 (25%) studies did not describe who conducted the self-report outcome assessment, and 1/6 (25%) had the person who delivered the intervention administer the questionnaires

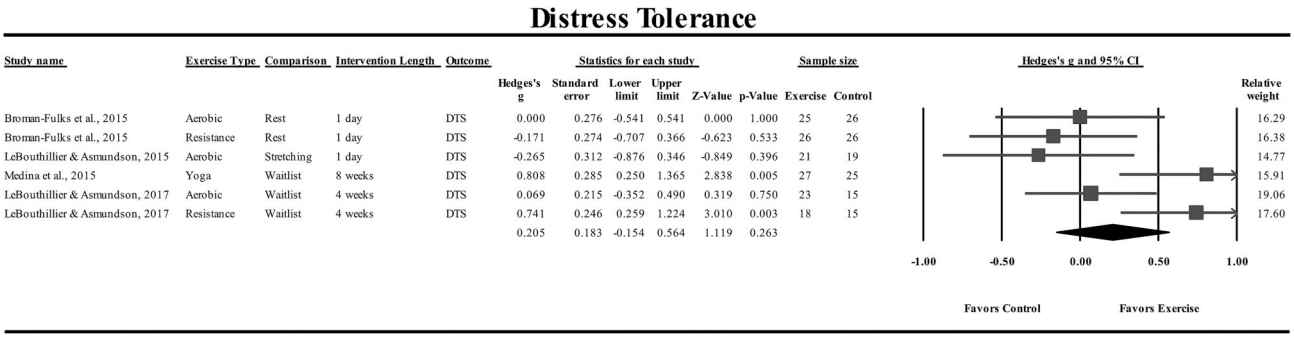

Fig. 4. Effect size estimates (Hedges's *g*) and 95% confidence intervals (CI) for the efficacy of exercise relative to control comparison groups on distress tolerance. DTS = Distress Tolerance Scale.

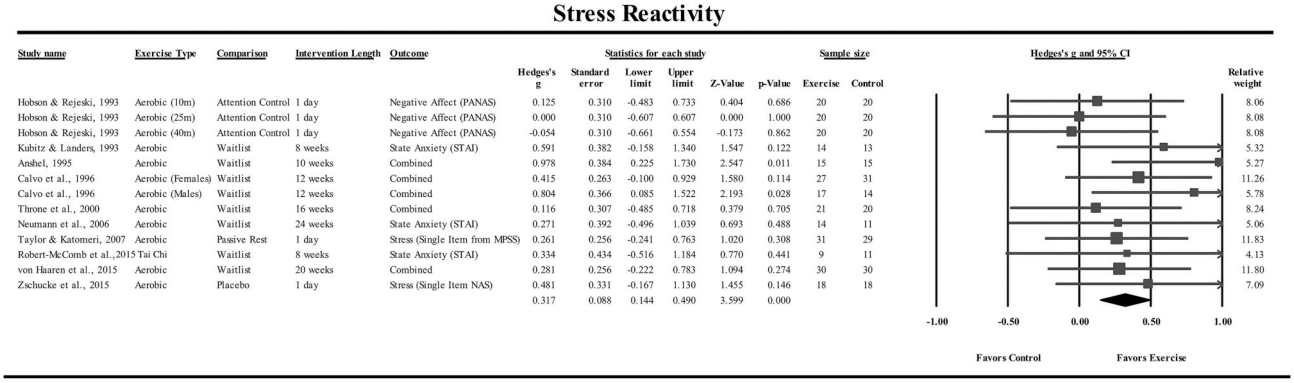

Fig. 5. Effect size estimates (Hedges's *g*) and 95% confidence intervals (CI) for the efficacy of exercise relative to control comparison groups on stress reactivity. Studies that used multiple relevant outcomes measures were included such that each measure contributed to the average effect size for that study. PANAS = Positive and Negative Affect Schedule, STAI = State-Trait Anxiety Index , MPSS = Mood and Physical Symptoms Scale, NAS = numerical analogous scale.

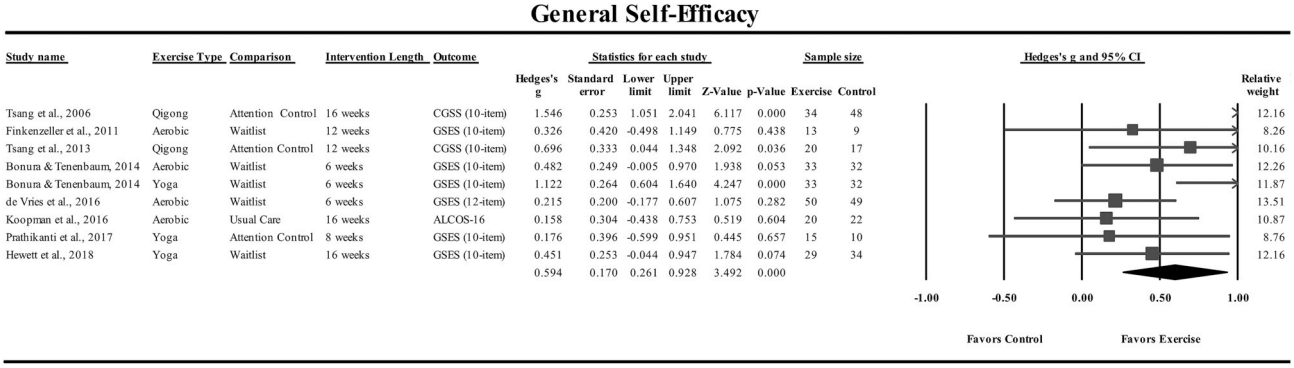

Fig. 6. Effect size estimates (Hedges's *g*) and 95% confidence intervals (CI) for the efficacy of exercise relative to control comparison groups on general self-efficacy. CGSS = Chinese General Self-efficacy Scale, GSES = General Self-Efficacy Scale, ALCOS = Algemene Competentie Schaal (Dutch Version of the General Self Efficacy Scale).

and therefore has a high risk for bias. All four studies had a low risk of bias in the 'incomplete outcome data' and selective outcome reporting domain (Fig. 2).

3.2.3. Stress reactivity

Among the studies examining stress reactivity (SR), sequence generation was adequate in 2/10 (20%) studies and allocation concealment was adequate in 1/10 (10%) studies. In 8/10 (80%) studies, blinding of participants and trial personnel was judged to be at high risk of bias. Blinded outcome assessment for self-report data was adequate in 2/10 (20%) studies; the other eight did not describe who conducted the self-report outcome assessments. Low risk of bias in the 'incomplete outcome data' domain was found in 4/10 (40%) studies and 1/10 (10%) studies were judged to be at high risk of bias in this domain. All ten had adequate ratings for the selective outcome reporting domain (Fig. 2).

3.2.4. General self-efficacy

Among the studies examining general self-efficacy (GSE), sequence generation was adequate in 4/8 (50%) studies and allocation concealment was adequate in 5/8 (63%) studies. In 4/8 (50%) studies, blinding of participants and trial personnel was judged to be at high risk of bias. Blinded outcome assessment for self-report data was adequate in 4/8 (50%) studies; the other four did not describe who conducted the self-report outcome assessments. Low risk of bias in the 'incomplete outcome data' domain was found in 6/8 (75%) studies and 1/8 (13%) was judged to be at high risk of bias in this domain. All eight had adequate ratings for the selective outcome reporting domain (Fig. 2).

3.3. Effect of exercise on transdiagnostic treatment targets

3.3.1. Effect of exercise on anxiety sensitivity

Data from six studies of 289 randomized participants were included in the analysis of effect sizes for anxiety sensitivity (AS). The effect of the exercise interventions versus control was 0.72 (95% CI [0.29, 1.15], $p = .001$) with high and significant heterogeneity ($I^2 = 78.54$, 95% CI [59.57, 88.61]; $Q = 37.28$, $p < .001$; Fig. 3). This suggests there is a medium to large, significant effect of exercise interventions for reducing AS.

3.3.2. Effect of exercise on distress tolerance

Data from four studies of 217 randomized participants were included in the analysis of effect sizes for distress tolerance (DT). The effect of the intervention versus control was 0.21 (95% CI [-0.15, 0.56], $p = .26$) with moderate and significant heterogeneity ($I^2 = 65.10$, 95% CI [16.21, 85.48]; $Q = 14.33$, $p = .01$; Fig. 4). This suggests there is a small, non-significant effect of exercise interventions for increasing DT.

3.3.3. Effect of exercise on stress reactivity

Data from ten studies of 468 randomized participants were included in the analysis of effect sizes for stress reactivity (SR). The effect of the intervention versus control was 0.32 (95% CI [0.14, 0.49], $p < .001$) with zero and nonsignificant heterogeneity ($I^2 = 0.00$, 95% CI [0, 42.21]; $Q = 8.99$, $p = .70$; Fig. 5). This suggests there is a small, significant effect of exercise interventions for reducing SR.

3.3.4. Effect of exercise on general self-efficacy

Data from eight studies of 484 randomized participants were included in the analysis of effect sizes for general self-efficacy (GSE). The effect of the intervention versus control was 0.59 (95% CI [0.26, 0.93], $p < .001$) with moderate and significant heterogeneity ($I^2 = 69.19$, 95% CI [38.44, 84.58]; $Q = 25.97$, $p = .001$; Fig. 6). This suggests there is a medium, significant effect of exercise interventions for increasing GSE.

3.4. Publication bias

For each outcome, a funnel plot was visually inspected and the Duval and Tweedie trim and fill procedure was used to test for missing studies. For AS, the funnel plot revealed asymmetry, but the Duval and Tweedie trim and fill procedure did not impute any studies or adjust the effect size (Supplemental Fig. 1a). Similarly, the funnel plot for DT revealed some asymmetry, but the Duval and Tweedie trim and fill procedure did not impute any studies or adjust the effect size (Supplemental Fig. 1b). For SR, a funnel plot and the Duval and Tweedie trim and fill procedure did not show evidence of publication bias (Supplemental Fig. 1c). For GSE, a funnel plot revealed some asymmetry, but the Duval and Tweedie trim and fill procedure did not impute any studies or adjust the effect size (Supplemental Fig. 1d).

4. Discussion

A range of strategies that engage therapeutic targets allows clinicians to attend to patient preferences when seeking to intervene on key mechanisms underlying the maintenance and improvement of anxiety and depressed mood. Hence, in the present study, we sought to complement studies documenting the anxiolytic and antidepressant effects of exercise with a meta-analytical review of the efficacy of exercise for engaging four putative transdiagnostic treatment targets, namely AS, DT, SR, and GSE. Our review of peer-reviewed published articles before April 1, 2018 yielded 28 studies examining a total of 1293 patients in RCTs evaluating the effect of exercise on AS, DT, SR, or GSE. Results from six studies yielded significant medium to large effect sizes of exercise for reducing AS and results from ten studies yielded significant but small effect sizes for reducing SR. Additionally, results from eight studies yielded significant medium effect sizes for increasing GSE. However, results from four studies yielded only a small, insignificant effect size of exercise for increasing DT. These findings provide the first estimates of controlled effect sizes of exercise for improving AS, DT, SR, and GSE, and suggest that exercise can successfully engage three of these four transdiagnostic targets thought to affect the course of anxiety disorders, unipolar depression, PTSD, and overall treatment progress.

As is the case for most meta-analytic reviews, there was considerable heterogeneity among the included studies not just in terms of the observed effects but also with respect to methodology (e.g., limited range in sample characteristics such as race, gender, and diagnostic composition; approach to assessment), the nature of the exercise intervention (e.g., type, duration), and the target population. Ideally, follow-up moderator analyses would allow us to obtain some insight as to whether the effects of exercise on these therapeutic targets would vary depending on any of these variables or their combinations/interactions. Indeed, it would be helpful to know, for example, whether there is a specific exercise intervention prescription that yields the best results for enhancing self-efficacy in adolescents vs. adults. You would expect that exercise prescriptions are most effective when they are personalized or matched to specific patient characteristics informed by what we know about how exercise can exert positive effects. Unfortunately, the sample of studies was too small to conduct such important analyses.

Aside from more studies with larger samples, this literature would benefit from research that pushes the envelope on methodology. Our analyses revealed that most studies failed to employ several of the recommended strategies that reduce bias (e.g., blinding, incomplete outcome data). In addition, the specificity of exercise effects can be assessed by employing control conditions that match the exercise condition on several aspects such as expectation of the putative ingredient. For example, in the smoking cessation literature, a wellness-control condition has been effectively used as a “placebo” control condition (Marcus et al., 1999; Smits et al., 2016), allowing researchers to make better inferences about the effects of adopting an exercise routine. Efforts toward a personalized prescription are probably also best guided by recognizing the importance of patient preferences as well the possibility that interventions may require modification as patients move through the different stages of treatment (e.g., acute phase, maintenance phase, continuation phase). It is plausible that matching the exercise activity to patients’ preferences is important for uptake and thus seeing effects during the acute phase, and that such preferences may change with exercise experiences (e.g., the feeling of being an active person, becoming more physically fit), allowing for the type (as well as dose) to change during later phases of treatment. Similarly, what is required in terms of the type and modality of exercise for improving patients on the four transdiagnostic treatment targets that are the subject of this paper may be different from what is required to maintain the gains and prevent relapse.

There are a number of other limitations to these conclusions that should be recognized. First, several studies compared two or more exercise interventions with the same control group and therefore contributed multiple effect sizes to the meta-analysis. These comparisons are not independent of each other and may have resulted in an artificially low heterogeneity and affected the omnibus effect size. Second, as no data from long-term follow-ups were included in our analyses, the findings represent relatively acute effects of these exercise interventions. Too few studies assessed the effect of exercise over a long-term follow-up period for an adequate meta-analytical analysis of the sustained effects of exercise interventions on AS, DT, SR, and GSE. Third, the small magnitude of the effects of exercise on DT may be directly related to the primary use of the Distress Tolerance Scale (DTS) for assessing this construct. The DTS assesses perceptions of one's ability to withstand negative emotional states but does not capture behavioral ability to actually withstand distress (Bernstein, Vujanovic, Leyro, & Zvolensky, 2011), which potentially develops prior to the cognitive

perceptions of one's ability to withstand negative emotional states. While the perception of one's ability to withstand negative emotional states appears to be a more clinically relevant transdiagnostic target (Marshall-Berenz, Vujanovic, Bonn-Miller, Bernstein, & Zvolensky, 2010; Vujanovic, Dutcher, & Berenz, 2017), including behavioral indices of DT in future work would be useful to fully understand the effect exercise interventions have on DT.

In summary, the current study provides the first meta-analytical analysis of the efficacy of exercise for engaging AS, DT, SR, and GSE; four putative transdiagnostic treatment targets. The results suggest that there is promise for using exercise to reduce AS and SR and increase GSE. We hope that these initial findings and some of our recommendations for future work stimulate further research in this area. There is no doubt that patients who adopt and maintain an exercise routine will benefit in terms of their overall well-being. It would be helpful to clinicians working in a transdiagnostic framework to be able to turn to a literature that can provide direction as to how to best prescribe exercise for specific targets and patients.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brat.2018.11.007.

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