

**A RANDOMIZED CONTROLLED TRIAL OF BIKRAM YOGA AND  
AEROBIC EXERCISE IN THE TREATMENT OF DEPRESSION:  
EFFICACY AND UNDERLYING PHYSIOLOGICAL AND PSYCHOLOGICAL  
MECHANISMS**

By

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## Abstract

Empirical interest in alternative treatment options for major depression has been on the rise, in part because of the shortcomings of conventional approaches. Despite a growing body of evidence supporting the use of various alternative treatments as either stand-alone or adjunctive therapies for depression (Ravindran et al., 2016), methodological limitations have plagued numerous individual trials. The current study aimed to examine the antidepressant effects of yoga in a study design that made several methodological improvements over previous trials. Bikram yoga was used as the yoga intervention because it is a standardized style of yoga that is readily available, thus lending itself well to subsequent replication. In addition to comparing its effects to those of no treatment, Bikram yoga was compared to an aerobic exercise intervention, as the latter has been well-supported for its mood-enhancing benefits and has even been incorporated into treatment guidelines for depression.

Participants were 53 adult women who met diagnostic criteria for a depressive disorder. They were randomized to one of three 8-week conditions: Bikram yoga, aerobic exercise, or waitlist control. Results from an intention-to-treat analysis demonstrated response rates (i.e., >50% reduction on the Hamilton Rating Scale for Depression; HAM-D; Hamilton, 1960) of 61.1%, 60.0%, and 6.7%, respectively, for the yoga, exercise, and waitlist groups. When considering the sample of completers, 73.3% and 80.0% of participants in the yoga and exercise groups, respectively, achieved remission (i.e., no longer meeting diagnostic criteria for depression and  $\text{HAM-D} \leq 7$ ) compared to only 8.3% in the waitlist condition.

A secondary objective of this study was to examine relevant physiological and psychological variables that may underlie the antidepressant effects of Bikram yoga and aerobic exercise. Physiological variables included pre- to post-treatment changes in heart rate, blood

pressure, and cortisol response to a psychological challenge test. Psychological variables were changes in level of perceived hassles, rumination, and mindfulness. Although these variables have been linked to depression and have also been found to be influenced by yoga and exercise, their role in mediating the antidepressant effects of yoga and exercise have gone largely unexplored. Rumination emerged as a significant mediator for both active treatment conditions. Acceptance, which is a component of mindfulness, also mediated the antidepressant effects of exercise. Possibly owing to methodological issues and extraneous factors that may have been inadequately controlled for, none of the physiological variables emerged as significant mediators. Suggestions for future research, including other potential mechanisms of action that may help better understand the mental health benefits of yoga and exercise, are highlighted.

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## **Chapter 1**

### **Introduction**

#### **Major Depressive Disorder and Current Conventional Treatments**

Major depressive disorder (MDD) is a common and highly recurrent psychiatric disorder, affecting approximately 3.9–4.7% of Canadians yearly and 9.9–11.3% across their lifetime (Lam et al., 2016; Patten et al., 2015). The cardinal features of MDD include intense and prolonged sadness and/or a loss of interest or pleasure in almost all activities (American Psychiatric Association, 2013). Additionally, individuals with depression experience a number of other symptoms that may include changes in weight and/or appetite, sleep disturbances, psychomotor changes, lack of energy, feelings of worthlessness or inappropriate guilt, difficulty concentrating, and recurrent thoughts of death (American Psychiatric Association, 2013). MDD is a particularly striking disorder due to its overarching effects on various dimensions of well-being. Further, it is predicted to become the single biggest medical burden on health by 2020 (World Health Organization). In line with the pervasive nature of its symptoms, MDD is associated with significant impairment in occupational and/or educational functioning, interpersonal relationships, and physical health, and with an increased risk of suicide (Angst, Stassen, Clayton, & Angst 2002; Lam et al., 2016; Patten et al., 2015). These serious implications affect not only the individual and their loved ones but also have important societal consequences. For example, the yearly economic burden of depression in Canada was estimated at \$14 billion in 1998, accounting for both direct treatment costs and indirect costs associated with reduced productivity and disability claims (Stephen & Joubert, 2001). A more recent report by The Conference Board of Canada estimated the yearly cost of depression to be a staggering \$32.3 billion (“Unmet Mental Health Care Needs,” 2016).

According to clinical practice guidelines set out by the Canadian Network for Mood and Anxiety Treatments (CANMAT), first-line treatment recommendations for individuals with acute MDD are pharmacotherapy, psychological treatment, specifically cognitive-behavioural therapy (CBT), interpersonal psychotherapy, and behavioural activation, or a combination of pharmacotherapy and psychological treatment (Kennedy et al., 2016; Parikh et al., 2016). Despite a strong basis of empirical support for the use of these conventional treatments, the application of these approaches to successfully treat MDD is confounded by a number of important limitations. First, there is an issue of limited acceptability and/or feasibility of conventional depression treatments. Epidemiological studies have revealed that only 55.7-63.1% of those with MDD in Canada seek professional services (i.e., family doctor, psychiatrist, psychologist, other mental health professional) for mental health reasons (Patten et al., 2015; Vasiliadis, Lesage, Adair, Wang, & Kessler, 2007), suggesting that a large proportion of afflicted individuals do not utilize conventional treatment options. Reasons to not seek treatment are likely varied, but may include limitations of the dominant model of mental health treatment (i.e., the delivery of therapeutic services by highly trained mental health professionals in one-to-one in-person appointments), attitudes towards conventional approaches (e.g., beliefs about medication side effects), and perceived stigma (Maddox, Levi, & Thompson, 1994; Masand 2003; Mitchell & Selmes, 2007). Importantly, treatment delays may lead to more entrenched symptoms and a worse long-term prognosis (Bukh, Bock, Vinberg, & Kessing, 2013; Wang et al., 2005). Second, conventional treatments for depression are often associated with poor adherence. For instance, it has been shown that among depressed individuals being treated with pharmacotherapy, 28-52% are non-adherent to some extent (Vergouwen, Bakker, Katon, Verheij, & Koerselman, 2003), 32% stop taking their medication within the first 6 weeks (Maddox et al., 1994), and 45-60% discontinue

medication with the first 3 months (Hotopf, Hardy, & Lewis, 1997; Lin et al., 1995; Maddox et al., 1994). Non-adherence has been found to be motivated by various factors, including the experience of adverse side effects, negative attitudes toward taking medication, a poor therapeutic alliance with one's treatment provider, and less severe symptomatology (Julius, Novitsky, & Dubin, 2009; Maddox et al., 1994; Mitchell & Selmes, 2007). Finally, even when considering the subset of individuals with MDD who both seek *and* adhere to conventional treatment, a significant portion do not experience adequate symptom improvement. It has been found that only 48-60% of individuals experience a clinically significant response (i.e., >50% reduction in symptom severity) to a trial of pharmacotherapy or psychotherapy, with 40-47% achieving remission based on a Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960) score of 7 or lower (Cuijpers et al., 2014; DeRubeis et al., 2005; Thase, Haight, & Richard, 2005; Trivedi et al., 2006).

### **Alternative Treatment Options for Depression**

Likely partly owing to the shortcomings of conventional treatments for MDD, interest in alternative approaches has been increasing. The term “complementary and alternative medicine” approaches (CAMs) is used to describe a group of diverse medical and health care practices, technologies, and treatments that fall outside the realm of conventional treatment and are used to improve a variety of aspects relating to mental and/or physical health. Examples of commonly used CAMs include herbal medicine (e.g., St. John's wort), vitamins and mineral supplements (e.g., omega-3 fatty acids), and physical or mind-body therapies (e.g., exercise, yoga, acupuncture, meditation, relaxation, massage). Although the use of CAMs is prevalent in the general population (i.e., approximately 36-79%; Barnes, Powell-Griner, McFann, & Nahin, 2004; Esmail, 2017; Tindle, Davis, Phillips, & Eisenberg, 2005), their use is even more common among

those with psychiatric problems. In fact, depression has been identified as one of the most frequent indications for CAM use (Freeman et al., 2010; Kessler et al., 2001), with national surveys revealing that approximately 60% of those with depression report using one or more CAMs to help alleviate their symptoms (Kessler et al., 2001; Unutzer et al., 2000; Wu et al., 2007). The most common reasons reported for using CAMs include a desire for treatment to be based on a “natural approach”, the unpleasant side effects of antidepressant medication, a lack of response to conventional treatments, and the high cost of conventional treatments (Astin, 1998; Tindle et al., 2005; Wu et al., 2007). Nevertheless, it appears that among CAM users with depression, these approaches are often used concurrently with conventional treatments rather than as alternatives (Solomon & Adams, 2015; Wahlström et al., 2008).

The evidence base pertaining to the use of CAMs in the alleviation of depression is now quite expansive (Freeman et al., 2010; Ravindran & da Silva, 2013; Solomon & Adams, 2015). In fact, there is solid empirical evidence to support the use of several CAMs as monotherapies or adjunctive therapies for specific types or severities of MDD. More specifically, CANMAT analyzed and summarized empirical findings of more commonly researched CAMs in the treatment of depression and developed guidelines for their use (Ravindran et al., 2016). For instance, according to these guidelines, there is support for the use of light therapy as a first-line monotherapy for seasonal MDD and as a second-line adjunctive therapy for mild to moderate non-seasonal MDD. St. John’s wort was identified as a first-line monotherapy in mild to moderate MDD and as a second-line adjunctive treatment for moderate to severe symptoms. Omega-3 fatty acids were deemed to be effective as a second-line monotherapy for mild to moderate MDD and as an adjunct to antidepressant medication for moderate to severe MDD.

Many other CAMs were also investigated in the CANMAT review (Ravindran et al., 2016), with varying levels of support found. Exercise and yoga, which are considered “physical therapies”, were two such approaches. These CAMs are particularly interesting from an antidepressant context as they are often anecdotally linked with various psychological benefits, such as a “runner’s high” or feelings of “zen” following yoga. According to the CANMAT guidelines (Ravindran et al., 2016), exercise and yoga have received a good deal of support for their antidepressant effects. In fact, Ravindran et al. (2016) concluded that there is support for the use of exercise as a first-line monotherapy for mild to moderate MDD and as a second-line adjunctive treatment for moderate to severe symptoms. Methodological weaknesses related to trials of both exercise and yoga were noted, which may limit interpretation of results (Ravindran et al., 2016); however, this appeared to be more of an issue for trials of yoga. Since this review, additional support has continued to accumulate for the use of CAMs in the treatment of depression. I have reviewed the relevant literature below, as well as highlighted methodological challenges that have plagued some of these studies, particularly those involving yoga. The primary objective of this investigation, therefore, was to examine the antidepressant effects of exercise and yoga using a methodologically rigorous study design. In addition to the efficacy of each approach relative to no treatment, I was interested in comparing exercise and yoga to each other, since the former has stronger empirical support for its antidepressant effects. As a secondary objective, I was interested in investigating various potential mechanisms by which exercise and yoga may improve mood. As the following literature review demonstrates, this is an area of increased empirical attention; however, *how* exercise and yoga may alleviate depression is not well understood.

## Chapter 2

### Theoretical Context

#### Exercise and Depression

Exercise is defined as planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness (American College of Sports Medicine, 2013). Empirical interest in its potential mood-enhancing benefits has likely been motivated by observed associations between activity levels and rates of depression. Results from prospective studies suggest that an inactive lifestyle (i.e., not meeting physical activity guidelines) or low cardiorespiratory fitness levels increase risk of depression (Jacka et al., 2011; Lucas et al., 2011; Schuch, Vancampfort, Sui, et al., 2016), whereas an active lifestyle decreases risk. For instance, numerous prospective studies using community samples have demonstrated that among physically active individuals, prevalence rates of depression at some later point in time are lower than those of less active individuals (for reviews, see Mammen & Faulker, 2013; Teychenne, Ball, & Salmon, 2008). This suggests that being physically active affords some protective or preventative effects against depression. Among individuals with a history of depression, Harris, Cronkite, and Moos (2006) found that increased physical activity was associated with lower recurrence of depression and better tolerance of life stressors over a 10-year period. Although there is some support for a dose-response relationship between increasing exercise and decreasing depression risk (Brown, Ford, Burton, Marshall, & Dobson, 2005; Teychenne et al., 2008), it appears that the buffering effects of exercise occur regardless of its intensity or type (Mammen & Faulker, 2013; Teychenne et al., 2008).

Expanding upon the correlational relation between exercise and depression, randomized controlled trials (RCTs) have been conducted to examine the antidepressant effects of exercise.

Studies have focused on the role of exercise as an adjunct to treatment as usual (TAU), as well as a stand-alone intervention, typically in comparison to conventional treatments (i.e., medication/placebo, psychotherapy), other non-exercise interventions (e.g., health education, meditation), or various control conditions. In most studies, exercise generally refers to aerobic exercise of a moderate to high intensity (e.g., jogging, brisk walking, cycling, or other cardiovascular training), which is administered for 30-60 minutes, usually three times per week for 8-20 weeks (Perraton, Kumar, & Machotka, 2010; Ravindran et al., 2009). Other studies, however, have also examined the antidepressant effects of as little as 7-10 days of daily exercise (e.g., Knubben et al., 2007). Comparisons of high versus low frequency have yielded mixed results (e.g., Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Legrand & Heuze, 2007), and no difference in benefit between high and low intensity exercise has consistently been found (Helgadóttir, Hallgren, Ekblom, & Forsell, 2016; Larun, Nordheim, Ekeland, Hagen, & Heian, 2006).

In terms of its adjunctive benefits, results from several RCTs suggest that exercise is a feasible and effective add-on strategy. For example, in a sample of 33 individuals with treatment-resistant MDD, Mota-Pereira et al. (2011) compared TAU to TAU in combination with a home-based exercise program (i.e., 30-45 min/day walks, 5 days/week, for 12 weeks). All participants had been undergoing combined pharmacological therapy for 9-15 months, without showing clinical remission, prior to study enrollment. Compared to those in the TAU-only group, individuals in the combination group experienced significantly greater reductions in depression severity on the HAM-D and the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996). Further, 26% of those in the combination group achieved remission by the end of treatment, compared to 0% in the TAU group. Similar findings have been found in the treatment of severe

MDD. Schuch et al. (2015) randomized 50 inpatients with severe MDD to either conventional treatment (pharmacotherapy and/or electroconvulsive therapy) alone or in combination with aerobic exercise. Exercise involved three sessions per week throughout the hospitalization period, with a goal dose of 16.5kcal/kg/week. The authors found that those in the combination group experienced significantly greater reductions in HAM-D scores and greater improvements in quality of life, according to the World Health Organization Quality of Life Assessment Instrument – Brief version (WHOQOL Group, 1998), at the end of the hospitalization period than the TAU group. Furthermore, although not a statistically significant difference, 48% of those in the combination group achieved remission, compared to 32% in the TAU group.

In a sample of 156 older adults with MDD, Blumenthal et al. (1999) compared the effects of aerobic exercise to antidepressant medication alone and combined exercise and medication. The authors found that following 16 weeks of treatment, all conditions resulted in significant and comparable treatment responses based on the HAM-D and BDI. The percentage of participants who were no longer classified as clinically depressed at the end of treatment did not differ across treatment group (exercise: 60.4%; medication: 68.8%; combination: 65.5%). Despite not providing clear evidence for the *additive* effects of exercise, results from this study suggest that exercise may be an important alternative stand-alone treatment of depression in older individuals. Using this same sample of participants, Babyak et al. (2000) demonstrated some interesting findings at 6-month follow-up. Remitted participants in the exercise group had significantly lower relapse rates (8%) compared to those in the medication group (38%) and combination group (31%). Across all three conditions, self-reported participation in exercise during the follow-up period was associated with a reduced probability of a depression diagnosis.

Results from the Blumenthal et al. (1999) and Babyak et al. (2000) studies underscore the value in investigating the independent antidepressant effects of exercise. Over the past several decades, dozens of RCTs have pursued this question, by comparing exercise not only to pharmacotherapy, but also to psychotherapy, other alternative treatments, and control conditions. For example, Blumenthal et al. (2007) randomly assigned 202 adults with MDD to one of four conditions: supervised exercise in a group setting, home-base exercise, antidepressant medication (sertraline), or placebo. Following a 16-week period, both exercise conditions resulted in symptom improvement on the HAM-D that was comparable to that of the medication group and superior to placebo. A recent large-scale RCT (Hallgren et al., 2015) compared the efficacy of exercise to internet-based CBT and TAU. A total of 946 primary care patients participated, the majority of whom reported a moderate severity of clinical depression at initial assessment. Following a 12-week intervention period, participants in the exercise and internet-based CBT groups experienced significantly greater reductions in depression symptoms on the Montgomery-Asberg Depression Rating Scale (Montgomery & Asberg, 1979) compared to those in the TAU group. These benefits were maintained at a 9-month follow-up (Hallgren et al., 2016).

Meta-analytic results have generally demonstrated the antidepressant effects of exercise to be superior to control activities (e.g., no treatment, TAU, waitlist, telephone conversations about general health) and other non-exercise interventions (e.g., bright light therapy, health education, stretching, meditation) and equivalent to pharmacotherapy and psychotherapy (e.g., Cooney et al., 2013; Kvam, Kleppe, Nordhus, & Hovland, 2016; Schuch, Vancampfort, Richards, et al. 2016). Nevertheless, possibly owing to varied inclusion criteria of meta-analyses, heterogeneity of studies examined, and poor quality of many trials, a wide range of effect sizes has been estimated (e.g., Cooney et al., 2013; Craft & Landers, 2008; Danielsson, Noras, Waern, &

Carlsson, 2013; Krogh, Nordentorft, & Sterne, 2011; Rethorst, Wipfli, & Landers, 2009). Recent meta-analytic reviews that have relied on careful selection of methodologically rigorous studies and accounted for publication bias, however, have demonstrated that exercise has moderate to large effects on depression (Kvam et al., 2016; Schuch, Vancampfort, Richards, et al. 2016). For instance, Schuch, Vancampfort, Richards, et al. (2016) calculated an overall standard mean difference of 1.11 in favour of exercise compared to control conditions, with even larger effects found for interventions using aerobic exercise, at moderate and vigorous intensities, for individuals with MDD. Similarly, using Hedges'  $g$  calculations, Kvam et al. (2016) found exercise to have a large and significant effect compared to no treatment ( $g = -1.24$ ) and a moderate to large significant effect relative to control conditions ( $g = -0.68$ ) and TAU ( $g = -0.48$ ). In line with these more recent meta-analytic findings, various associations, including CANMAT, are incorporating exercise into their treatment guidelines for depression (e.g., British Association for Psychopharmacology, Scottish Intercollegiate Guidelines Network; Cleare et al., 2015; Ravindran et al., 2016; SIGN, 2010). For example, the National Institute for Health and Care Excellence recommends a structured 45-60 min group exercise class, three times per week for 10-14 weeks, as an initial intervention for mild to moderate depression (NICE, 2016).

### **Yoga and Depression**

Although the majority of RCTs investigating the antidepressant effects of physical therapies have utilized aerobic exercise programs (Perraton et al., 2010), there has been a recent increase of empirical interest in yoga. Yoga is defined as an ancient Indian system of philosophy and practice that promotes the interconnection of mind, body, and spirit (Iyengar, 1993; Salmon, Lush, Jablonski, & Sephton, 2009). The Sanskrit word *yoga* literally means “union” and describes the interconnection of mind, body, and spirit that is believed to ultimately lead to

self-awareness (Choudhury, 2007; Iyengar, 1993). Although the first published trials of yoga appeared as early as 1975, the majority of research on yoga's therapeutic potential has occurred post-millennial, with drastic year-to-year increases occurring since 2011 (Cramer, Lauche, & Dobos, 2014).

Yoga is practiced by an estimated 200 million people worldwide (Kasturi, 2013), including 16% of Canadian adults in 2016 and 27% across their lifetime (Esmail, 2017). In Western society, higher rates of use have been found among those who are Caucasian, female, middle-aged, and college-educated (Barnes et al., 2004; Birdee et al., 2008; Ipsos Public Affairs, 2016). It appears that yoga practitioners in Western society often start a yoga practice explicitly to improve their health (Cramer, Lauche, & Dobos, 2014). Consistent with this, the experience of musculoskeletal conditions, asthma, and mental health concerns have been independently associated with higher rates of use (Birdee et al., 2008). Accordingly, health care providers, such as family physicians, are more commonly recommending yoga as a treatment method to their patients (Nerurkar, Yeh, Davis, Birdee, & Phillips, 2011; Wardle, Adams, & Sibbritt, 2014).

Although different forms of yoga have emerged, each with unique approaches and theoretical underpinnings, Hatha yoga is the most commonly practiced form in North America (Salmon et al., 2009). Hatha yoga includes breath control (*pranayama*), physical postures (*asanas*), and meditation (*dhyana*; Raub, 2002). Many styles of Hatha yoga exist, with variations in their emphasis on *pranayama*, *asanas*, and *dhyana*. For instance, in Iyengar yoga, the focus is on correct alignment of the body, and students may practice it for many years before working with the breath. In contrast, in Vinyasa yoga, the focus is on breath-linked movement. That is, practitioners move from one posture to the next while coordinating their breath with each movement. In Kundalini yoga, the focus is on awakening kundalini energy via the use of the

three components of Hatha yoga in combination with mantra chanting. Other styles of Hatha yoga (e.g., Sudarshan Kriya Yoga [SKY]) focus almost exclusively on breathing or meditation.

A substantial body of research has accumulated attesting to the therapeutic benefits of yoga, including favorable changes in cardiovascular functioning, body weight, physical pain, cholesterol, blood glucose levels, and strength and flexibility (e.g., Balasubramaniam, Telles, & Doraiswamy, 2013; Cramer, Lauche, & Haller, et al., 2014; Field, 2011). Further, it has been found to result in improvements in stress management, overall well-being, sleep quality, and mood (e.g., Balasubramaniam et al., 2013; Evans, Tsao, Sternlieb, & Zeltzer, 2009; Field, 2011; Innes, Bourguignon, & Taylor, 2005; Raub, 2002; Streeter et al., 2017; Yang, 2007). With respect to clinical depression, approximately two dozen empirical trials have now examined the effects of yoga in comparison to control activities (e.g., no treatment, TAU, waitlist, social support), exercise interventions (e.g., running), relaxation exercises (e.g., progressive muscle relaxation, listening to relaxing music), and conventional treatments (e.g., pharmacotherapy, ECT). The studies that have been conducted to date have generally demonstrated yoga's potential as an antidepressant approach (for reviews, see Cabral, Meyer, & Ames, 2011; Cramer, Anheyer, Lauche, & Dobos, 2017; Cramer, Lauche, Langhorst, & Dobos, 2013; Pilkington, Kirkwood, Rampes, & Richardson, 2005). For instance, there is evidence that yoga in combination with antidepressant medication is superior to antidepressant medication alone. Sharma, Das, Mondal, Goswami, and Gandhi (2005) randomly assigned 30 adults with MDD to either medication alone or in combination with Sahaj yoga, a style of yoga that emphasizes meditation. Although both groups experienced significant reductions in symptoms based on the HAM-D following 8 weeks of treatment, those in the combination group improved to a significantly greater degree and were more likely to achieve remission compared to the medication-only group (46.6% vs. 13.3%). It is

important to highlight, however, that these low remission rates suggest problems with the study's pharmacological intervention, which was not described in detail and brings into question the validity of the results. In a study by Gangadhar, Naveen, Rao, Thirthalli, and Varambally (2013), 137 outpatients with a depressive disorder self-selected into one of three treatment conditions: yoga, antidepressant medication, or a combination of yoga and antidepressant medication. The yoga intervention was a series of physical postures, relaxation techniques, breathing exercises, and chanting meditation that was previously developed by the research team to target specific symptoms of depression (Naveen et al., 2013). Following a 12-week intervention period, those in the yoga and combination groups experienced significantly greater reductions in HAM-D scores and higher rates of treatment response (i.e., HAM-D  $\leq$  7) than the medication-only group (yoga: 93.3%; combination: 81.2%; medication: 31.25%).

There is also some support for the use of yoga as an adjunctive approach for depressed individuals who are not responding adequately to medication (Sharma, Barrett, Cucchiara, Gooneratne, & Thase, 2017; Uebelacker et al., 2017). Sharma et al. (2017) randomized 25 outpatients who continued to experience symptoms of MDD despite a course of antidepressant treatment (i.e.,  $\geq$  8 weeks) to either 8 weeks of SKY or a waitlist control group. Those in the yoga group experienced significantly greater reductions in depression symptoms, measured by the HAM-D and BDI, than those in the waitlist group. Uebelacker et al. (2017) also examined the adjunctive benefits of Hatha yoga versus health education classes (i.e., control group) in a sample of 122 individuals with treatment-resistant MDD. The yoga program used was developed specifically for the study and included breathing exercises and meditation, a variety of physical postures that instructors could choose from, and relaxation. Following a 10-week intervention period, rates of treatment response (i.e.,  $>50\%$  reduction in symptom severity) did not differ

across the two groups, which the authors reasoned was due to the difficult-to-treat sample and the use of a control group that was matched for time and non-specific factors (e.g., social support from both an instructor and from peers with depression). Nevertheless, at a 6-month follow-up, 51% of those in the yoga group demonstrated a treatment response, which was significantly greater than the 31% rate observed in the health education group.

Yoga's potential as a stand-alone treatment has also been examined. A particularly noteworthy study examined the effects of SKY versus electroconvulsive therapy (ECT) versus antidepressant medication (Janakiramaiah et al., 2000). Forty-five inpatients with MDD were randomly assigned across treatment conditions. Significant and comparable reductions in HAM-D and BDI scores over the 4-week trial were found in all three groups. Although the response rate (i.e., HAM-D  $\leq$  7) in the ECT group (93%) was significantly higher than the other two conditions, 67% of those in the yoga group experienced a clinically significant response, which did not differ statistically from the medication group (73%). Results from this study are important because it is one of few RCTs that has been deemed to be high methodological quality and low risk of bias (Cramer et al., 2013). A recent meta-analysis of the effects of yoga on elevated depression symptoms revealed consistent evidence for the beneficial short-term effects of yoga compared to TAU and control conditions, as well as limited support for its superiority to relaxation and aerobic exercise (Cramer et al., 2013). In a subsequent systematic review of RCTs specifically involving MDD, yoga was deemed to be superior to placebo and generally comparable to other evidence-based interventions (e.g., exercise, medication, ECT; Cramer et al., 2017). Although promising, it has been highlighted that because of a high degree of heterogeneity across yoga interventions and, often, low methodological quality, caution must be taken when interpreting results. Studies have varied widely in terms of the length of intervention, ranging

from 3 days to 24 weeks, frequency of intervention, and type of yoga (Cramer et al., 2013; Pilkington et al., 2005; Ravindran et al., 2009). In numerous studies, limited to no information has been provided regarding the nature of the yoga intervention and qualifications of yoga instructors (e.g., Broota & Dhir, 1990; Khumar, Kaur, & Kaur, 1993; Shahidi et al., 2011; Veale et al., 1992). Furthermore, the majority of previous investigations have suffered from important methodological weaknesses, such as a lack of a standardized instruments to diagnose depression, insufficient randomization procedures, failure to report attrition rates, absence of baseline measures, lack of blinding or insufficient information to ensure blinding, use of non-standardized depression outcome measures, and insufficient treatment length (Cramer et al., 2013; Pilkington et al., 2005; Uebelacker, Epstein-Lubow, et al., 2010).

Despite methodological drawbacks of previous investigations, it appears that yoga is a CAM approach that holds a great deal of potential as a treatment option for depression. As a critical next step in establishing a better understanding of yoga's antidepressant effects, methodologically rigorous studies that improve upon the abovementioned limitations are needed. Additionally, and equally important, studies need more consistency in the implementation of yoga. Previous authors have highlighted that the lack of a definitive definition of yoga, along with the variety of forms of yoga studied, has hampered empirical investigation in this area (Lutz, Dunne, & Davidson, 2007; Uebelacker, Epstein-Lubow, et al., 2010). Without increased consistency, it will remain unknown whether the mood-enhancing effects of yoga are general or specific to certain approaches. It has been suggested that future studies use a standardized style of yoga (Uebelacker, Epstein-Lubow, et al., 2010). This approach would mirror manualized psychotherapy protocols, such as CBT, allowing for replication and for the benefits of yoga to be better evaluated and understood. In response to this, a limited number of yoga programs have

been developed for use in research (Gangadhar et al., 2013; Naveen et al., 2013; Uebelacker et al., 2017; Weintraub & Duncan, 2007), typically based on “expert” opinion of yoga instructors. As an alternative option, investigators may want to consider Bikram yoga, which is an existing standardized form of yoga.

Bikram yoga is a specific form of Hatha yoga that consists of an unchanging 90-minute sequence of 26 physical postures and two breathing exercises, practiced in a heated environment (40.6°C, 40% humidity; Choudhury, 2007; see Appendix A for a diagram of the sequence and *asana* names). Practitioners are continuously instructed to keep their eyes open and to focus on themselves in the mirror. Lights remain on for the entire class and no music is played. These instructional and environmental factors presumably help foster mindful awareness and the mind-body connection (Choudhury, 2007). This physically demanding style of yoga has gained widespread popularity, with estimates of 930-1650 studios worldwide (Moss, 2012; Shakespeare, 2006). Standardization comes into play in that only instructors who have undergone an intense certification course are permitted to teach Bikram yoga classes,<sup>1</sup> and they must deliver a scripted and consistent dialogue (i.e., instruction). Such consistency enhances the validity of research using Bikram yoga, as commonalities across studios and instructors allow for certain variables to be controlled and for a certain degree of generalizability. As such, Bikram yoga is an ideal candidate for the application of yoga in a research setting. In fact, a handful of studies have now examined some of its therapeutic benefits. It has been found to be associated with increased muscular strength and improved balance (Hart & Tracy, 2008), above average bone mineral

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<sup>1</sup> Bikram yoga certification consists of an intense 9-week teacher training program that is run by Bikram Choudhury and his faculty (i.e., medical doctors, certified Bikram yoga instructors, researchers) two times per year. Daily training activities include two Bikram yoga classes, anatomy classes, lectures, and posture clinics. In addition to attending these daily activities, trainees must also pass anatomy tests, memorize and deliver the scripted dialogue to Bikram’s satisfaction, and demonstrate proficiency in all Bikram yoga postures.

density (Mukherjee, Mukherjee, & Rude, 2010), decreased cortisol reactivity (Hopkins et al., 2016), and improved arterial stiffness (Hunter et al., 2016). In terms of psychologically-related variables, Bikram yoga has been linked to decreases in affective eating (Hopkins et al., 2016), increased emotional well-being (Hunter et al., 2016), and significant improvements in perceived stress, self-efficacy, and health-related quality of life (Hewett, Pumpa, Smith, Fahey, & Cheema, 2018).

### **Mechanisms Underlying the Antidepressant Effects of Exercise and Yoga: The Importance of the Stress Response**

As empirical investigations into the antidepressant effects of CAM approaches have increased, so has interest in potential underlying mechanisms of action. Numerous mediators by which aerobic exercise and yoga may exert their mood-enhancing effects have been suggested. These mediators tend to fall into two broad categories – biological/physiological mechanisms (e.g., changes in metabolism and the function of several biomarkers such as serotonin, endocannabinoids, brain-derived neurotrophic factor, oxidative stress, inflammation) and psychological mechanisms (e.g., increased self-esteem and self-efficacy, distraction from negative thoughts, connectedness to others). Although still in the early stages of investigation (Blumenthal et al., 2007; Rimer et al., 2012; Krogh, Petersen, Timmermann, Saltin, & Nordentoft, 2007; Pascoe & Bauer, 2015; Uebelacker, Epstein-Lubow, et al., 2010), there is a growing body of research evidence that supports the belief that exercise and yoga improve mental health via changes in one's stress response (Kinser, Goehler, & Taylor, 2012; McCall, 2013; Riley & Park, 2015; Ross & Thomas, 2010; Salmon, 2001; Streeter, Gerbarg, Saper, Ciraulo, & Brown, 2012).

The stress response is an integrated psychological and physiological process that is initiated in the face of a stimulus, typically referred to as a “stressor”. The large majority of stressors are believed to be psychosocial in nature (Girdano, Dusek, & Everly, 2009), as opposed to physical or “biogenic” (e.g., exposure to extreme cold or heat; ingestion of certain medications or substances). Psychosocial stressors are defined as real or imagined environmental events that set the stage for the elicitation of the stress response (Boyle, 2013). That is, they do not directly cause the stress response but trigger it via cognitive appraisal mechanisms (Boyle, 2013). Therefore, an individual’s interpretation of a stimulus is central to whether the stimulus is perceived as a threat, challenge, or aversive event. If it is viewed in this way (i.e., as a stressor), emotional arousal typically results (Boyle, 2013). These cognitive appraisals and emotional reactions are believed to then trigger a subsequent physiological response, and they may continue to influence physiological changes, depending on the individual and duration of the stressor.

The physiological component of the stress response begins in the amygdala (Ulrich-Lai & Herman, 2009), an area of the brain that contributes to emotional processing. When danger is perceived by the amygdala, a neural signal is sent to the hypothalamus (Roldan, Alvarez-Pelaez, & de Molina, 1974; Ulrich-Lai & Herman, 2009). The hypothalamus acts a command centre and stimulates two inter-related systems, the sympathoadrenalmedullary (SAM) system, which provides a rapid response to stress, followed by the hypothalamic-pituitary-adrenal (HPA) axis, a slower acting system (Herman, McKlveen, Solomon, Carvalho-Netto, & Myers, 2012; Ulrich-Lai & Herman, 2009). With respect to SAM activity, the hypothalamus signals the sympathetic branch (i.e., sympathetic nervous system; SNS) of the autonomic nervous system (ANS), stimulating the adrenal medulla. This leads to the release of catecholamines (norepinephrine and epinephrine; Boyle, 2013). Norepinephrine and epinephrine facilitate numerous physiological

changes that represent the classic “fight or flight” response, such as increased heart rate, vasoconstriction, accelerated breathing, dilation of pupils, and inhibition of digestion (see Boyle, 2013). The function of these physiological changes is to provide the body with increased strength and speed in anticipation of fighting or fleeing. In terms of HPA axis stimulation, the hypothalamus releases corticotropin releasing hormone (CRH), which triggers the production and release of adrenocorticotrophic hormone (ACTH) from the pituitary gland (Ulrich-Lai & Herman, 2009). ACTH in turn stimulates the release of glucocorticoids (cortisol in humans and corticosterone in rodents) from the adrenal cortex (Ulrich-Lai & Herman, 2009). Circulating glucocorticoids then promote the mobilization of stored energy, suppress the immune system, and potentiate numerous sympathetically-mediated effects, such as vasoconstriction (Ulrich-Lai & Herman, 2009). This allows sympathetic activity to continue in the face of an ongoing stressor and demonstrates the synergistic actions of the SAM system and HPA axis during stress. Following the termination of a stressor, elevations in glucocorticoid levels typically downregulate the physiological stress response through negative feedback mechanisms at various levels of the HPA axis (Herman et al., 2012; Jacobson & Sapolsky, 1991; Munck, Guyre, & Holbrook, 1984). The parasympathetic division (i.e., parasympathetic nervous system; PSNS) of the ANS, which is responsible for actions that are generally opposite those of the SNS, acts to further dampen the stress response and restore the body to a restful state (Ulrich-Lai & Herman, 2009).

**Dysregulation of Stress-Related Processes in Depression.** The hypothesis that the antidepressant effects of exercise and yoga may be mediated by changes in the stress response seems plausible when considering the strong link between stress and depression. It is well-established that stressful life events are one of the most powerful predictors of depression onset (e.g., Kendler, Gardner, & Prescott, 2002; Kendler, Gardner, & Prescott, 2006; Kessler, 1997;

Mazure, 1998). Specifically, the experience of a recent major life stressor increases the risk of developing a depressive episode by 2.5-12 times (Kendler et al., 1995; Shrout et al., 1989). Imaging studies have also been useful in revealing links between depression and structural and functional abnormalities in numerous stress-related brain areas, including the amygdala, hippocampus, pituitary gland, and anterior cingulate cortex (Cotter, Mackay, Landau, Kerwin, & Everall, 2001; Frodl et al., 2002; Kempton et al., 2011; Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). Some of the most consistent findings in biological psychiatry relate to dysregulation of the HPA axis in depression. In fact, hyperactivity of the HPA axis among depressed individuals has been documented for decades. Much of this research has examined HPA axis activity at rest (i.e., basal levels) and in response to pharmacological challenge tests designed to assess negative feedback mechanisms of the system. Cortisol continues to be the most commonly-used indicator of HPA axis activity.

In terms of basal HPA axis activity, depression has been linked to elevated cortisol concentrations in the saliva, urine (Carroll, Curtis, Davies, Mendels, & Sugerman, 1976), plasma (Gibbons & McHugh, 1963), and cerebrospinal fluid (Carroll, Curtis, & Mendels, 1976), and elevated awakening cortisol levels (Bhagwagar, Hafizi, & Cowen, 2005; Pruessner, Hellhammer, Pruessner, & Lupien, 2003). Depression has also been associated with non-suppression of cortisol in response to a dexamethasone (DEX) suppression challenge (Carroll et al., 1981), increased cortisol reactivity to an ACTH test (Amsterdam, Winokur, & Abelman, 1983), and enlarged adrenal glands (Nemeroff et al., 1992), all of which indicate hyperactivity of the HPA axis. It has been suggested that such hyperactivity during depressive episodes is due to impairments or dysregulation of negative feedback mechanisms within the HPA axis (Musselman, Evans, & Nemeroff, 1998; Plotsky, Owens, & Nemeroff, 1998).

Psychological challenge paradigms, such as the commonly-used Trier Social Stress Test (TSST; Kirschbaum, Pirke, & Hellhammer, 1993), have also revealed depression-specific abnormalities in HPA axis functioning. These laboratory stress tests assess cortisol reactivity and recovery to an acute stressor, from which an individual's response to stressful life events in real life may be deduced. The TSST is a particularly valuable psychological stress test, as it combines two elements that have been associated with the largest HPA axis reactivity and longest recovery times - high levels of sustained social-evaluative threat and uncontrollability (Dickerson & Kemeny, 2004). On average, cortisol levels in response to the stressor peak 20-30 minutes after its onset and recover back to baseline over the course of up to 60 min following its offset (Dickerson & Kemeny, 2004). Meta-analyses relying primarily on studies using the TSST have demonstrated that depressed individuals show blunted cortisol reactivity (Burke, Davis, Otte, & Mohr, 2005; Zorn et al., 2017) and impaired stress recovery (Burke et al. 2005) in response to psychological stress compared to controls. These response patterns appear to be particularly pronounced in studies with older and more severely depressed adults (Burke et al., 2005) and may be specific to women (Zorn et al., 2017). There is also evidence to suggest that the chronicity and/or recurrence of depression may influence cortisol reactivity to psychological stress (Booij, Bouma, de Jonge, Ormel, & Oldenhinkel, 2013). Using a stress protocol inspired by the TSST, Booij et al. demonstrated that individuals with a more recent onset of depressive symptoms exhibited a higher cortisol response compared to controls, whereas those with more chronic (i.e., persistent or recurrent) symptoms showed a blunted response. Results from this study (Booij et al., 2013) highlight an important question regarding the permanency of HPA axis dysregulation in depression. Empirical findings are inconsistent, however, with some support for the normalization of initial HPA axis dysregulation among remitted individuals (e.g., Hennings et

al., 2009; Zorn et al., 2017) and other support for continued dysregulation despite symptom improvement (e.g., Ahrens et al., 2008; Deuschle et al., 2003).

Given the interconnectedness of the HPA axis and the SAM system, it is not surprising that dysregulation of sympathetically-mediated responses during depressive episodes have also been observed. Concentrations of norepinephrine (NE) have often been the focus of investigation, as NE is the primary neurotransmitter of the SNS (Veith et al., 1994). Compared to healthy controls, depressed individuals have been shown to have elevated basal levels of NE and/or its metabolites in urine (Maas et al., 1987), plasma (Lake et al., 1982; Roy, Pickar, DeJong, Karoum, & Linnoila, 1988; Veith et al., 1994), and cerebrospinal fluid (Roy et al., 1988). Successful treatment with antidepressant medication has been shown to reduce concentrations of NE and its metabolites in both urine and plasma (e.g., Linnoila, Karoum, Calil, Kopin, & Potter, 1982; Linnoila et al., 1986). Pharmacological challenge studies have been useful in understanding the relation of SNS and HPA axis dysregulation in depression. For instance, following the administration of DEX, Roy et al. (1988) found significant correlations between levels of NE and its metabolites and plasma cortisol levels among individuals with MDD. Moreover, those who were classified as non-suppressors had significantly greater cerebrospinal levels of NE metabolites compared to both depressed individuals who were cortisol suppressors or controls. The authors concluded that dysregulation of the noradrenergic system and HPA axis occur together in some depressed individuals. Similar results have been found in earlier DEX studies looking at plasma NE (Barnes et al., 1983; Rubin, Price, Charney, & Heninger, 1985) and epinephrine (Barnes et al., 1983).

In addition to catecholamine levels, depression has been associated with other physiological indicators of increased SNS activity, including elevated basal heart rate (Lake et

al., 1982; Veith et al., 1994) and mean arterial blood pressure (Veith et al., 1994) and reduced heart rate variability (Dalack & Roose, 1990; Miyawaki & Salzman, 1991). Heart rate variability (HRV), which is the amount of fluctuation around the mean heart rate (i.e., beat-to-beat variation in heart rate), is believed to be the most precise non-invasive measure of sympathetic-parasympathetic autonomic balance (Malik et al., 1996; van Ravenswaaij-Arts, Kollee, Hopman, Stoeltinga, & van Geign, 1993). A low HRV has been consistently linked to the development of various risk factors for cardiovascular disease and may indicate underlying stress, overtraining, or inflammation, whereas a high HRV has been associated with good health and reduced cardiovascular disease risk (Malik et al., 1996; Thayer, Yamamoto, & Brosschot, 2010). Finally, eliciting SNS reactivity to psychological challenge tests has also revealed differences between depressed and nondepressed individuals. For example, Heim et al. (2000) examined SNS reactivity to the TSST in a sample of women with MDD and healthy controls. The authors found that depressed women, particularly those with a history of early life stressors (i.e., physical, sexual, and/or emotional abuse, and general traumas), exhibited significantly higher heart rate responses to the TSST compared to non-depressed individuals.

Empirical studies have clearly demonstrated dysregulation of the HPA axis and SNS during depressive episodes. This implies that the physiological stress response of depressed individuals functions differently from that of nondepressed individuals, at least during an acute episode of depression. As previously described, however, the stress response is more complex than simply endocrine and autonomic processes. Cognitive appraisals and emotional reactions to potentially stressful stimuli play an important role in triggering and perpetuating the physiological stress response. Therefore, it is important to also consider psychological processes that are linked to depression, as these may interact with physiological responses to stress in

predicting depressive symptoms. For instance, it has been shown that higher levels of perceived stress in daily life are associated with elevated awakening cortisol levels and depression symptoms (Pruessner, Hellhammer, et al., 2003), as well as other indicators of heightened SNS activity (Dishman et al., 2000). Perceived stress levels have also been linked to altered cortisol response to acute psychological stress (i.e., TSST), even when the acute stressor itself was believed to be of low challenge or threat (Schlotz, Hammerfald, Ehlert, & Gaab, 2011). This implies that an individual's own perception of how "stressed out" he or she feels can impact how that individual responds, physiologically, to subsequent stress. In addition to perceived stress, several cognitive styles and emotional-regulation strategies have been implicated in depression (e.g., pessimistic inferential style, dysfunctional attitudes, thought suppression; Aldao, Nolen-Hoeksema, & Schweizer, 2010; Hong & Cheung, 2015), with rumination being one of the most widely studied constructs for its role in the etiology, maintenance, and worsening of depression symptoms.

According to the Response Styles Theory (Nolen-Hoeksema, 1991), rumination is a style of thinking involving repetitive and passive past-oriented thoughts about negative content (i.e., one's depressive symptoms, negative self-aspects) without engagement in active coping or problem solving (Nolen-Hoeksema, 1991). This stable cognitive trait has emerged as one of the most robust risk factors for depression (Aldao et al., 2010). It has been prospectively associated with increases in symptoms (Nolen-Hoeksema & Davis, 1999; Nolen-Hoeksema, Parker, & Larson, 1994), heightened risk for new onsets of major depression (Just & Alloy, 1997; Nolen-Hoeksema, 2000), and greater chronicity of depressive episodes (Nolen-Hoeksema, Morrow, & Fredrickson, 1993; Robinson & Alloy, 2003). In contrast to rumination, the Response Styles Theory also highlights the role of an alternative response to one's depressive symptoms –

distraction (Nolen-Hoeksema, 1991). Distraction is defined as an adaptive coping style that involves actively turning one's attention away from symptoms and on to pleasant or neutral thoughts or actions (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Whereas ruminative coping is proposed to amplify and prolong depression, distraction is believed to play a role in the discontinuation of depression (Nolen-Hoeksema, 1991).

Rumination is interesting when considering psychological components of the stress response, as there is a growing body of evidence highlighting its role in linking the experience of stress to subsequent negative affect (Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013; Moberly & Watkins, 2008; Morrison & O'Connor, 2005). For instance, in a study using two samples spanning different developmental periods (i.e., adolescents, adults; Michl et al., 2013), exposure to stressful life events was prospectively associated with increased engagement in rumination in both samples. Further, rumination mediated the longitudinal relationship between exposure to stressors and symptoms of depression in the adult sample. A recent study by Connolly and Alloy (2017) used smartphone ecological momentary assessment to examine the role of rumination, both independently and in interaction with stress, in predicting depressive symptoms among undergraduate university students. Two types of rumination were examined: ruminative self-focus and stress-reactive rumination (i.e., rumination in response to the experience of stress). Both measures of rumination were found to interact with the experience of stress to predict higher subsequent depressive symptoms. Stress-reactive rumination also exerted a significant independent effect in predicting increases in daily depression symptoms.

In addition to mediating the relation between stressful life events and depression symptoms, rumination has also been associated with various physiological indicators of stress (Brosschot, Gerin, & Thayer, 2006). It has been linked to higher basal levels of systolic blood

pressure (Chambers & Davidson, 2000), prolonged blood pressure elevations and slower recovery following anger-induction tasks (Schwartz, Gerin, Davidson, & Christenfeld, 2000; Suchday, Carter, Ewart, Larkin, & Desiderato, 2004), and slower heart rate recovery following psychological stress tests (Aldao, McLaughlin, Hatzenbuehler, & Sheridan, 2014; Roger & Jamieson, 1988; Shapero, McClung, Bangasser, Abramson, & Alloy, 2017). In terms of its relation to cortisol reactivity, several studies have demonstrated heightened cortisol reactivity and delayed recovery following a psychological stressor in those with higher levels of trait rumination (Roger & Najarian, 1998; Shapero et al., 2017; Stewart, Mazurka, Bond, Wynn-Edwards, & Harkness, 2013; Zoccola, Quas, & Yim, 2010); however, the absence of a relation and negative associations (i.e., blunted cortisol reactivity) have also been found (Nolen-Hoeksema & Morrow, 1991; Zoccola & Dickerson, 2012; Zoccola, Dickerson, & Zaldivar, 2008). Despite these mixed findings, there appears to be strong evidence for the role of rumination in modulating the physiological effects of stress. Individuals with a tendency to ruminate have been found to exhibit a reduced ability to disengage attention from negative emotional information (Joorman, 2006), difficulties in effective problem solving (Lyubomirsky & Nolen-Hoeksema, 1995; Watkins & Baracaia, 2002), and a decreased willingness to engage in positive coping activities (Lyubomirsky & Nolen-Hoeksema, 1993). These difficulties may in turn amplify, maintain, or reactivate physiological responses to stress (Brosschot et al., 2006), particularly in those with elevated depressive symptoms who may already have some degree of dysregulation in stress reactivity.

**Exercise- and Yoga-Induced Alterations in Stress-Related Processes.** The associations between depression and dysregulation of various stress-related processes provide a foundation from which empirical studies can be designed that investigate mechanisms underlying the

antidepressant effects of treatment approaches. Although interconnections between physiological and psychological components of the stress response, as they relate to depression, are not fully understood, both domains are important to consider when trying to understand how exercise and yoga may improve depressive symptoms. In fact, numerous studies have now demonstrated various physiological and psychological effects of exercise and yoga, suggesting that these CAM approaches may induce adaptive alterations to the stress response. Some of this research is reviewed below and will provide rationale for the secondary objective of the current investigation. In terms of physiological variables, the literature review below focuses on associations between SNS/HPA axis activity and acute exercise/yoga (i.e., during or following a single session) or longer-term exercise/yoga (e.g., following a trial or training period of exercise or yoga; differences between exercise-trained and untrained individuals). With respect to psychological changes that may occur via these CAM approaches, the focus is on changes in perceived stress, rumination, and mindfulness following prolonged exercise or yoga.

***The Autonomic Nervous System.*** Numerous measurements of ANS activity, particularly those relating to the sympathetic branch, have been examined in studies of exercise and yoga. These measurements have typically included heart rate, blood pressure, and HRV, although given the ANS's regulatory control over the cardiovascular system, other cardiovascular parameters have also been examined as indicators of autonomic activity. Acutely, exercise has been shown to increase SNS activity, including heart rate, blood pressure, and respiration (De Vries, 1980; McArdle, Katch, & Katch, 1991), as well as increase catecholamine concentrations (e.g., Hartley et al., 1972; Zouhal, Jacob, Delamarche, & Gratas-Delamarche, 2008). Exercise training, on the other hand, has generally been found to result in the opposite effects. That is, it has been linked to reductions in basal heart rate and blood pressure (Blair, Goodyear, Gibbons, & Cooper, 1984;

Paffenbarger, Jung, Leung, & Hyde, 1991; Paffenbarger et al., 1983; Winder, Hagberg, Hickson, Ehsani, & McLane, 1978), decreased catecholamine concentrations (Hartley et al., 1972; Winder et al., 1978; Winder, Hickson, Hagberg, Ehsani, & McLane, 1979), and other indicators of improved autonomic tone, most notably increased HRV (e.g., Levy et al., 1998; Sandercock, Bromley, & Brodie, 2005). Exercise training has also been associated with changes in cardiovascular functioning, including reductions in peripheral resistance (i.e., overall resistance to blood flow through blood vessels; Hambrecht et al., 2000) and arterial stiffness (i.e., rigidity of arterial walls; Collier et al., 2008; Mustata, Chan, Lai, & Miller, 2004), and increases in cardiac output (i.e., volume of blood per minute pumped by the heart; Mazzeo et al., 1998). The effects of exercise training on *stress reactivity* is one of the most important questions to consider when trying to understand physiological mechanisms by which exercise alleviates depression. Numerous investigations have been conducted looking at the effects of exercise training on SNS and HPA axis reactivity to stressors, as well as differences in stress reactivity between exercise-trained and untrained individuals. Although these studies have used a variety of laboratory tasks to elicit the stress response, the most commonly used stressors are psychological (e.g., TSST) and physiological (e.g., an exercise test) in nature.

Exercise training has been shown to reduce SNS reactivity and improve recovery to psychological challenge tests (Forcier et al., 2006; Jackson & Dishman, 2006; Klaperski, von Dawans, Heinrichs, & Fuchs, 2014). Findings such as these are particularly interesting with respect to potential physiological mechanisms by which exercise improves depression, given the pattern of heightened SNS activity that is typically observed in depression. Spalding, Lyon, Steel, and Hatfield (2004), for instance, compared the effects of 6 weeks of aerobic exercise training, 6 weeks of weight training, and no treatment on blood pressure and heart rate during and following

an acute stressor involving mental arithmetic combined with distraction. Relative to the other two conditions, the aerobic exercise group had a significantly lower heart rate during the stressor and recovery periods. Overall systolic blood pressure was also lower in this group compared to no treatment. Meta-analytic results have provided additional support (Crews & Landers, 1987; Forcier et al., 2006). Forcier et al. (2006) analyzed 18 studies that examined the effects of fitness levels of cardiovascular reactivity and recovery from acute psychological stressors. The authors found that “fit” individuals (i.e., those of high initial fitness or following completion of an exercise training program) showed significantly attenuated heart rate and systolic blood pressure reactivity, with a trend toward reduced diastolic blood pressure reactivity, compared to “unfit” individuals (i.e., those of low initial fitness or prior to beginning an exercise training program). Further, fit individuals demonstrated faster heart rate and blood pressure recovery, all of which point to reduced stress reactivity. These findings suggest that exercise is associated with changes in how one responds physiologically to stressors that are not necessarily physiological in nature. This idea has been previously discussed in the context of the “cross-stressor adaptation” hypothesis (Sothmann, 2006; Sothmann et al., 1996). This hypothesis proposes that regular exercise leads to biological alterations that contribute to reduced physiological reactions or sensitivity not only to exercise-related stressors but also to non-exercise stress (Sothmann, 2006).

Although less research has been conducted in the domain of yoga, relative to exercise, there is emerging evidence for the beneficial effects of yoga on SNS functioning (Pascoe & Bauer, 2015; Pascoe, Thompson, & Ski, 2017; Streeter et al., 2012). Similar to exercise, it appears that yoga has differential short-term (i.e., during or following a single class) versus long-term (i.e., following a trial) effects. That is, variables such as heart rate and blood pressure have been found to increase during a yoga class (e.g., Field, Diego, Delgado, & Medina, 2013; Sinha,

Ray, Pathak, & Selvamurthy, 2004) but decrease across trials of yoga (Pascoe et al., 2017). In a sample of 238 individuals with hypertension, Sujatha and Judie (2014) demonstrated that a 12-week Hatha yoga program was associated with decreased basal heart rate and blood pressure, anxiety, and perceived stress, compared to a waitlist control group. Another study found that 8 weeks of either Iyengar yoga or walking was associated with decreased blood pressure, self-reported anxiety and depression symptoms, and perceived stress (McDermott et al., 2014), with no significant differences emerging between the two interventions. An interesting study by Telles et al. (2004) demonstrated that following 1 month of an intense daily yoga practice, novice practitioners achieved significantly greater voluntary control over their heart rate compared to a control group. Overall, these results provide strong support for the beneficial effects of yoga on blood pressure and heart rate, and these effects appear to be generalizable across various adult populations (e.g., restless-leg syndrome, hypertension, osteoarthritis, elevated blood glucose, healthy control; Bharshankar, Bharshankar, Deshpande, Kaore, & Gosavi, 2003; Ebnezar, Nagarathna, Yogitha, & Nagendra, 2012; Innes & Selfe, 2012; Kanojia et al., 2013; Pascoe et al., 2017; Roche & Hesse, 2014). With respect to other ANS-related measurements, there is some evidence for decreased basal levels of norepinephrine and epinephrine (Granath, Ingvarsson, von Thiele, & Lundberg, 2006; Selvamurthy et al., 1998), favourable changes in HRV (Pascoe et al., 2017; Tyagi & Cohen, 2016), and improvements in vascular functioning (e.g., Duren, Cress, & McCully, 2008; Ross & Thomas, 2010; Sarang & Telles, 2006).

The effects of yoga on SNS reactivity to stress has received little empirical attention, with only a handful of studies conducted to date. These studies have involved a high degree of methodological heterogeneity, including the use of varied laboratory stressors to induce physiological reactivity. For example, in a study of 21 young adult males, the effects of 2 months

of Hatha yoga on heart rate and blood pressure in response to the Harvard step test were examined (Madanmohan, Bhavanani, Shatapathy, & Sahai, 2004). The Harvard step test is an exercise test that involves stepping up and down a platform for a rate of 30 steps per minute for 5 min or until fatigued. The results demonstrated significantly reduced increases in heart rate and systolic blood pressure in response to the test from pre- to post-yoga training. Similarly, Telles and Naveen (2004) found basal heart rate and lowest heart rate achieved during a 6-min exercise test to be significantly reduced following 30 days of yoga practice. Consistent reductions in SNS reactivity have been demonstrated in additional studies using isometric hand-grip (Kanojia et al., 2013; Vijayalakshmi, Madanmonhan, Bhavanani, Patil, & Babu, 2004) and cold pressure (Kanojia et al., 2013) tests. Only one study was identified that has examined the effects of yoga on SNS reactivity to a more psychologically-relevant stressor (Hagins, Haden, & Daly, 2013). In a sample of 30 6<sup>th</sup> grade students, changes in blood pressure and heart rate in response to a “behavioural” stressor (i.e., mental arithmetic and mirror tracing tasks) were examined following either 15 weeks of Hatha yoga or 15 weeks of physical education (Hagins et al., 2013). Contrary to expectations, no significant decreases in SNS reactivity were found in either group. Rather, significant *increases* in systolic and diastolic blood pressure were found.

Based on this small body of evidence, the effects of yoga on SNS stress reactivity are not well-understood. Nevertheless, this question warrants further investigation when considering alterations in SNS reactivity that result from interventions that share commonalities with yoga. For example, meditation and relaxation, both of which are emphasized to some degree in virtually all styles of Hatha yoga, have been shown to significantly reduce blood pressure and heart rate response to psychological stressors (e.g., Barnes, Treiber, & Davis, 2001; Goleman & Schwartz, 1976; Knight & Rickard, 2001; McCubben et al., 1996). Therefore, the possibility that

yoga may alleviate depressive symptoms by reducing SNS reactivity to stress appears to be a worthwhile area of continued investigation.

***The Hypothalamic-Pituitary-Adrenal Axis.*** The effects of exercise on the HPA axis have been examined in studies of both animals and humans. Animal models have demonstrated complex changes at various levels of the HPA axis in response to exercise, including stressor-specific changes in HPA hormone response (e.g., Droste, Chandramohan, Hill, Linthorst, & Reul, 2007; Droste et al., 2003). For example, Droste et al. (2003) examined the effects of long-term voluntary exercise (i.e., 4 weeks of wheel running) on HPA axis response to subsequent stress tests. Compared to control mice, exercising mice demonstrated an exaggerated corticosterone response to a stressor involving a strong physical component (i.e., forced swimming) but a diminished hormone response when faced with a mild psychological stressor (i.e., exposure to a novel environment). It was hypothesized that this heightened response to the physical stressor was due to alterations in the HPA axis and SAM system that occurred as a function of increased metabolic demand during wheel running. The diminished response to the psychological stressor was suggested to be indicative of decreased anxiety. Animal studies have also demonstrated exercise-induced increases in adrenal gland weights, adaptive changes in ACTH levels, and normalization of glucocorticoids (Droste et al., 2007; Droste et al., 2003; Morgan, Corrigan, & Baune, 2015).

Similar to findings relating to the effects of exercise on SNS activity, human studies have consistently shown that acute exercise results in increased activity of the HPA axis, evidenced by elevations in cortisol levels from baseline to post-exercise (e.g., Gispen-de Wied, Jansen, Duyx, Thijssen, & van Engeland, 2000; Kiive, Maaros, Shlik, Tõru, & Harro, 2004; van der Pompe, Bernards, Meijman, & Heijnen, 1999). However, with prolonged exercise training, HPA axis

activity and cortisol levels appear to habituate to the exercise, resulting in a decrease in the magnitude of the response at a given workload (Kjaer, 1992). The effects of exercise training on cortisol levels at rest have generally been nonsignificant, with no differences emerging between trained and untrained individuals (Duclos, Gouarne, & Bonnemaïson, 2003; Heuser, Wark, Keul, & Holsboer, 1991; Kargotich et al., 2007; Krogh, Nordentoft, Mohammad-Nezhad, & Westrin, 2010).

Both psychological and physiological stressors have been used to examine the relation of exercise to cortisol reactivity. Generally, findings from these studies have indicated that higher levels of physical activity are associated with reduced cortisol reactivity but not necessarily improved recovery. In a cross-sectional study, Rimmelmeier et al. (2007) found significantly lower cortisol response to the TSST in exercise-trained men (i.e., elite sportsmen) compared to untrained men. Similarly, using a sample of young women who were classified according to self-reported exercise levels (i.e., none/little, moderate, vigorous), reduced cortisol reactivity to the TSST was found among the more active groups (Klaperski, von Dawans, Heinrichs, & Fuchs, 2013). No group differences in cortisol recovery were found (Klaperski et al., 2013). In an investigation of the impact of acute exercise on cortisol reactivity (Zschucke, Renneberg, Dimeo, Wustenberg, & Strohle, 2015), 40 young men were randomized to a single session of moderate exercise or placebo activity (i.e., light stretching exercises). Ninety minutes following the assigned task, participants underwent cortisol assessment and an fMRI experiment using an adapted version of the Montreal Imaging Stress Task (MIST), a psychological challenge test that is similar to the TSST. The authors found that participants in the exercise group showed a significantly reduced cortisol response to the stress test, particularly among those with a higher aerobic fitness level. Furthermore, those in the exercise group displayed patterns of brain

activation that indicated sustained activity in negative feedback loops and, therefore, greater dampening of further HPA responses. Finally, in an experimental trial, Klaperski et al. (2014) randomly assigned 149 healthy men to a 12-week exercise, relaxation, or waitlist control group. The authors found that participants in the exercise and relaxation groups experienced significant reductions in cortisol reactivity to the TSST from pre- to post-intervention, whereas those in the waitlist group did not. Improvements in cortisol recovery were found but only among those in the relaxation group. Consistent results have been demonstrated in studies using exercise tests as precipitating stressors (Luger et al., 1987; Mathur, Toriola, & Dada, 1986; Rudolph & McAuley, 1995); nevertheless, there is also some evidence suggesting no effect of exercise training on cortisol reactivity to acute physiological stress (Krogh et al., 2010).

Investigations of yoga-induced alterations to HPA axis activity have revealed that individual yoga classes result in decreased salivary cortisol levels from pre- to post-class (Field et al., 2013; Michalsen et al., 2005; Newham, Wittkowski, Hurley, Aplin, & Westwood, 2014; West, Otte, Geher, Johnson, & Mohr, 2004), with additional support for an overall decrease across yoga trials (Banasik, Williams, Haberman, Blank, & Bendel, 2011; Newham et al., 2014; Rocha et al., 2012; Vadiraja et al., 2009; Vedamurthachar et al., 2006). For instance, in a sample of healthy adult men, Rocha et al. (2012) found that 6 months of combined yoga and exercise was associated with significantly lower salivary cortisol levels upon awakening, depression and anxiety symptoms, and stress, when compared to exercise alone. Vadiraja et al. (2009) demonstrated that relative to brief supportive counselling, 6 weeks of yoga resulted in significant decreases in waking and bedtime salivary cortisol among breast cancer patients. Further, these changes in cortisol corresponded to reduced depression, anxiety, and perceived stress. A recent meta-analysis concluded that yoga interventions with an emphasis on *asanas* produce significant

reductions in waking, afternoon, and evening salivary cortisol (Pascoe et al., 2017). With respect to cortisol reactivity, using a sample of 52 women at risk for obesity, Hopkins et al. (2016) examined the effects of 9 weeks of Bikram yoga on cortisol response to a modified TSST protocol. The authors found that participants in the yoga group experienced significantly greater reductions in cortisol reactivity to the stress test over the course of the study than those in a waitlist control group. Importantly, however, this effect was observed only among participants with elevated cortisol reactivity at pre-treatment (“high reactors”) and was not observed among “low reactors.”

Despite some support for a dampening effect of yoga on cortisol levels, other studies have provided contrasting results, including no effect (Beddoe, Yang, Kennedy, Weiss, & Lee, 2009; Bosch, Traustadottir, Howard, & Matt, 2009; Granath et al., 2006; Sarubin et al., 2014; Yoshihara, Hiramoto, Sudo, & Kubo, 2011) and an increasing effect (Vera et al., 2009). For example, in a sample of 31 men and women with self-reported stress-related problems, Granath et al. (2006) found no change in salivary cortisol levels following 4-months of Kundalini yoga. In the only RCT known of to examine the effects of yoga on cortisol levels in the context of MDD, Sarubin et al. (2014) randomized 60 inpatients to 5 weeks of combined yoga and medication or medication only. HPA axis reactivity was assessed via cortisol concentrations in response to serial DEX/CRH tests. Cortisol decreased from pre- to post-treatment in both groups, but no evidence was found in support of an additive benefit of yoga on downregulating the HPA axis. Based on the current state of the research, it appears that the effects of yoga on HPA axis reactivity are not well-understood.

***Attitudes About Stress.*** A decrease in stress levels is one of the most common benefits reported by individuals who engage in activities such as exercise and yoga (Michalsen et al.,

2005; Vadiraja et al., 2009). Therefore, in addition to alterations in the physiological components of the stress response, understanding how exercise and yoga affect one's self-reported perception of, or attitudes about, stress and daily hassles may also be important in the context of their antidepressant effects. The beneficial impact of yoga on levels of perceived stress has been consistently demonstrated in various samples and using different styles of yoga (e.g., Chattha, Raghuram, Venkatram, & Hongasandra, 2008; Chong, Tasunaka, Tsang, Chan, & Cheung, 2011; Gard et al., 2012; Granath et al., 2006; Hewett et al., 2018; Rizzolo, Zipp, Stiskal, & Simpkins, 2009; West et al., 2004). For instance, in a recent study by Hewett et al. (2018), 63 physically inactive adults with high baseline levels of stress were randomized to 16 weeks of Bikram yoga, practiced 3-5 times weekly, or a waitlist control group. Significant improvements in self-reported stress levels were observed in the yoga group relative to the control group. Moreover, higher attendance was associated with a larger reduction in perceived stress. In a sample of 24 women with high levels of emotional distress, Michalsen et al. (2005) examined the effects of 3 months of Iyengar yoga, practiced twice weekly, on perceived stress and associated psychological outcomes. The authors found significantly greater reductions in perceived stress in the yoga group, compared to a waitlist control group, as well as significant improvements in state and trait anxiety, overall well-being, vigor, fatigue, and depression symptoms.

Several studies have also compared the influence of yoga versus exercise on levels of perceived stress. West et al. (2004) compared the effects of a single 90-min Hatha yoga class to a single 90-min African dance class and a non-exercise control group (college lecture). Both the yoga and exercise class yielded significant improvements in self-reported stress levels and negative affect from pre- to post-class, with no significant change in the control group. These results are interesting as they suggest that even a single yoga or exercise class has a positive

impact on perceived stress levels. Longer-term trials of yoga and exercise have also been compared. For instance, in a sample of 120 menopausal women, the effects of 8 weeks of Hatha yoga were compared to 8 weeks of low intensity exercise (Chattham et al., 2008). Participation in either activity occurred for 1 hour daily, 5 days per week, in addition to lectures and individual counselling on concepts relating to healthy living, the physiology of menopause, and stress management techniques. Consistent with hypotheses, the authors found significantly greater decreases in perceived stress and neuroticism scores over the course of the 8 weeks in the yoga group compared to the exercise group. In a sample of 36 healthy men from the Brazilian army, Rocha et al. (2012) investigated the effects of 6 months of combined Iyengar yoga plus exercise (two sessions of each per week) to exercise alone (four sessions per week) on various psychophysiological and memory parameters related to stress. Relative to the exercise-only group, participants in the combined group experienced significantly greater improvements in symptoms of stress, depression, and anxiety, as well as decreases in salivary cortisol levels and improvements in memory performance. The authors concluded that these effects were not merely due to a physical practice, since all participants engaged in two sessions of exercise per week.

Although it appears that a yoga practice may result in greater benefit in terms of perceived stress, there is consistent evidence indicating that exercise also has a significant impact. Cross-sectional studies have found negative relations between levels of exercise and perceived stress, particularly when more strenuous types of exercise are engaged in (Aldana, Sutton, Jacobson, & Quirk, 1996; Ng & Jeffery, 2003; Nguyen-Michel, Unger, Hamilton, & Spruijt-Metz, 2006; Skirka, 2000). For example, Nguyen-Michel et al. (2006) examined the relation of self-reported exercise to perceived stress and the severity of commonly encountered hassles in an ethnically diverse sample of 814 college students. A significant negative relationship was found between

exercise and hassles, with a trend-level association emerging between exercise and perceived stress. Various trials of exercise have also provided support for the link between exercise and changes in one's perception of stress levels (Askari, Saberi-Kakhki, Taheri, & Yassini, 2017; Cramer, Nieman, & Lee, 1991; Oaten & Cheng, 2006). Cramer et al. (1991) randomized 35 physically inactive women to either a 15-week moderate exercise training group (5 days/week, 45 min/session) or a control group. Participants in the exercise group, but not the control group, experienced a significant reduction in the frequency of daily hassles over the course of the trial. That is, the occurrence of daily events in one's environment that were considered by that individual to be stressful were rated as less frequent. In a sample of 24 physically inactive university students, Oaten and Cheng (2006) investigated whether the practice of self-regulation could lead to improvements in regulatory strength and other psychological variables, including perceived stress. The self-regulation activity used was a 2-month exercise program. The authors found that compared to a control period, participants reported significant decreases in perceived stress at post-intervention, as well as improvements in emotional distress, healthful behaviours, and regulatory strength, measured via a visual tracking task. Finally, in a sample of 45 women with MDD, the effects of a low/moderate intensity exercise program (60 min/session, 3 sessions/week) on categories of depression symptoms (i.e., affective, cognitive, somatic) were examined, along with the potential mediating role of perceived stress (Askari et al., 2017). Participants in the study were assigned, albeit not randomly, to one of three groups: exercise plus usual pharmacotherapy (TAU), psychotherapy (i.e., behavioural activation) plus TAU, or TAU only. In addition to significant post-treatment improvements in all three categories of depression symptoms, both combination groups resulted in significant decreases in perceived stress compared to the TAU-only condition. No differences between the combination groups were

observed, suggesting that adjunctive exercise was as effective as adjunctive psychotherapy in terms of the outcome variables. Unfortunately, the authors failed to properly test a mediation model; therefore, the role of perceived stress in the observed antidepressant effects of exercise remains unexamined.

***Rumination.*** As previously described, a tendency to ruminate conveys a strong risk for the onset and maintenance of depression (Aldao et al., 2010; Just & Alloy, 1997; Nolen-Hoeksema et al., 1993). This maladaptive tendency is, therefore, likely an important target or mechanism of change in the alleviation of depression. In contrast, the use of distraction as a response style has been associated with improvements in depression among individuals with MDD (e.g., Joormann, Siemer, & Gotlib, 2007). Effective types of distraction are believed to include activities that are engaging and likely to result in positive reinforcement (Nolen-Hoeksema, 1991). By their very nature, exercise and yoga appear to be activities that potentially fit these criteria, making them worthy of investigation. Despite this possibility, there exists only a small body of preliminary research that has looked at the impact of exercise and yoga on rumination. In the exercise literature, Puterman et al. (2011) examined whether a physically-active lifestyle moderated the association between rumination in response to a laboratory stressor (i.e., TSST) and cortisol reactivity/recovery to the stressor. Participants were 46 women, classified as “active” or “sedentary” based on self-reported exercise on three consecutive days. The authors found that higher levels of stressor-induced rumination were associated with a more rapid initial increase in cortisol, a later peak in reactivity, and a delayed recovery, but only among sedentary individuals. Among active participants, cortisol trajectories did not differ across levels of rumination, suggesting that a physically-active lifestyle may buffer against the effects of rumination on HPA axis response to stress. In a within-subject design,

Bernstein and McNally (2017) compared the effects of three different 25-min interventions (i.e., resting, stretching, aerobic exercise) on emotional reactions to a psychological stressor. The stressor involved a combination of time-limited verbal puzzles and mental arithmetic. It was found that higher levels of rumination following the stressor were associated with more persistent negative affect. This association, however, was attenuated when exercise preceded the stressor, suggesting that acute exercise may facilitate subjective emotional recovery from stress. Finally, using a quasi-experimental design involving a trial of exercise, Craft (2005) examined the role of psychological mechanisms, including changes in rumination, underlying the antidepressant effects of aerobic exercise. Nineteen women with MDD self-selected into either a 9-week moderate intensity exercise program (2-4 times weekly) or a control group. A significant reduction in depression severity was observed at week 9 for participants in the exercise group but not for those in the control group. Further, exercise was associated with a decrease in rumination throughout the course of the study, although this effect was also observed, albeit to a lesser degree, in the control group. Contrary to expectations, there was no significant association between depression symptoms and rumination.

Comparatively few studies have been conducted with respect to yoga's impact on rumination. In a small pilot study of the acceptability and feasibility of 8 weeks of Vinyasa yoga as an adjunct treatment for depression, Uebelacker, Tremont, et al. (2010) examined pre- to post-intervention changes in rumination, mindfulness, and behavioural activation as potential mechanisms of action. Participants were 10 adult men and women with elevated symptoms of depression who had been using antidepressant medication without adequate response for a minimum of 2 months. Although rumination scores decreased as predicted, the degree of change was not significant, perhaps owing to the small sample size. Kinser and colleagues published an

interesting series of quantitative and qualitative studies that help shed light on the link between yoga and ruminative thoughts (Kinser, Bourguignon, Taylor, & Steeves, 2013; Kinser, Bourguignon, Whaley, Hauenstein, & Taylor, 2013; Kinser, Elswick, & Kornstein, 2014). Twenty-seven women with MDD took part in a larger parent study and were randomly assigned to 8 weeks of either Hatha yoga or health education (Kinser, Bourguignon, Whaley, et al., 2013). Several mechanisms of action were examined across these studies, one of which was changes in rumination. In their qualitative study (Kinser, Bourguignon, Taylor, et al., 2013), semi-structured interviews and daily logs were used to understand the experiences of women who participated in the yoga intervention. When describing their experiences of depression, a common theme that emerged across participants was the presence of persistent negative thoughts or rumination. When asked how they perceived yoga to help with depression symptoms over the course of the intervention, most participants described yoga as a self-care strategy that was helpful for interrupting negative thinking patterns. These findings lend support the authors' suggestion that levels of ruminative thinking be included as an outcome measure in all intervention studies for depression (Kinser, Bourguignon, Whaley, et al., 2013). In terms of quantitative analyses, the authors found that despite no significant pre- to post-treatment difference in depression improvement across the two groups, there was a trend for decreased rumination among the yoga group only (Kinser, Bourguignon, Whaley, et al., 2013). At a 1-year follow-up, those in the yoga group demonstrated sustained and significant improvements in depression symptoms and rumination relative to baseline (Kinser et al., 2014). Interestingly, these sustained benefits were evident regardless of whether an individual continued to practice yoga following the initial intervention period.

Finally, Schuver and Lewis (2016) examined the effects of a mindfulness-based yoga intervention on depression symptoms and rumination in a sample of 40 women with MDD. Participants were randomized to 12 weeks of the yoga intervention or a walking control group. Those in the yoga intervention were asked to follow a home-based yoga DVD that had been commercially developed for the management of depression and anxiety symptoms (Weintraub & Duncan, 2007) two times per week. In addition to following the DVD, they participated in mindfulness education sessions delivered over the phone. Participants in the control condition followed a home-based walking DVD twice per week and received health education sessions conducted over the phone. Significant reductions in depression symptoms emerged in both groups, with no difference between the conditions. In terms of rumination, however, individuals in the yoga group experienced significantly greater reductions than those in the control group. A test of mediation was not conducted.

Investigations into the effects of prolonged exercise and yoga on rumination are limited and characterized by various methodological issues. Nevertheless, the role of rumination in the antidepressant effects of these CAMs is deserving of further attention in more rigorously designed studies. The abovementioned studies have provided preliminary, but general, support for the premise that exercise and yoga help to reduce ruminative thinking, which is important given the strong link between rumination and depression. As well, rumination's association with mindfulness, another construct of interest that may help account for the antidepressant effects of exercise and yoga, provides additional rationale to further investigate this area. That is, there appears to be a negative association between rumination and mindfulness (e.g., Campbell, Labelle, Bacon, Faris, & Carlson, 2012; Jain et al., 2007; Lykins & Baer, 2009). For example,

Jain et al. (2007) found that a decrease in distress following mindfulness meditation training was partially mediated by the training's effects on reducing rumination.

***Mindfulness.*** Mindfulness is defined as “the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment” (Kabat-Zinn, 2003, p. 145). Although this construct is rooted in ancient Buddhist practices, it has become widely popularized in Western society and contemporary psychotherapy through the pioneering work of Jon Kabat-Zinn and his followers (Kabat-Zinn, 2003). In general, a consistent mindfulness practice is believed to help buffer against the effects of stress, as nonjudgmental present-moment focus helps free the mind from excessive orientation toward the past or future when dealing with stressors (Kabat-Zinn, 2003). Various forms of mindfulness-based interventions have been developed, including Kabat-Zinn's original mindfulness-based stress reduction program (MBSR; Kabat-Zinn, 1982) and more recent innovations such as mindfulness-based cognitive therapy (MBCT; Segal, Williams, & Teasdale, 2002), acceptance and commitment therapy (Hayes, Strosahl, & Wilson, 1999), and dialectical behavior therapy (Linehan, 1993). These interventions have been applied across a variety of conditions (e.g., depression, anxiety, eating disorders, borderline personality disorder, substance use problems, psychosis) and settings (e.g., hospitals, prisons, schools, veterans' centers), highlighting the wide applicability of mindfulness.

In terms of depression more specifically, MBCT was originally developed to help decrease the risk of relapse and recurrence among individuals with MDD (Segal et al., 2002; Teasdale et al., 2000). MBCT combines elements of the MBSR program (e.g., mindfulness meditation) with aspects of CBT for depression and theorizes that when individuals with a history of depression become distressed, they return to automatic cognitive processes that can trigger

another depressive episode (Teasdale et al., 2000). The goal of MBCT is to, therefore, interrupt these automatic processes by teaching individuals to become more aware of thoughts and feelings and to relate to them from a different, more compassionate, perspective (Jain et al., 2007; Teasdale et al., 2000). Meta-analytic results have consistently demonstrated that MBCT is an effective intervention for relapse prevention in MDD, particularly among individuals with three or more previous depressive episodes and/or more pronounced residual symptoms (e.g., Chiesa & Serretti, 2011; Kuyken et al., 2016; Piet & Hougaard, 2011), with some support for its use in targeting acute symptoms (e.g., Hofmann, Sawyer, Witt, & Oh, 2010; Kenny & Williams, 2007; Kingston, Dooley, Bates, Lawlor, & Malone, 2007).

Some researchers have posed the question of whether mindfulness can be fostered via methods that do not fall under the psychotherapy techniques noted above (Asztalos et al., 2012; Carmody & Baer, 2008). This line of inquiry may be particularly relevant for depressed individuals who could benefit from improved mindfulness but are not good candidates for a more formal practice because of barriers such as intense negative thinking and concentration difficulties (Uebelacker, Epstein-Lubow, et al., 2010). Given that mindfulness is a key element to most styles of yoga, it seems intuitive that it could be developed through a consistent yoga practice. Focus during yoga is oriented to the present moment and typically directed toward the breath, purposeful movement, and physical sensations that arise. Therefore, it may be possible to learn mindfulness through yoga, even if various barriers that may hinder a formal mindfulness practice are present (Uebelacker, Epstein-Lubow, et al., 2010). Presumably this skill would then generalize beyond yoga, helping to reduce negative or ruminative thoughts and increase focus on the present moment.

Empirical findings have provided consistent support for the hypothesis that yoga enhances mindfulness. In a cross-sectional study, Brisbon and Lowery (2009) found significantly higher levels of mindfulness, as well as lower levels of stress, among advanced yoga practitioners compared to beginners. Similar findings were produced by Satin, Linden, and Millman (2014), who demonstrated that relative to experienced runners and inactive individuals, yoga practitioners reported higher levels of mindfulness at a trend level. In addition to scoring higher on mindfulness scales than comparison groups, yoga practitioners may also hold beliefs about their practice being associated with enhanced mindfulness. For instance, a survey of yoga practitioners found that 89.7% of students and 96.7% of instructors reported that their perceived mindfulness had improved as a result of their yoga practice (Park, Riley, & Braun, 2016). In terms of the prospective relation between yoga and mindfulness, an uncontrolled study with 51 healthy adults demonstrated that 8 weeks of Bikram yoga resulted in significant increases in mindfulness levels, as well as adaptive changes in other psychological and physical outcomes (Hewett, Ransdell, Gao, Petlichkoff, & Lucas, 2011). Consistent findings have been found in trials using other styles of Hatha yoga, such as Iyengar yoga and Kripula yoga (Bowden, Gaudry, An, & Gruzelier, 2012; Curtis, Osadchuk, & Katz, 2011; Gard et al., 2012).

Three studies have now been published looking at the impact of yoga on mindfulness in the context of elevated depression symptoms (Battle, Uebelacker, Magee, Sutton, & Miller, 2015; Falsafi, 2016; Uebelacker, Tremont, et al., 2010). All three studies found significant improvements in depression and mindfulness from pre- to post-intervention; however, despite two of the studies proposing a mediating role of mindfulness in the antidepressant effects of yoga (Battle et al., 2015; Uebelacker, Tremont, et al., 2010), none of the studies tested such a model. Interestingly, the Falsafi (2016) study compared Hatha yoga to a mindfulness intervention that

was formal in nature and progressed from simple exercises (e.g., guided meditation on the breath) to more complex mindfulness practices (e.g., forgiveness meditation). The yoga intervention, on the other hand, placed a strong emphasis on physical postures but did not explicitly emphasize mindfulness. Falsafi (2016) found that both interventions resulted in significantly greater reductions in depression and increases in mindfulness compared to a waitlist control group, but did not differ from each other. These results are exciting because they suggest that a more physical intervention, such as the style of Hatha yoga used, may lead to improvements in mindfulness that are similar to those achieved through a more formal mindfulness practice.

There have also been suggestions that involvement in regular exercise has the potential to enhance mindfulness (Asztalos et al., 2012; de Bruin, van der Zwan, & Bogels, 2016; Demarzo et al., 2014; Mothes, Klaperski, Seelig, Schmidt, & Fuchs, 2014; Salmon, Hanneman, & Harwood, 2010). Several lines of reasoning to support this hypothesis have been noted. For instance, Kee and Wang (2008) suggested that involvement in exercise may increase mindfulness through the opportunities it fosters for moment-to-moment attention. This may be especially likely for exercises that contain predictive and repetitive breathing and movements, such as running, cycling, and swimming (Mothes et al., 2014). Consistent with this idea, Salmon et al. (2010) proposed that long-distance running promotes “sustained, essentially nonjudgmental attention that can be directed at will toward a wide range of internal and external experiential cues” (p. 150). Therefore, it has been suggested that the promotion of a mind-body connection or increased capacity to self-regulate attention, resulting from exercise, helps foster mindfulness (Kee & Wang, 2008; Salmon et al., 2010). de Bruin et al. (2016) expanded on this idea by proposing that present-moment attention on the body during exercise also precludes one’s ability to ruminate about the past or future. Despite these lines of reasoning, very little empirical attention has been

allocated to examining the effects of exercise on mindfulness. Cross-sectional studies have demonstrated positive associations between self-reported exercise levels and mindfulness (Loucks, Britton, Howe, Eaton, & Buka, 2015; Ulmer, Stetson, & Salmon, 2010). For example, using an accelerometer to provide an objective measure of physical activity across 7 days, Kangasniemi, Lappalainen, Kankaanpää, and Tammelin (2014) found significantly higher levels of mindfulness among physically active individuals compared to those who were less active. As well, the authors found a significant positive relationship between minutes engaged in moderate-to-vigorous intensity exercise and mindfulness scores. Interestingly, results from these cross-sectional studies have generally been interpreted as supporting the hypothesis that higher mindfulness leads to healthier behaviours (i.e., initiation and maintenance of regular exercise; Mothes et al., 2014).

Mothes et al. (2014) conducted the first RCT of its kind to investigate the effects of regular exercise on mindfulness in a sample of 149 physically inactive men. Participants were randomized to one of three 12-week groups: exercise training, relaxation training, or waitlist. Exercise involved a heart rate-controlled running group (i.e., 60-80% of maximal heart rate), and relaxation training was a group-based program that consisted mainly of progressive muscle relaxation and autogenic training. Group sessions occurred twice weekly, for 60 min per session. As hypothesized, the authors found a significant increase in mindfulness scores over the course of the study in the exercise group but not in the relaxation training or waitlist groups. Further, there was a significant positive correlation between changes in mindfulness and changes in self-reported emotional functioning. A subsequent RCT by de Bruin et al. (2016) compared the effects of aerobic exercise, mindfulness training, and HRV-biofeedback on various cognitive processes in a sample of 126 adults with elevated stress levels. Each condition was practiced

daily for 5 weeks. It was hypothesized that individuals in the mindfulness group would demonstrate the greatest improvements on measures of attention control, executive functioning, self-compassion, worrying, and mindful awareness, given that these cognitive processes are targeted in mindfulness training. Contrary to expectations, all three interventions resulted in significant improvements on all cognitive measures and, importantly, did not differ from each other. Similar to the Falsafi (2016) study that compared Hatha yoga to mindfulness training, these results suggest that exercise can enhance mindfulness in a way that is equivalent to that achieved through a formal mindfulness practice.

## Chapter 3

### Objectives and Hypotheses of the Current Investigation

This study was conducted with a sample of adult women who were experiencing symptoms indicative of a clinical depressive disorder (i.e., MDD, Dysthymia, adjustment disorder with depressed mood, depressive disorder not otherwise specified). They were recruited from a university (i.e., students, staff) and larger surrounding community and took part in two pre-treatment assessment sessions, followed by a post-treatment session approximately 8 weeks later. During the first pre-treatment appointment (i.e., psychological assessment), women participated in a diagnostic clinical interview to assess their mood and overall mental health history. They were also asked to complete self-report measures of depression symptoms, perceived hassles, rumination, and mindfulness. At the second pre-treatment appointment (i.e., physiological assessment), they took part in numerous physiological measurements relating to cardiovascular functioning and stress reactivity. This was followed by an exercise test to determine fitness level or aerobic capacity. There has been some debate regarding whether an antidepressant response following physical activity is dependent on improvements in physical fitness (Rimer et al., 2012).

At the end of the second pre-treatment appointment, women were randomly assigned to one of three 8-week conditions: Bikram yoga, aerobic exercise, or a waitlist group. An 8-week duration was chosen to accommodate the short academic semesters of university students who made up a portion of the sample. Women in the active treatment conditions (i.e., Bikram yoga and aerobic exercise) were asked to attend two classes per week for 8 weeks. These classes were offered in already-established group settings in the community. Women in the yoga group attended classes at a local Bikram yoga studio and those in the exercise group attended classes at

a local YMCA facility. During the 8-week period, participants in all three conditions were asked to complete an online battery of questionnaires on a weekly basis. At the final post-treatment appointment (i.e., combined psychological and physiological assessments), participants were asked to take part in an abbreviated clinical interview to assess depression symptoms and they repeated all physiological measurements, including the exercise test.

### **Goal 1: Antidepressant Effects of Bikram Yoga**

The first main goal of this study was to examine the antidepressant effects of yoga in a study design that addressed important methodological issues that have been criticisms of previous investigations. The first major improvement made in this study was its selection of yoga type. Bikram yoga was chosen specifically because of its standardization. That is, it was not believed to be superior to other styles of yoga in alleviating depression symptoms. In addition to evaluating whether Bikram yoga effectively reduces clinical depression, the randomized controlled design of this study allowed for comparisons to two important treatment conditions, a waitlist group and aerobic exercise. The waitlist comparison was critical since this was the first investigation using Bikram yoga for the treatment of depression (Kinser & Robins, 2013). This comparison would help to determine if Bikram yoga is superior to no treatment. As well, the use of a waitlist group would help control for various factors, including the passage of time, repeated measurements, and participant expectations. It was also important to compare Bikram yoga to another treatment modality that has received support for its antidepressant effects and would be similar in terms of nonspecific aspects of the intervention (e.g., environment, frequency and duration, social support, attention from facilitators or instructors, etc.; Kinser & Robins, 2013). Therefore, for the purposes of this study, aerobic exercise was chosen as an appropriate comparison group. In addition to the careful selection of treatment conditions, this study also

improved upon previous investigations, and presumably decreased risk of bias, by using standardized instruments to diagnose depression and assess pre- to post-treatment changes, proper randomization procedures, blinding of outcome assessors, an intention-to-treat analysis, and sufficient treatment lengths.

In terms of hypotheses relating to the first goal, I predicted a treatment group (i.e., yoga vs. exercise vs. waitlist) by time (i.e., pre- vs. post-treatment) interaction, such that those in the active treatment conditions would experience significant improvements in depression symptoms from pre- to post-treatment, whereas those in the waitlist group would not. Several commonly used treatment outcome variables were examined in this study. First, I examined the change in depressive symptoms from pre- to post-treatment, based on HAM-D scores. Second, I looked at treatment outcome dichotomously via treatment *response*, defined as a 50% reduction from baseline total scores on the HAM-D (Prien, Carpenter, & Kupfer, 1991; Depression Guideline Panel, 1993), and by the more stringent measure of *remission*, defined as no longer meeting diagnostic criteria for a depressive disorder according to the Structured Clinical Interview for DSM-IV Axis I Disorders (First, Spitzer, Gibbon, & Williams, 2002) and a HAM-D score of 7 or lower (Frank et al., 1991). Given that psychological outcome studies using Bikram yoga are lacking, the predicted superiority of Bikram yoga over the waitlist group was based on findings from relevant RCTs with various styles of yoga (Cramer et al., 2013; Pilkington et al., 2005). That is, an assumption was made that Bikram yoga would lead to similar antidepressant effects as other styles of yoga and, therefore, result in greater improvements in depression symptoms compared to no treatment. In terms of the anticipated effects of Bikram yoga versus aerobic exercise, there was limited empirical evidence to base predictions on. Veale et al. (1992) demonstrated that group-based aerobic exercise resulted in comparable antidepressant effects to

an undefined yoga program. Shahidi et al. (2011) found no significant difference between the effects of a jogging/stretching intervention and “Laughter Yoga” (i.e., unconditional laughter with yogic breathing) on depression symptoms. In a study by Schuver and Lewis (2016), although there was a significant group difference in post-treatment levels of rumination, mindfulness-based yoga led to similar improvements in mood compared to a walking intervention. In light of these previous findings, there was not enough evidence to make a specific prediction about the superiority of Bikram yoga’s antidepressant effects over aerobic exercise, or vice versa. Therefore, this study simply sought to examine how these conditions compare in terms of alleviating depression symptoms in an exploratory fashion.

## **Goal 2: Potential Mediating Factors Underlying the Antidepressant Effects of Aerobic Exercise and Bikram Yoga**

The second main goal of this study was to examine potential underlying mechanisms of action by which exercise and yoga alleviate depressive symptoms. Given associations between depression, stress, and various stress-related processes, I focused on variables that have been shown to be affected by exercise and yoga and may play a role in one’s depressogenic response to stress. Despite some evidence demonstrating the impact of exercise and yoga on these potential mediating variables, most of the studies conducted to date have not considered these effects in the context of elevated depression symptoms. Furthermore, of the studies that have considered depression symptoms, none have tested mediation models. Therefore, the goal of this study was to examine group differences in pre- to post-treatment changes in these variables, as well as the mediating role of changes in the variables in the proposed antidepressant effects.

**Physiological Mediators.** Physiological variables examined in this study included changes in heart rate, blood pressure, and cortisol response to the TSST (Kirschbaum et al.,

1993). Examining these variables would presumably provide insight into exercise- and yoga-induced changes to both SNS and HPA axis reactivity to stress. As previously noted, the TSST is a commonly used psychological challenge paradigm. More specifically, it involves mentally preparing and delivering a short speech in front of a panel of researchers, followed by a mental arithmetic task. Heart rate and blood pressure measurements were taken continuously throughout the TSST, beginning approximately 20 min before it commenced and continuing until approximately 60 min following its completion. During this period, saliva samples were taken at eight time points. Reactivity variables were derived for all three physiological variables. Additional details about the timing and derivation of these measurements are provided in the Method section.

In terms of SNS reactivity to the TSST, I predicted a treatment group by time interaction, such that those in the active treatment groups would show significant reductions in both heart rate reactivity and blood pressure reactivity from pre- to post-treatment. I did not anticipate any changes in SNS reactivity in the waitlist group. This prediction was based on previously reviewed research findings, which demonstrated elevated SNS reactivity among depressed individuals (Heim et al., 2000; Lake et al., 1982; Veith et al., 1994), as well as general dampening effects of prolonged exercise and yoga on SNS activity (Forcier et al., 2006; Spalding et al., 2004; Telles & Naveen, 2004; Telles et al., 2004). Although the evidence for yoga-associated reductions in SNS reactivity is currently somewhat limited, it appears that it outweighs findings suggesting otherwise. Finally, I also expected that pre- to post-treatment reductions in the SNS reactivity variables would mediate the antidepressant effects of exercise and yoga, such that these changes would help account for improvements in depression symptom severity.

In terms of generating hypotheses relating to changes in cortisol reactivity to the TSST, it

was important to keep in mind the following research findings: depressed individuals, particularly those who are older and have more severe symptoms, show blunted cortisol reactivity in response to psychological challenge tests (Burke et al. 2005; Zorn et al., 2017); exercise has been found to decrease cortisol reactivity to such tests (Klaperski et al., 2014; Rimmele et al., 2007); and yoga's impact on cortisol reactivity remains inconclusive (Granath et al., 2006; Hopkins et al., 2016; Sarubin et al., 2014). Further complicating the ability to generate firm hypotheses was the possibility that the sample of community-based participants in the current study varied with respect to depression severity and degree of HPA axis dysregulation. Although it was anticipated that exercise and yoga would have some regulatory effects on cortisol reactivity, group differences were examined in an exploratory way. Nevertheless, I did not expect a significant change in cortisol reactivity among participants in the waitlist group. The mediating role of changes in cortisol reactivity in the antidepressant effects of exercise and yoga was also investigated without specific predictions.

**Psychological Mediators.** Psychological variables examined in this study included changes in perceived hassles, rumination, and mindfulness. These variables were assessed at pre-treatment and weekly or biweekly thereafter, via an online link. Attitudes about hassles was considered a subjective measurement of stress. Participants were asked to give weekly ratings of how much various situations or events were considered hassles or irritants. Despite some evidence demonstrating a greater effect of yoga on perceived stress relative to exercise (Chattha et al., 2008; Rocha et al., 2012), both CAMs have been consistently linked to reductions in perceived stress and/or severity of hassles (e.g., Askari et al., 2017; Cramer et al., 1991; Hewett et al., 2018; Michalsen et al., 2005). Therefore, I predicted a treatment group by time interaction, such that both active treatment groups would be associated with significant reductions in

perceived hassle ratings from pre- to post-treatment, whereas the waitlist group would not. Further, I hypothesized that these changes would mediate improvements in depression symptom severity.

Rumination was assessed biweekly following the pre-treatment assessment. Given preliminary, but supportive, evidence demonstrating improvements in rumination following exercise and yoga (e.g., Craft, 2005; Kinser, Bourguignon, Whaley, et al., 2013; Schuver & Lewis, 2016), I predicted a treatment group by time interaction. That is, I hypothesized that there would be significant reductions in rumination scores from pre- to post-treatment in the active treatment groups but not in the waitlist group. Finally, I predicted that changes in rumination would mediate the antidepressant effects of exercise and yoga, such that these changes would predict improvements in depression symptom severity.

Similar hypotheses were made with respect to mindfulness, which was measured weekly. Specifically, I predicted a treatment group by time interaction, such that mindfulness would improve from pre- to post-treatment in the active treatment groups but not in the waitlist group. This prediction was based on consistent evidence of enhanced mindfulness following yoga (e.g., Battle et al., 2015; Falsafi, 2016; Gard et al., 2012), as well rationale and preliminary evidence linking exercise to increased mindfulness (de Bruin et al., 2016; Kee & Wang, 2008; Mothes et al., 2014). Similar to the other psychological variables, I expected that improvements in mindfulness would mediate the antidepressant effects of exercise and yoga

## Chapter 4

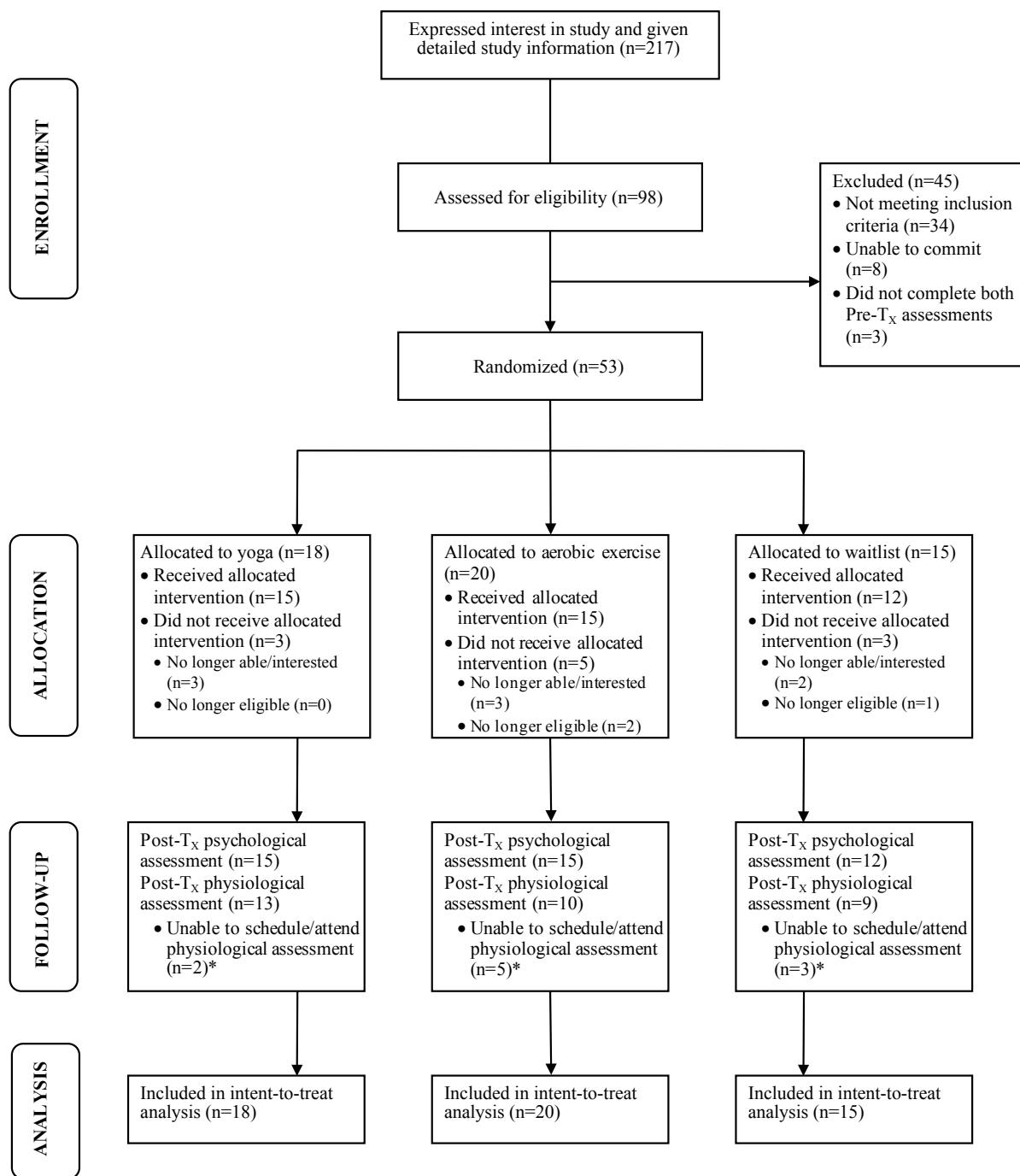
### Method

#### Participants

Participants were recruited from Queen's University and the larger Kingston community, via flyers, social media, and word of mouth. A CONSORT diagram (Consolidated Standards of Reporting Trials; Moher et al., 2012) depicting participant flow throughout the study is presented in Figure 1. A total of 217 women expressed interest in the study and were provided with detailed information about the main objectives and procedures, and 98 women went on to participate in a telephone screening interview. Of these, 56 women participated in the pre-treatment psychological assessment. Fifty-three women, ranging in age from 18 to 60 ( $M = 33.08$ ;  $SD = 14.71$ ), returned for the pre-treatment physiological assessment (held 1-7 days later) and were randomly assigned to one of three 8-week treatment groups: Bikram yoga ( $n = 18$ ), aerobic exercise ( $n = 20$ ), or waitlist control ( $n = 15$ ). Forty-two women completed the post-treatment psychological assessment; however, ten of these individuals were unable to attend an in-person appointment. For these women, the psychological assessment was conducted over the phone and physiological data were not collected.

To be eligible for inclusion in the study, participants had to meet DSM-IV-TR (American Psychiatric Association, 2000) criteria for a current episode of a non-chronic, unipolar depressive disorder (i.e., MDD, adjustment disorder with depressed mood, depressive disorder not otherwise specified). Exclusion criteria included the presence of a psychotic disorder, bipolar disorder, substance dependence, current suicidality beyond simple ideation, a medical condition that could be the cause of depression, a pre-existing physical condition that could interfere with participation in physical activity (e.g., cardiovascular disease, untreated hypertension, etc.), and a

change in the type or dose of antidepressant medication or change in frequency of sessions of psychotherapy/counseling in the previous 3 months. Women who were pregnant or actively trying to get pregnant were also excluded, as were those participating regularly in yoga or group exercise classes (i.e., on a biweekly or more basis) during the 3-month period prior to study onset or on a long-term basis in the past 2 years. It was necessary that participants had a schedule that allowed for attendance in two yoga or exercise classes per week. Those who were currently exercising in a non-group format were asked to maintain their original level of physical activity throughout the duration of the study, in addition to yoga or exercise classes according to group assignment. Inclusion and exclusion criteria were assessed during a telephone screening interview and during pre-treatment assessments.



**Fig. 1.** CONSORT diagram representing participant flow through the phases of the study.  
 \* Participants unable to schedule/attend the post-treatment physiological assessment were administered the psychological assessment over the phone.

## Measures: Interviews and Questionnaires

**Telephone Screen Interview.** A semi-structured telephone screen interview was conducted prior to the pre-treatment assessments (see Appendix B). It was used to provide detailed information about the study procedures to interested individuals and to collect enough information to assess most inclusion and exclusion criteria to a high degree of certainty. As part of the screening interview, items from the Physical Activity Readiness Questionnaire (Thomas, Reading, & Shephard, 1992; see below) were administered verbally. Questions regarding various medical diagnoses (e.g., cardiovascular, metabolic, or pulmonary disease) and risk factors for cardiovascular disease were also asked. Risk factors included age  $\geq 55$ , family history of cardiovascular disease, history of cigarette smoking, sedentary lifestyle, obesity, hypertension, and dyslipidemia (American College of Sports Medicine, 2013). Individuals who were otherwise deemed eligible for the study but reported physical health information that increased their risk of participation (i.e., “moderate” or “high” cardiovascular risk) were informed that medical clearance (see “Physician Clearance Form” below and Appendix C) was required from their family physician prior to further consideration for the study. Moderate cardiovascular risk indicated an individual who was asymptomatic and had not been diagnosed with any cardiovascular, metabolic, or pulmonary disease but reported two or more risk factors for cardiovascular disease. High cardiovascular risk was applied to an individual who was symptomatic or had been previously diagnosed with cardiovascular, metabolic, or pulmonary disease. For high risk individuals who successfully received medical clearance from their family physician, a final requirement for eligibility was approval by Dr. Kyra Pyke.<sup>2</sup>

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<sup>2</sup> Although two individuals were deemed high cardiovascular risk and reported that they would seek medical clearance from their family physician, these individuals did not follow-up with research personnel. Therefore, no participants were of high cardiovascular risk.

**Physician Clearance Form.** For individuals who reported symptoms or diagnoses of cardiovascular, metabolic, or pulmonary disease, or two or more risk factors associated with cardiovascular disease, a physician clearance form was required (see Appendix C). This form was also required for individuals who did not disclose such information but whose laboratory findings from the pre-treatment physiological assessment indicated cardiovascular risk factors. The Physician Clearance Form described the nature of the study, including details regarding the treatment groups and exercise test, and outlined why the individual was deemed to be of moderate or high cardiovascular risk. For individuals who required this form, it was completed and emailed to them. They were asked to take it to their family physician for review. Instructions on the form asked the physician to consider his or her knowledge of a patient's current and past physical health and to indicate whether that individual was a good candidate for the study. Family physicians were instructed to fax the completed form back to the investigators.

**Demographic.** A structured interview was administered to collect basic demographic information, including age, ethnicity, educational attainment, relationship status, current and past treatment history, current physical activity levels, and yoga an exercise class experience.<sup>3</sup>

**Physical Activity Readiness.** The Physical Activity Readiness Questionnaire (PAR-Q; Thomas et al., 1992) is a 7-item medical health questionnaire that was used to screen participants for pre-existing conditions that may interfere with participation (e.g., high blood pressure, heart condition, joint pain). The PAR-Q is recommended by the Canadian Society for Exercise

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<sup>3</sup> Each of the following demographic variables was dichotomized for subsequent analyses: ethnicity, educational attainment, and relationship status. For ethnicity, the two groups were White and Other (i.e., self-reporting as Asian, African American, Native American, Hispanic, Mixed Race, or Other). The educational attainment groups included those who had completed high school and/or some college or university versus those with a university degree (i.e., undergraduate or graduate). For relationship status, the two groups were unmarried (i.e., single, dating, common-law, divorced) or married.

Physiology as a medical clearance tool for moderate intensity physical activity. Participants whose responses suggested a relevant risk factor, symptom, or medical condition were either excluded from the study at that point or asked to seek medical clearance from a family physician prior to further consideration for the study

**Medical Screening Interview.** The Medical Screening Interview (MSI) is a 14-item semi-structured interview that was developed for the purposes of this study (see Appendix D), to further assess physical health and medical history. This interview included seven items adapted from the PAR-Q, in addition to items inquiring about symptoms, diagnoses, and medications relating to problems with the following: heart or blood vessels; nerves or brain; breathing or lungs; hormones, thyroid, or diabetes; muscles, joints, or bones; and other. Additional questions inquired about smoking habits.

**Diagnostic.** The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P; First et al., 2002) was administered to assess for current and past DSM-IV diagnoses. The SCID-I/P has demonstrated excellent reliability and validity (Williams et al., 1992). Senior undergraduate research assistants or I administered the Mood Module of the SCID-I/P during the telephone screen interview. During the in-person assessment appointments, I or another graduate student in Clinical Psychology administered the SCID-I/P. Dr. Kate Harkness trained each of us to “gold standard” reliability status and continued to provide ongoing supervision in its use. In order to achieve gold standard reliability status, we sat in on diagnostic interviews being conducted by gold standard interviewers, conducted these interviews while being observed by gold standard interviewers, and matched diagnoses on at least three consecutive interviews.

**Depression Symptoms.** The Beck Depression Inventory – II (BDI; Beck et al., 1996) and the Hamilton Rating Scale for Depression (HAM-D; Hamilton, 1960) were used to assess the

presence and severity of depression symptoms. The BDI is a 21-item self-report questionnaire in which participants responded on a scale from 0 to 3, with higher total scores indicating more severe depressive symptoms. The BDI has demonstrated excellent reliability and validity in studies of depression with adults (Dozois, Dobson, & Ahnberg, 1998; Segal, Coolidge, Cahill, & O'Riley, 2008). In the current study, the internal consistency was  $\alpha = 0.86$ .

The HAM-D is a 17-item semi-structured interview that assesses the severity of depressive symptoms in the past week. The item ratings range from 0 to 2 or from 0 to 4 based on severity, with a total score from 0 to 50. Higher scores indicate more severe depressive symptoms, with cut-off scores for severity as follows: 0-7 = normal/absence of symptoms; 8-16 = mild depression; 17-23 = moderate depression; >23 = severe depression (Zimmerman, Martinez, Young, Chelminski, & Dalrymple, 2013). The HAM-D has largely been regarded as the “gold standard” measure of depression severity (Demyttenaere & De Fruyt, 2003; Williams, 2001), with adequate psychometric properties (Bagby, Ryder, Schuller, & Marshall, 2004). I or another advanced graduate student in Clinical Psychology administered the HAM-D during pre- and post-treatment assessments.

**Hassles.** A revised version of the Hassles and Uplifts Scale (HUS; DeLongis, Coyne, Dakof, Folkman, & Lazarus, 1982; Kanner, Coyne, Schaefer, & Lazarus, 1981), which has been used in previous research (e.g., DeLongis, Folkman, & Lazarus, 1988), was used in this study. This scale examines commonly encountered events that may be considered irritants (i.e., hassles) and/or positive experiences (i.e., uplifts). More specifically, participants were asked to give weekly ratings of 53 events based on how much each event was a hassle and how much each event was an uplift in the previous week with the following scale: 0 = *None or not applicable*, 1 = *Somewhat*, 2 = *Quite a bit*, 3 = *A great deal*. The events fall into several domains, including

relationships (e.g., family-related obligations), work (e.g., job security), activities (e.g., recreation), the environment (e.g., the weather), finances (e.g., enough money for emergencies), practical considerations (e.g., housework), and health (e.g., medical care). Scores across items were summed to give separate cumulative scores for hassles and uplifts. For the purposes of this study, only hassles were examined in subsequent analyses. The internal consistency for the hassles subscale was  $\alpha = 0.94$ .

**Rumination.** The Ruminative Responses Scale (RRS) of the Response Styles Questionnaire (Nolen-Hoeksema & Morrow, 1991) was administered to assess the tendency to ruminate in response to depressive symptoms. The RRS has 22 items, rated on a 4-point scale ranging from 1 (*almost never*) to 4 (*almost always*) and asks respondents to indicate what they “generally do when feeling down, sad, or depressed”. In this study, instructions were modified slightly in that participants were asked to indicate their general tendencies within a specific time frame (i.e., during the past 2 weeks). Items on the RRS assess the tendency to focus on oneself (e.g., “I think, ‘Why do I react this way?’”), depressive symptoms (e.g., “I think about how hard it is to concentrate”), or possible causes and consequences of depression (e.g., “I think, ‘I won’t be able to do my job because I feel so badly’”). An overall score was computed by summing responses across all items. The RRS has been shown to have good validity for predicting depression (Just & Alloy, 1997; Spasojevic & Alloy, 2001) and demonstrated an internal consistency of  $\alpha = 0.89$  in the current study.

**Mindfulness.** The Philadelphia Mindfulness Scale (PHLMS; Cardaciotto, Herbert, Forman, Moitra, & Farrow, 2008) is a relatively new questionnaire that was designed to re-evaluate the multi-facetedness and inter-facet correlations of other questionnaires (e.g., Kentucky Inventory of Mindfulness Skills; Baer, Smith, & Allen, 2004; Five-Faceted

Mindfulness Questionnaire; Baer et al., 2007). The 20-item PHLMS was used to assess two components of mindfulness, present-moment awareness and acceptance, which have been highlighted in numerous definitions of mindfulness (Bishop et al., 2004; Cardaciotto et al., 2008). Awareness refers to the ongoing monitoring of internal and external experiences, with a focus on current experiences rather than on past or future events. Examples of items on this subscale include, “I am aware of what thoughts are passing through my mind,” and “When I am startled, I notice what is going on inside my body.” Acceptance refers to an attitude of nonjudgment, openness, and even compassion about one’s experience. Examples of items on this subscale include, “I try to distract myself when I feel unpleasant emotions,” and “There are things I try not to think about.” Participants responded to each item on a 5-point scale, ranging from 1 (*Never*) to 5 (*Very Often*). Scores across items were summed to give separate cumulative scores for awareness and acceptance. Prior to calculating the acceptance score, all acceptance-related items were reverse coded. The PHLMS has demonstrated good internal consistency in clinical and nonclinical samples (Baer, Walsh, & Lykins, 2009; Cardaciotto et al., 2008) and independence of subscales (Cardaciotto et al., 2008). In the current study, the internal consistency for the awareness subscale was  $\alpha = 0.77$  and for the acceptance subscale it was  $\alpha = 0.76$ .

**Treatment Participation.** The Treatment Participation Questionnaire (TPQ) is a 5-item questionnaire that was developed for the purposes of this study to track the use of applicable treatments within a specified time frame (see Appendix E). This questionnaire asked participants to report how many times they attended a Bikram yoga or aerobic exercise class in the past week, and to estimate the portion of time that they were *not* engaged in the class (i.e., sitting down, lying down, or standing still). More specifically, participants in the Bikram yoga group were asked to estimate the number of postures they did not attempt, and participants in the exercise

group were asked to estimate the portion of class (in minutes) that they did not participate.<sup>4</sup>

Participants were reminded that taking breaks in class, as needed, was completely acceptable. An open-ended question asked about the experience of any adverse events related to study participation. The use of antidepressant medication or psychotherapy/counseling during the past week was also assessed. Open-ended questions inquired about any changes to participants' pre-existing treatments (i.e., dose or type of antidepressant medication, frequency of psychotherapy/counseling sessions) in the past week.

### **Laboratory Procedures**

**Heart Rate and Blood Pressure.** Heart rate (HR) was assessed using three ECG electrodes on the chest and abdomen. Mean arterial pressure (MAP), defined as the average blood pressure during a single cardiac cycle, was assessed using an automated blood pressure device called a finger photoplethysmography (Finometer PRO, Finapres Medical Systems, Amsterdam, The Netherlands). Both variables were measured continuously for the entire duration of the physiological assessments and recorded in LabChart (AD Instruments, Colorado Springs, CO, USA) for subsequent analysis.

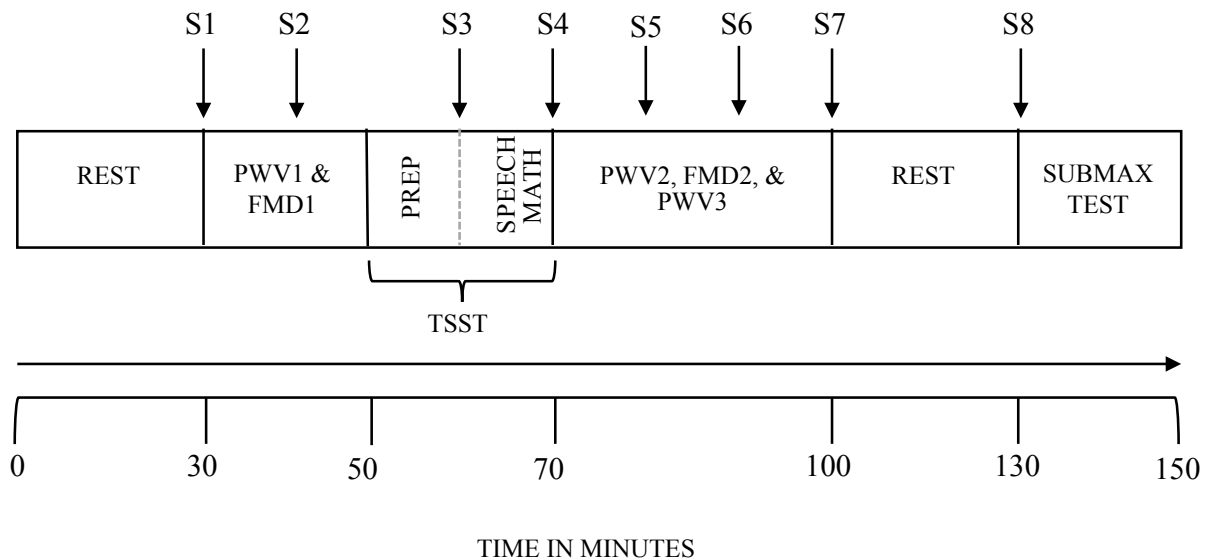
**Trier Social Stress Test (TSST).** Two variations of the TSST were used to prevent habituation over the two physiological assessments (i.e., pre-treatment and post-treatment). An unfamiliar panel of two research personnel read instructions to the participant. Participants were told that they had 10 min to prepare a 5-min speech. They were told that the speech would be videotaped and subsequently analyzed for nonverbal behavior. In one speech, participants were required to explain why they deserved a particular job opportunity after being recently fired. In

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<sup>4</sup> Due to problems with missing data from online questionnaires, adherence rates were calculated based on the number of classes that participants signed in for at the Bikram yoga studio or Kingston Family YMCA. Missing data, along with some apparent difficulties in understanding questions relating to the portion of time *not* engaged in a class, meant that a reliable variable of *engagement* in class could not be derived.

the other speech task, they were required to defend themselves against a false accusation of shoplifting. Participants were told to continue talking, to maintain eye contact, and to stay still for the entire 5 min by way of standard prompts. Immediately following the speech task, participants underwent a mental arithmetic task in which they were asked to serially subtract 13 from a 4-digit prime number. They were again told to maintain eye contact and to stay still for the duration of the arithmetic task. Periodically, participants were told that their answer was incorrect (even if correct) to increase the uncontrollability of the task as this has been shown to elicit greater cortisol responses (Dickerson & Kemeny, 2004) and to start again from the original 4-digit number.

**Saliva Sampling.** The procedure outlined by Kirschbaum et al. (1993) in defining the time points for saliva sampling during the TSST was followed but with the inclusion of two additional samples (Figure 2). Samples were taken between the hours of 1500 and 1700 h because this is a period of low cortisol relative to the morning (Groschl, Raug, & Dorr, 2003). Participants were asked to suck on a synthetic swab (Sarstedt Salivette; Poll et al., 2007) for approximately 2 min or until saturated. The saliva samples were then stored in the fridge until the data collection session was completed. At the end of each physiological assessment, samples were centrifuged at 4°C for 2.5 min at 2500 rpm and 1070 relative centrifugal force (IEC-Centra MP4R; International Equipment Company, MA, USA). Once the samples were spun, the swabs were removed and samples were stored in a -80°C freezer for subsequent analysis (Garde & Hansen, 2005). At the time of analyses, samples were thawed to room temperature, vortexed, centrifuged at 1500g for 15 min, and assayed in triplicate using enzyme-linked immunoassay (ELISA) according to the kit instructions (No. 1-3002; Salimetrics, State College, PA, USA).



**Fig. 2.** Depiction of the timed protocol followed for pre- and post-treatment physiological assessments. Saliva samples are represented by S1, S2, etc. PWV = pulse wave velocity task; FMD = flow-mediated dilation task; TSST = Trier Social Stress Test; Submax test = submaximal exercise test

**Submaximal Exercise Test.** The YMCA submaximal cycle ergometer test (Golding, Myers, & Sinning, 1989) was used to estimate maximal oxygen uptake ( $VO_{2max}$ ; also called maximal aerobic capacity), which is defined as the maximum rate of oxygen consumption attainable during maximal or exhaustive exercise (Wilmore & Costill, 2005).  $VO_{2max}$  is considered to be one of the best indicators of cardiovascular fitness level (McArdle et al., 2001; Wasserman, Hansen, Sue, Casaburi, & Whipp, 1999). It can be directly measured using a gas analyzer during a progressive and maximal exercise test. However, this requires a well-equipped laboratory with expensive instruments and highly trained personnel. Therefore, submaximal exercise test protocols that *predict*  $VO_{2max}$  have been developed. The YMCA test is widely-used submaximal protocol that predicts  $VO_{2max}$  by utilizing three (or more) consecutive 3-min stages

on a cycle ergometer (Golding et al., 1989). It is a graded test, which means that it involves a progressive increase in power output or workload (measured in watts [W]).

Prior to beginning the test, participants were asked to sit and relax on the cycle ergometer for several minutes to get a stable estimate of basal HR. A Sportline Elite Cardio 660 women's HR monitor watch with a coded chest strap was used to continuously monitor HR throughout the test. To help minimize unnecessary fluctuations in HR, participants were kept unaware of their HR and it was monitored by study investigators. Participants were also asked to keep relatively quiet throughout the exercise test, as speaking can artificially inflate HR. Once a stable basal HR had been achieved, the test was conducted according to the description in the *Y's Way to Physical Fitness* (Golding et al., 1989). Each participant began exercising on the cycle ergometer at 25W at a cadence of 50 rpm. At each stage, HR from the last 15 s of min 2 and 3 was recorded in 5-s increments. For instance, for min 2, HR was recorded for each of the following (min:s): 2:45, 2:50, 2:55. Values from the 5-s increments were averaged separately for min 2 and 3. If these averages differed by more than 5 bpm, an additional minute was added to that stage (Golding et al., 1989). This was continued until HR values for the last 2 min were within +/- 5 bpm. If the participant's HR did not plateau or the participant did not maintain cadence, the test was considered invalid.

The test was designed to have three stages: one 25W warm-up stage and two additional submaximal stages. Power output progression for the submaximal stages was based on the participant's HR response to the warm-up stage (if HR for last min in warm-up stage is < 80 bpm: 125W; 80-90 bpm: 100W; 90-100 bpm: 75W; and >100 bpm: 50W; Golding et al., 1989). The test assumes a well-known linear relationship between HR and  $\text{VO}_2\text{max}$ , which does not occur until HR is > 110 bpm. Therefore, the test was terminated once two stages were completed

with HR values between 110 and 150 bpm. For some individuals, this required a third submaximal stage to be added. Upon completion of the test, resistance on the cycle ergometer was reduced and participants were instructed to continue cycling at a slower pace until their HR was within 10 bpm of initial basal HR.

VO<sub>2</sub>max was estimated according to the *Y's Way to Physical Fitness* (Golding et al., 1989) from a participant's age-predicted maximal HR (APMHR = 220 – Age). That is, the YMCA test uses an extrapolation method in which recorded power output and HR points are extrapolated to APMHR. This method predicts the workload at the maximal HR, from which VO<sub>2</sub>max is then predicted. In this study, VO<sub>2</sub>max ranged from 15.48 to 43.41 ( $M = 29.06$ ,  $SD = 6.07$ ) at pre-treatment and from 16.78 to 41.01 ( $M = 29.80$ ,  $SD = 6.28$ ) at post-treatment, with higher scores indicating greater maximal aerobic capacity.

## **Study Procedure**

**Screening Procedure.** Individuals who inquired about the study (via telephone or email) first underwent a semi-structured telephone screen interview to assess inclusion and exclusion criteria. These interviews were conducted by senior undergraduate research assistants or me. Participants were informed of the purpose of the screening procedure and given a brief overview of the study and its procedures. They were then asked a series of questions to determine eligibility, including questions regarding physical health, cardiovascular risk factors, and depression symptoms. Pre-treatment assessments were booked over the phone for eligible individuals. If a Physician Clearance Form was required based on information disclosed during the telephone screen, an individual was informed about this. If interested in proceeding, she was emailed a copy of the completed form and asked to take it to her family physician for review.

Once the form had been received from the family physician, the individual received a follow-up call and pre-treatment assessments were booked if appropriate.

**Pre-Treatment Assessments.** Participants attended two pre-treatment assessment appointments. The first appointment was a 2-hr psychological assessment that took place in the Mood Research Lab of the Psychology Department. I facilitated this appointment. Each participant received a verbal description of the study, accompanied by a detailed Queen's University Health Sciences Research Ethics Board-approved consent form. Participants were told that they were participating in a study investigating the antidepressant effects of Bikram yoga and aerobic exercise, as well as potential mechanisms of action to help understand how these approaches may help with depression symptoms. They were informed that they would be randomly assigned to one of three 8-week conditions (i.e., Bikram yoga, aerobic exercise, or a waitlist control group). Expectations for class attendance for participants randomly assigned to the active treatment groups were discussed. Participants were told that those who were assigned the waitlist group would subsequently gain access to 8 weeks of either Bikram yoga or aerobic exercise classes following completion of the study protocol. Additional study procedures were discussed, including the three in-person assessments (i.e., two pre-treatment assessments, one post-treatment assessment) and the use of clinical diagnostic interviews, self-report questionnaires, various physiological measurements, and an exercise test. The potential risks and benefits of the treatment conditions and study procedures were discussed. Participants were informed that participation in the study was completely voluntary and that they were free to withdraw at any time.

Upon verbal and written explanation, participants were asked to sign the consent form stating that they understood the purpose of the study and were physically healthy enough to

participate in 8 weeks of moderate to vigorous physical activity. Next, participants completed a battery of measures, including the Medical Screening Interview, a demographic interview, the full SCID-I/P, and the HAM-D. Self-report measures included the BDI, HUS, RRS, and PHLMS. Upon completion of the pre-treatment psychological assessment, participants were provided with directions to and special instructions for the physiological appointment. They were informed to bring running shoes and wear comfortable clothes suitable for exercise, and to refrain from specific substances or activities for a minimum length of time prior to the appointment (i.e., eating and smoking cigarettes, 6 hr; caffeine and alcohol, 12 hr; exercise, 24 hr).

The second appointment was a 3-hr physiological assessment conducted in the Cardiovascular Stress Response Lab of the Kinesiology Department, supervised by Dr. Kyra Pyke. It took place within a week of the pre-treatment psychological assessment. I facilitated this appointment with a member of the Cardiovascular Stress Response Lab (i.e., lab coordinator or graduate student). The first 30 min of this appointment was used to set-up the physiological measurements and allow enough time for participants to become familiarized and comfortable with the laboratory setting. Following this, a carefully timed experimental protocol was followed, during which HR and MAP were measured and recorded continuously. The TSST began approximately 30 min into the protocol. As displayed in Figure 2, saliva sampling occurred at eight time points. Two additional experimental procedures (i.e., pulse-wave velocity and flow-mediated dilation measurements) occurred as part of the protocol. These procedures were not conducted for the purposes of this study; therefore, they are simply displayed in Figure 2 and not otherwise discussed. Next, participants engaged in the YMCA submaximal cycle ergometer test. At the end of the physiological assessment, participants were randomly assigned via a computer-generated random sequence to one of the treatment conditions. Group assignment was revealed

via sealed envelopes that had been previously prepared by research personnel. I did not have access to the random assignment list. Information regarding the assigned group was provided and participants were given the opportunity to ask questions. No participants refused their group assignment.

**Intervention Period.** Participants in the Bikram yoga group were asked to attend two classes per week for 8 weeks (16 classes in total) at a local affiliated Bikram yoga studio. Certified Bikram yoga teachers instructed all classes using a scripted instructional dialogue. Each 90-min class was held in a temperature-controlled room (40.6°C, 40% humidity). The class opened with a deep breathing exercise and continued with 50 min of standing *asanas* and 40 min of floor-based *asanas*, including a quick, forceful breathing exercise to finish (see Appendix A; Choudhury, 2007). All but the last *asana* (i.e., spine-twisting) were performed twice. *Savasana*, which is a restorative and relaxation posture, was performed between *asanas* throughout the floor series and at the end of class (Choudhury, 2007). The yoga studio regularly offered 22 class times per week, all of which were accessible to participants.

Participants in the aerobic exercise group were asked to attend two group aerobic exercise classes per week for 8 weeks (16 classes in total) at the Kingston Family YMCA. They were provided with a modified schedule of the YMCA group classes, which included only classes with a strong aerobic component and excluded those involving yoga, pilates, or cycling. Selecting these classes was done in consultation with the general manager of the YMCA, who was familiar with each class type. Classes involving the following components were available to participants: choreography-based cardio, aerobics, light muscular conditioning, and stretching; cardio, plyometric, and strength training exercises; high intensity aerobic exercise with intermittent rest periods; circuit-based cardio and strength training exercises; stepper-based exercises; and Latin-

inspired dance/fitness. Classes were 50-60 minutes in duration. Participants were not required to select only one class type but were able to attend any of the offered classes each week. Although the YMCA's group exercise class schedule changed slightly each season, participants had approximately 18-22 classes in total to choose from each week.

Participants in the active treatment groups had access to classes free-of-charge. Prior to participating in any classes, they were required to sign a liability waiver that absolved the establishment of their assigned intervention of any and all liability in the case of injury. Participants were instructed to commence their classes within a week of their pre-treatment physiological assessment and to email the investigator following their first class. They were informed about sign-in procedures and the importance of reporting adverse events.

Waitlisted individuals were not able to access yoga or exercise classes throughout the intervention period but participated in the rest of the study protocol. Following the post-treatment assessment, they received access to the class type of their choosing.

Throughout the intervention period, participants received a weekly email with a link to online questionnaires (SurveyMonkey). This online battery of questionnaires included the HUS (weekly), RRS (bi-weekly), PHLMS (weekly), and TPQ (weekly), which were randomly ordered.

**Post-Treatment Assessment.** Following completion of the intervention period, participants attended a 3½ hr post-treatment assessment in the Cardiovascular Stress Response Lab. They adhered to the previously given instructions regarding appropriate attire and avoidance of specific substances/activities for a minimum length of time prior to the appointment. Following a 30-min resting period, all physiological procedures and measurements were repeated, including the submaximal exercise test. The second variation of the TSST was used. I facilitated this appointment with a member of the Cardiovascular Stress Response Lab (i.e., lab

coordinator or graduate student). Following this, participants were administered the Mood Module of the SCID-I/P and the HAM-D to assess changes in diagnostic status and depression severity. This portion of the assessment was facilitated by another advanced graduate student in Clinical Psychology who was trained to gold standard reliability status in diagnostic assessment. These graduate students were unaware of participants' group assignment and were otherwise not involved in the study. Participants were compensated \$50 at the end of this appointment.

### **Data Analysis**

Analyses were conducted using several software programs, including the Statistical Program for the Social Sciences (SPSS) Software Version 24, LabChart (AD Instruments, Colorado Springs, CO, USA), and HLM 7 Software (Raudenbush, Bryk, & Congdon, 2017). For each set of analyses, demographic and clinical variables were examined with respect to the outcome variable and/or mediator variable/s to identify relevant covariates. Demographic variables included age, ethnicity, educational attainment, relationship status, and BMI.<sup>5</sup> Clinical variables included initial age of onset of a depressive disorder, total number of depressive episodes, pre-treatment depression severity scores (i.e., BDI, HAM-D), the presence/absence of a comorbid disorder, and current treatment status.

**Objective 1: Group Differences in Treatment Outcome Variables.** For the treatment outcome objective of this study, both intention-to-treat (ITT) and as-treated analyses were performed. The ITT analyses included all participants who were randomly assigned to one of three conditions ( $n = 53$ ), regardless of subsequent withdrawal or deviation from study protocol. The last observation carried forward method was used to address missing post-treatment data (i.e., HAM-D scores) in this sample. The last observation carried forward method, which is still

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<sup>5</sup> Body mass index (BMI) was computed at pre-treatment and post-treatment, based on objective measurements of the demographic variables height and weight, according to the following equation:  $BMI = \text{weight}(\text{kg})/\text{height}^2(\text{m})$ .

commonly used in ITT analyses (Blumenthal et al., 2007; Danielsson, Papoulias, Petersson, Carlsson, & Waern, 2014; Hallgren et al., 2016; de Manincor et al., 2016; Sharma et al., 2017), assumes no change from pre-treatment HAM-D scores for noncompleters. It was believed to be a more appropriate method for dealing with missing data in this case compared to other approaches such as multiple imputation, as it would presumably provide the most conservative test of treatment efficacy. Treatment outcome variables examined in the ITT approach included change in HAM-D scores from pre- to post-treatment (i.e., post-treatment minus pre-treatment) and response (i.e., >50% reduction in HAM-D scores from pre- to post-treatment). Since the remission variable was derived from a combination of post-treatment HAM-D scores and categorical diagnostic impressions (i.e., no longer meeting diagnostic criteria for a depressive disorder and  $\text{HAM-D} \leq 7$ ), it was excluded from the ITT analyses. As-treated analyses included only those participants who completed the post-treatment psychological assessment ( $n = 42$ ) and all treatment outcome variables (i.e., change in HAM-D scores, response, remission).

When treatment outcome was defined as change in HAM-D scores, a repeated-measures analysis of covariance (ANCOVA) was used. Partial  $\eta^2$  was used as the index of effect size, with .04, .12, and .26 corresponding to small, medium, and large effects, respectively. Significant interactions were followed up with pairwise comparisons between means, using a Bonferroni correction to adjust for the number of comparisons. When treatment outcome was defined by either response or remission, a two-way contingency table analysis with a chi-square test was used. Cramer's  $V$  was used to indicate the strength of relationship, with .10, .30, and .50 representing small, medium, and large effects, respectively. Follow-up pairwise comparisons, using a Bonferroni correction, were conducted to evaluate the difference among the proportions.

## **Objective 2: Mechanisms of Action.**

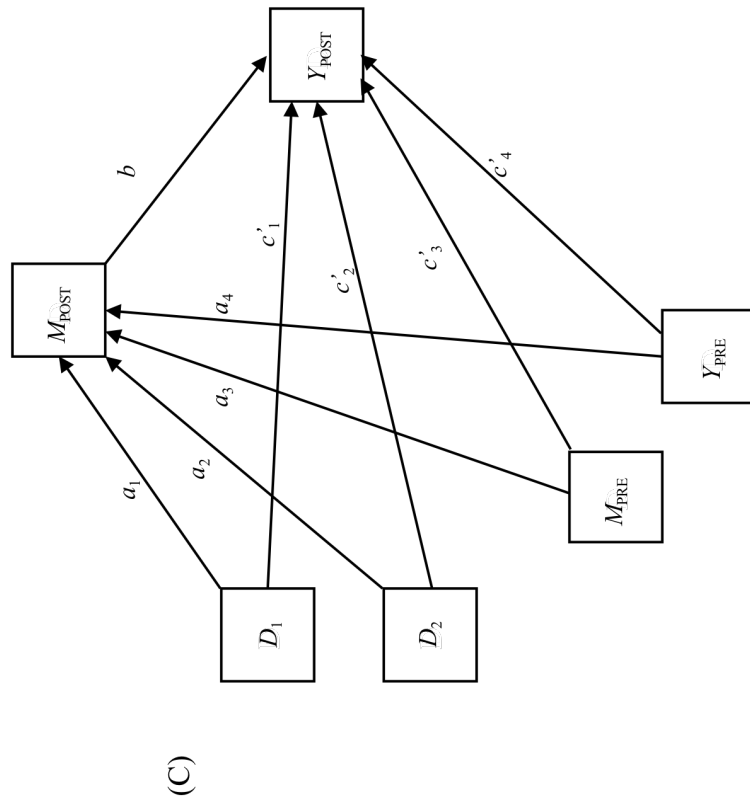
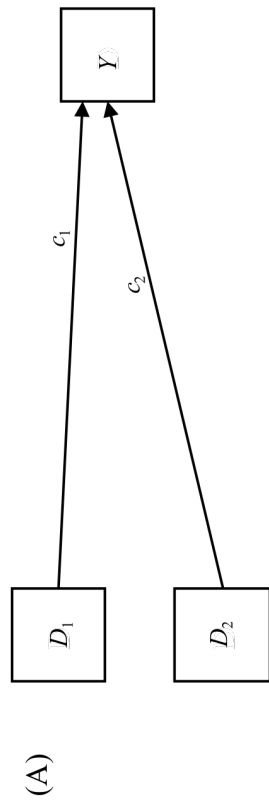
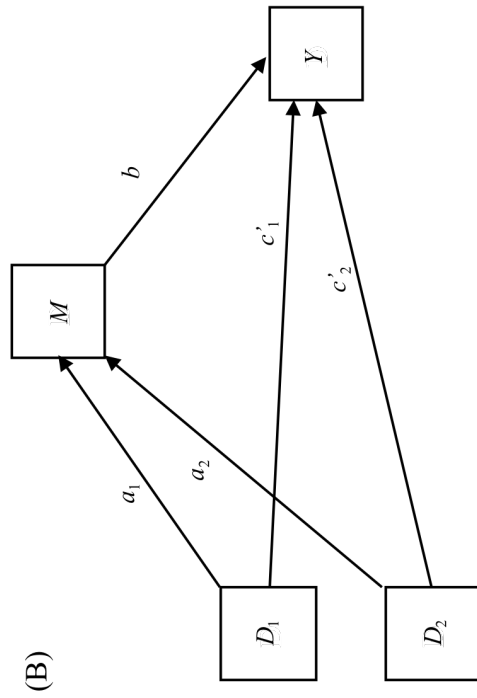
***Physiological Stress Reactivity Analyses.*** HR, MAP, and salivary cortisol were analyzed to characterize stress reactivity. HR and MAP were analyzed offline in LabChart and compiled into 1-min average time bins. Baseline HR (in bpm) and MAP (in mm Hg) were taken as the 1-min average collected during the baseline minute of a physiological task (i.e., flow-mediated dilation task) that was conducted immediately prior to the TSST but not for the purposes of the current study. Physiological reactivity to the TSST was quantified as the peak 1-min average of HR and MAP during the task, minus baseline and then divided by baseline (denoted HR reactivity, MAP reactivity).

Salivary cortisol sample 2 (see Figure 2) was used as participants' baseline against which to gauge differences in response to the TSST and across treatment groups. Sample 2 was believed to be a better indicator of salivary cortisol levels at rest than sample 1. Sample 8, which was collected approximately 60 min following the end of the TSST, was excluded from analyses given an unusual and unexpected increase in cortisol concentration for many participants. It is possible that this increase may have occurred in anticipation of a subsequent submaximal exercise test (at pre- and post-treatment) and group assignment (at pre-treatment). Given the substantial positive skew and kurtosis for several pre- and post-treatment cortisol samples, all cortisol samples were common logarithm transformed prior to main analyses. There were no extreme outliers (i.e., cases  $\pm 3$  SD from the mean) within the transformed variables. In addition to raw baseline cortisol concentrations in  $\mu\text{g/dL}$  (i.e., sample 2; denoted baseline CORT), two other cortisol variables were derived from the transformed scores: (a) 'cortisol reactivity' to the TSST, defined as peak cortisol concentration (sample 4) minus baseline (sample 2) divided by baseline (denoted CORT reactivity), and (b) 'area under the curve with respect to increase'

(denoted  $AUC_i$ ; see formula from Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003).  $AUC_i$  is a measure of the total cortisol output over the course of the TSST, calculated as the sum of the area of the five trapezoids bounded by the baseline value and framed by the cortisol concentration in the six saliva samples (samples 2-7). Untransformed estimated marginal means are presented in figures for ease of interpretability. Repeated-measures ANCOVAs were used to assess group differences in the change in physiological stress reactivity variables from pre- to post-treatment. Significant interactions were followed up with pairwise comparisons between means, using a Bonferroni correction to adjust for the number of comparisons.

Next, mediation models looking at separate mediation effects of HR reactivity, MAP reactivity, CORT reactivity, and  $AUC_i$  were tested using the PROCESS macro version 3.0 (Hayes, 2013), which is a computational add-on for SPSS. PROCESS is designed for modeling mediation and moderation analyses with ordinary least squares regressions, and uses a bootstrapping approach to evaluate the 95% confidence intervals (CIs) for the inference of indirect (mediation) effects. In this approach, effects are significant when the upper and lower bound of their bias-corrected 95% CI does not contain zero. The bootstrapping approach implemented in PROCESS has become an increasingly favoured method to testing mediation relative to the highly familiar Baron and Kenny (1986) causal steps approach on logical grounds (e.g., Hayes, 2009), as well as for its increased sensitivity to detecting true indirect effects (e.g., MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). Prior to running the mediation models, outliers were examined visually and statistically using three distance measures (i.e., Mahalanobis, Cook's, and Leverage values) with their respective cut-off scores (Tabachnick & Fidell, 2007). Participants with outlier scores on at least two of the three distance measures were excluded from analyses (Buchanan, 2015).

Bootstrapping with 10,000 resampling iterations was used. Treatment group was specified as a multicategorical predictor in PROCESS, which automatically creates  $k - 1$  variables  $D_1, D_2, \dots, D_{k-1}$  and adds them to the model. The indicator coding option was chosen, which treats the group coded with the smallest numerical value (i.e., waitlist group) as the reference category. See Figure 3B for the uncontrolled model used in this study in path diagram form, in which treatment group  $X$  (coded as  $D_1$  or  $D_2$ ) was proposed to exert its effects on  $Y$  through a single mediator  $M$ . As displayed in Figure 3B, the direct effect of  $D_1$  or  $D_2$  on  $Y$  (denoted  $c'_1$  and  $c'_2$ ) represents the mean difference between the groups (i.e., yoga vs. waitlist, exercise vs. waitlist) on  $Y$ , independent of  $X$ 's effect on  $M$ . An indirect effect of  $D_1$  or  $D_2$  represents the mean difference between the two groups on  $Y$  that results from  $X$ 's influence on  $M$ , which in turn affects  $Y$ , and was of particular interest in these analyses as it represents the “mediation” effect. An indirect effect is calculated as  $c$  minus  $c'$ , with  $c$  being the total effect of  $X$  on  $Y$  (see Figure 3A). In addition to  $D_1$  and  $D_2$ , other predictor variables were entered in each mediation model. When modeling change over time, it has been suggested to predict later measures (i.e., post-treatment values) of  $M$  and  $Y$  from independent variables of interest while controlling for earlier measures (i.e., pre-treatment values) of  $M$  and  $Y$  (Darlington & Hayes, 2017; Hayes & Rockwood, 2017). Therefore, post-treatment values of the physiological variable and HAM-D were entered as  $M$  and  $Y$ , respectively, and pre-treatment values of these variables were entered as covariates (see Figure 3C). These covariates were specified to predict both  $M$  and  $Y$ . Any additional covariates identified in preliminary analyses were entered in the same way (not depicted in Figure 3).



**Fig. 3.** A mediation model in path diagram form with the multicategorical independent variable, treatment group.  $D_1$  and  $D_2$  represent dummy variables (waitlist coded as reference group),  $M$  represents the mediator, and  $Y$  represents the dependent variable. Figure 3(A) depicts the *total effect* of the independent variable on  $Y$  (i.e., direct plus indirect effects), denoted by  $c$ . Figure 3(B) depicts the *direct effect* of the independent variable on  $Y$ , denoted by  $c'$ . Indirect effects of the dummy variables were calculated as  $c$  minus  $c'$ . Figure 3(C) depicts the mediation model with the addition of pre-treatment levels of the mediator and outcome variables as covariates ( $M_{PRE}$ ,  $Y_{PRE}$ ), and post-treatment levels of these variables specified as the actual mediator ( $M_{POST}$ ) and outcome variable ( $Y_{POST}$ ).

***Psychological Variable Analyses.*** Group differences in psychological variables measured repeatedly throughout the course of the intervention were analyzed using multilevel modeling (MLM) with HLM 7 software (Raudenbush et al., 2017). The psychological variables were perceived hassles, rumination, and mindfulness scores. Perceived hassles and mindfulness were measured weekly; therefore, measurements for these variables were taken at pre-treatment, followed by every week from week 1 to week 8 (i.e., post-treatment). Rumination was measured bi-weekly; therefore, measurements for this variable were taken at pre-treatment, week 2, week 4, week 6, and week 8 (i.e., post-treatment). Multilevel modeling was used to assess group differences in these variables, as it is ideal for analyzing data that have a nested or hierarchical structure (Raudenbush & Bryk, 2002). Further, it incorporates information from all measurement points to estimate slopes of change during treatment and uses a better mechanism for missing data than listwise deletion (Price, Anderson, & Henrich, 2008), which is traditionally used in regression. That is, MLM can accommodate missing data at Level 1 by excluding the data point from analysis and assigning greater statistical weight to complete participant data (Raudenbush & Bryk, 2002). Random intercepts and slopes were specified to allow for unique individual growth trajectories. Model parameters were estimated by restricted maximum likelihood.

In the MLM models, repeated measurements of each psychological variable (Level 1) were nested within participants (Level 2). Two iterations of each model were required for all pairwise comparisons between the three groups to be made (i.e., yoga vs. waitlist, exercise vs. waitlist, yoga vs. exercise). Dummy variables were used to examine changes in the psychological variables as a function of group. In each iteration, two dummy variables were defined. In the first iteration, Dummy1 was the comparison of exercise to waitlist, and Dummy2 was the comparison of yoga to waitlist. In the second iteration, Dummy1 was the comparison of yoga to exercise, and

Dummy2 was the comparison of waitlist to exercise. It is important to note that Dummy1 of the first iteration and Dummy2 of the second iteration were the exact same comparison (i.e., exercise vs. waitlist = waitlist vs. exercise); therefore, only one of these comparisons is presented in subsequent analyses. Time was entered as a fixed effect at Level 1 and coded such that the intercept of the model represented values of the psychological variable at post-treatment. The slopes represented the rate of change in the psychological variable from pre- to post-treatment. Between subject predictors, including the dummy variables and relevant covariates, were included at Level 2. The Level 1 function for a general uncontrolled model for a psychological variable of interest was:

$$Y_{it} = \pi_{0i} + \pi_{1i}(\text{Time}) + e_{it}$$

where  $Y_{it}$  is participant  $i$ 's psychological variable at time  $t$ ,  $\pi_{0i}$  is participant  $i$ 's psychological variable at post-treatment (i.e., week 8),  $\pi_{1i}$  is the instantaneous rates of linear change in the psychological variable at post-treatment for participant  $i$ , and  $e_{it}$  is the residual variance in repeated measurements of the psychological variable for participant  $i$  that cannot be accounted for by post-treatment psychological variable values ( $\pi_{0i}$ ) or linear change in the psychological variable over time. The Level 2 equations were as follows:<sup>6</sup>

*Intercept*

$$\pi_{0i} = \beta_{00} + \beta_{01}(\text{Dummy1}) + \beta_{02}(\text{Dummy2}) + r_{0i}$$

*Slope*

$$\pi_{1i} = \beta_{10} + \beta_{11}(\text{Dummy1}) + \beta_{12}(\text{Dummy2}) + r_{1i}$$

To examine pre-treatment group differences in psychological variables, the same two model iterations described above were conducted for each psychological variable with Time

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<sup>6</sup> In models with covariates, the covariates were included as predictors for both the intercept and slope equations at Level 2.

coded a second way. That is, Time at Level 1 was coded such that the intercept of the model represented values of the psychological variable at pre-treatment. This model was run as a control, to test whether the groups differed on the psychological variable prior to any intervention.

Next, to examine the psychological variables (i.e., perceived hassles, rumination, mindfulness) as mediators in the proposed antidepressant effects of yoga and exercise, mediation models were tested using PROCESS and the same approach previously described. That is, mediation was assessed by the indirect effect of treatment group (mediated through changes in the psychological variable of interest) on changes in HAM-D scores, while accounting for the direct effects of treatment group on changes in the psychological variable and HAM-D scores. Mediator variables were defined as post-treatment values of the psychological variable of interest, and post-treatment HAM-D scores were entered as the dependent variable in all models. Again, in addition to any relevant demographic or clinical variables, pre-treatment values for the psychological variable of interest and pre-treatment HAM-D scores were entered as covariates.

## Chapter 5

### Results

#### Treatment Outcome Analyses

**Preliminary Analyses.** A total of 53 participants took part in the complete pre-treatment data collection protocol (see Figure 1 for CONSORT diagram). Demographic and clinical characteristics of this sample are displayed in Table 1. Three participants did not complete the pre-treatment protocol and, therefore, have been excluded from all subsequent analyses. The 53 participants with complete pre-treatment data were randomly assigned as follows: Bikram yoga:  $n = 18$ , aerobic exercise:  $n = 20$ , and waitlist control:  $n = 15$ . One-way ANOVAs and chi-square tests were used to assess for group differences on relevant demographic and clinical variables. As displayed in Table 2, there were no significant differences between groups.

Of the participants who were originally randomized, 42 were considered “completers”. The majority of these individuals (76.2%) participated in both post-treatment assessments (i.e., psychological and physiological), although a small subset (23.8%) were unable to attend an in-person appointment and, therefore, post-treatment physiological data were not collected. Of the 53 participants randomized, completion rates were 83.3% for the yoga group, 75.0% for the exercise group, and 80.0% for the waitlist group. A total of 11 participants were considered “noncompleters”, resulting in an attrition rate of 20.8%. The most common reasons for withdrawing from the study included the interference of life stressors and difficulty complying with study expectations. Two participants did not provide a reason for withdrawing from the study. Three participants became ineligible during the study protocol, resulting in the termination of their involvement. Independent samples  $t$ -tests and  $\chi^2$  tests were used to compare completers and noncompleters with respect to demographic and clinical variables (see Table 3).

The presence of a comorbid disorder was differentially distributed, with a significantly higher comorbidity rate among noncompleters compared to completers (72.7% vs. 35.7%).

Importantly, the distribution of noncompleter status was not significantly associated with group assignment,  $\chi^2(2, N = 53) = 0.41, p = .816$ , Cramer's  $V = .088$  (yoga = 16.7%, exercise = 25.0%, waitlist = 20.8%).

***Adverse Events.*** Adverse events associated with participation in yoga or exercise classes were assessed weekly using the TPQ. As well, participants were instructed to report any adverse events to members of the research team (i.e., Dr. Kate Harkness, Dr. Kyra Pyke, myself) as soon as possible. No adverse events were reported to research personnel, and no serious adverse events were reported on the TPQ. Minor adverse events reported included transient muscle soreness, transient stiffness, and feeling hot and/or uncomfortable during a Bikram yoga class. No participants withdrew from the study due to the experience of an adverse event.

Table 1

*Detailed Demographic and Clinical Characteristics of Initial Sample (N=53)*

	<i>M</i>	<i>SD</i>	<i>n</i>	<i>%</i>
Age	33.08	14.71		
Ethnicity				
White			39	73.6
Asian			8	15.1
Mixed			2	3.8
Other			4	7.5
Highest education level				
Grade 12			1	1.9
Some college/university			28	52.8
Undergraduate degree			16	30.2
Graduate degree			8	15.1
Relationship status				
Single/dating			27	50.9
Common-law/engaged			6	11.3
Married			19	35.8
Divorced			1	1.9
Pre-T <sub>x</sub> BMI	26.67	6.13		
Current depressive disorder				
MDD			46	86.8
DDNOS			4	7.5
ADJ-D			3	5.7
Age of initial onset	19.34	6.11		
Total # of episodes				
1			8	15.1
2			16	30.2
3			13	24.5
4			5	9.4
5+			11	20.8
Pre-T <sub>x</sub> BDI	31.96	9.74		
Pre-T <sub>x</sub> HAM-D	13.02	3.56		
Current treatment				
None			29	54.7
Psychotherapy			4	7.5
Medication			15	28.3
Both			5	9.4
Comorbid disorder				
Social anxiety disorder			11	20.8
Panic disorder			3	5.7
Generalized anxiety disorder			6	11.3
Obsessive-compulsive disorder			1	1.9
Specific phobia			8	15.1

*Note.* Pre-T<sub>x</sub> BMI = body mass index at pre-treatment; MDD = major depressive disorder; DDNOS = depressive disorder not otherwise specified; ADJ-D = adjustment disorder with depressed mood; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment; Pre-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at pre-treatment.

Table 2

*Demographic and Clinical Characteristics Stratified by Group Assignment (N=53)*

	Yoga (n = 18)	Exercise (n = 20)	Waitlist (n = 15)	Test statistic	p
Age (M/SD; F)	34.17/15.75	34.85/15.15	29.40/13.08	0.65	.524
Ethnicity (n/%; $\chi^2$ )				0.47	.792
White	13/72.2	14/70.0	12/80.0		
Other	5/27.8	6/30.0	3/20.0		
Highest education level (n/%; $\chi^2$ )				0.35	.838
Grade 12/Some university	10/55.6	10/50.0	9/60.0		
University degree	8/44.4	10/50.0	6/40.0		
Relationship status (n/%; $\chi^2$ )				0.77	.680
Unmarried	11/61.1	12/60.0	11/73.3		
Married	7/38.9	8/40.0	4/26.7		
Pre-T <sub>x</sub> BMI (M/SD; F)	25.52/6.71	27.37/6.94	27.10/4.12	0.47	.625
Age of onset (M/SD; F)	19.78/5.00	19.35/7.09	18.80/6.27	0.10	.904
Total # of episodes (M/SD; F)	4.11/3.39	2.80/1.32	3.53/2.88	1.19	.321
Pre-T <sub>x</sub> BDI (M/SD; F)	33.89/8.50	28.33/11.42	34.00/8.17	2.01	.145
Pre-T <sub>x</sub> HAM-D (M/SD; F)	13.39/3.07	12.00/3.77	13.93/3.71	1.44	.248
Current treatment: Yes (n/%; $\chi^2$ )	8/44.4	9/45.0	7/46.7	0.02	.991
Comorbid disorder: Yes (n/%; $\chi^2$ )	8/44.4	10/50.0	5/33.3	0.98	.612

Note. Pre-T<sub>x</sub> BMI = body mass index at pre-treatment; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment; Pre-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at pre-treatment.

Table 3

*Demographic and Clinical Characteristics of Completers and Noncompleters (N=53)*

	Completers (n = 42)	Noncompleters (n = 11)	Test statistic	p
Age (M/SD; t)	32.81/15.00	34.09/14.23	0.26	.800
Ethnicity (n/%; $\chi^2$ )			0.01	.942
White	31/73.8	8/72.7		
Other	11/26.2	3/27.3		
Highest education level (n/%; $\chi^2$ )			.048	.488
Grade 12/Some university	24/57.1	5/45.5		
University degree	18/42.9	6/54.5		
Relationship status (n/%; $\chi^2$ )			0.01	.968
Unmarried	27/64.3	7/63.6		
Married	15/35.7	4/36.4		
Pre-T <sub>x</sub> BMI (M/SD; t)	26.34/6.11	27.91/6.35	0.75	.456
Age of onset (M/SD; t)	19.24/6.49	19.73/4.56	0.23	.816
Total # of episodes (M/SD; t)	3.21/2.35	4.36/3.50	1.30	.201
Pre-T <sub>x</sub> BDI (M/SD; t)	31.88/9.98	32.27/9.26	0.12	.906
Pre-T <sub>x</sub> HAM-D (M/SD; t)	12.83/3.80	13.73/2.45	0.74	.464
Current treatment: Yes (n/%; $\chi^2$ )	21/50.0	3/27.3	1.82	.178
Comorbid disorder: Yes (n/%; $\chi^2$ )	15/35.7	8/72.7	4.86	.027

Note. Pre-T<sub>x</sub> BMI = body mass index at pre-treatment; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment; Pre-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at pre-treatment.

**Identification of Covariates.** Relationships among relevant demographic/clinical variables and treatment outcome variables were examined in a series of bivariate correlations and independent samples *t*-tests. See Tables 4 and 5, respectively, for the ITT (i.e., randomized) and as-treated (i.e., completer) samples. For the ITT sample, there was a significant difference in post-treatment HAM-D scores across ethnicity. Participants from Other ethnicity scored significantly lower than White participants on HAM-D scores at post-treatment ( $M = 6.71$ ,  $SD = 6.65$  vs.  $M = 11.10$ ,  $SD = 7.10$ ). Therefore, ethnicity was included as a covariate in a subsequent ITT analysis involving change in HAM-D scores across the intervention period. As would be

expected, there were significant and positive relations between pre-treatment depression severity scores (i.e., BDI, HAM-D) and post-treatment HAM-D scores. Pre-treatment HAM-D scores were also significantly associated with response in the ITT sample. Participants who achieved a response had significantly lower HAM-D scores at pre-treatment than those who did not achieve a response ( $M = 11.92, SD = 3.30$  vs.  $M = 13.93, SD = 3.57$ ).

Table 4

*Relations Between Demographic and Clinical Characteristics and Treatment Outcome Variables in Randomized Sample (N = 53)*

	Post-T <sub>x</sub> HAM-D			Response		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>t</i>	$\chi^2$	<i>p</i>
Age	-.01		.957	0.22		.827
Ethnicity		2.02	.049		2.77	.096
Highest education level		0.87	.390		0.01	.942
Relationship status		1.03	.306		0.65	.422
Pre-T <sub>x</sub> BMI	.19		.173	1.23		.223
Age of onset	-.26		.064	1.17		.246
Total # of episodes	.24		.085	1.80		.077
Pre-T <sub>x</sub> BDI	.38		.007	1.88		.066
Pre-T <sub>x</sub> HAM-D	.51		.000	2.12		.039
Current treatment		0.06	.950		0.01	.942
Comorbid disorder		0.66	.510		0.05	.817

*Note.* Pre-T<sub>x</sub> BMI = body mass index at pre-treatment; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment; Pre-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at pre-treatment; Post-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at post-treatment.

Within the as-treated sample, significant and positive relationships emerged between post-treatment HAM-D scores and both pre-treatment depression severity scores. Initial age of

onset of a depressive episode was negatively correlated with post-treatment HAM-D scores, indicating that a lower age of onset is associated with higher depression severity at post-treatment. Therefore, age of onset was included as a covariate in a subsequent as-treated analysis involving change in HAM-D scores. In terms of the response and remission outcome variables, it is important to note that there was a 100% correspondence between them. That is, participants who experienced a response also achieved remission and vice versa. Since this resulted in identical statistics for both variables, they are referred to collectively in subsequent relevant analyses. None of the demographic or clinical variables were significantly related to response/remission.

Table 5

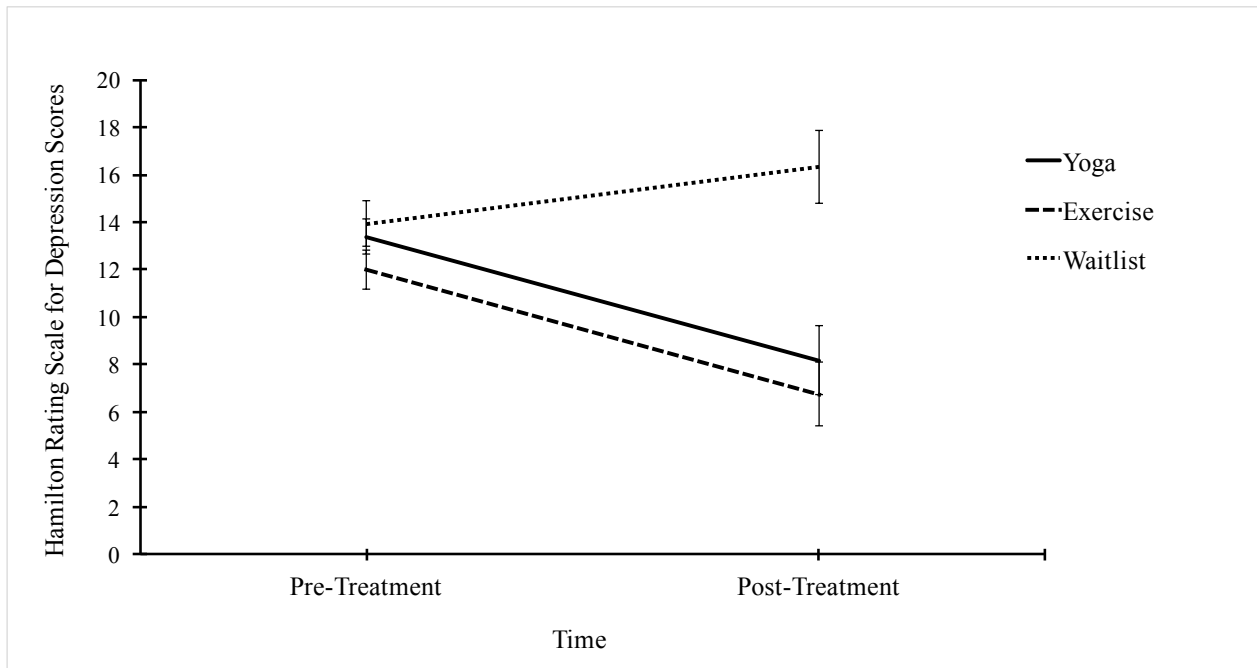
*Relations Between Demographic and Clinical Characteristics and Treatment Outcome Variables in Sample of Completers (N = 42)*

	Post-T <sub>x</sub> HAM-D			Response/remission		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>t</i>	$\chi^2$	<i>p</i>
Age	-.09		.587	0.11		.912
Ethnicity		1.89	.066		3.71	.054
Highest education level		1.17	.248		0.20	.653
Relationship status		1.59	.120		0.86	.353
Pre-T <sub>x</sub> BMI	.10		.524	0.99		.326
Age of onset	-.36		.019	1.37		.177
Total # of episodes	.14		.376	1.50		.142
Pre-T <sub>x</sub> BDI	.38		.016	2.03		.050
Pre-T <sub>x</sub> HAM-D	.50		.001	1.86		.070
Current treatment		0.33	.744		0.39	.533
Comorbid disorder		0.33	.743		0.86	.353

*Note.* Pre-T<sub>x</sub> BMI = body mass index at pre-treatment; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment; Pre-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at pre-treatment; Post-T<sub>x</sub> HAM-D = Hamilton Rating Scale for Depression scores at post-treatment.

**Primary Analyses: Intention-to-Treat Sample.** A repeated-measures ANCOVA was conducted when treatment efficacy was defined as change in HAM-D scores across the intervention period. This allowed for the examination of the effect of treatment group (i.e., yoga vs. exercise vs. waitlist) on the dependent variable of time (i.e., pre- vs. post-treatment HAM-D scores), over and above the covariate of ethnicity. The inclusion of ethnicity did not significantly alter findings; therefore, for ease of interpretation and simplicity, the uncontrolled analyses are presented. There was a significant interaction between group assignment and time,  $F(2, 50) =$

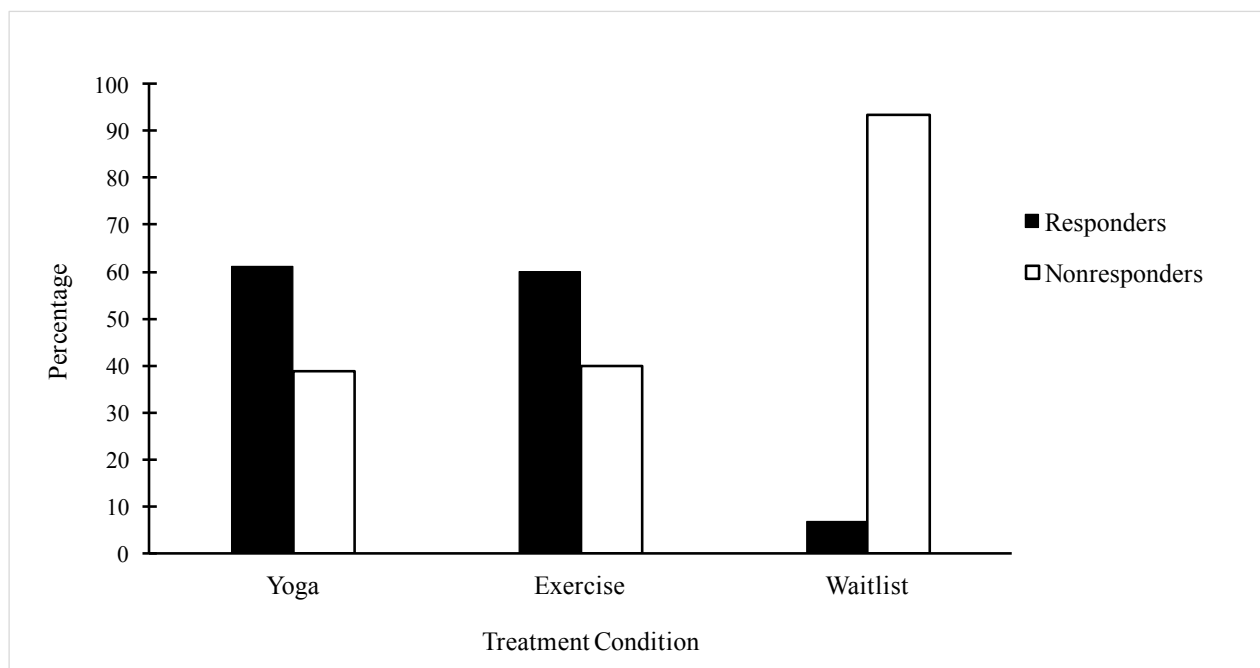
11.41,  $p < .001$ , partial  $\eta^2 = .31$ . Post-hoc analyses revealed that HAM-D scores significantly decreased from pre- to post-treatment in both the yoga group,  $t(17) = 3.70$ ,  $p = .001$  ( $M = 13.39$ ,  $SE = 0.72$  vs.  $M = 8.17$ ,  $SE = 1.45$ ), and the exercise group,  $t(19) = 4.38$ ,  $p < .001$  ( $M = 12.00$ ,  $SE = 0.84$  vs.  $M = 6.75$ ,  $SE = 1.35$ ). In contrast, HAM-D scores were found to increase in the waitlist group,  $t(14) = -2.21$ ,  $p = .044$  ( $M = 13.93$ ,  $SE = 0.96$  vs.  $M = 16.33$ ,  $SE = 1.51$ ). See Figure 4.



**Fig. 4.** Significant interaction between time and treatment condition with respect to Hamilton Rating Scale for Depression scores in randomized sample.

When treatment outcome was defined as *response*, a two-way contingency table analysis with a chi-square test was used. Group assignment and response were significantly related,  $\chi^2(2, N = 53) = 12.60$ ,  $p = .002$ , Cramer's  $V = .49$ . The percentage of participants who experienced a significant response in the ITT sample was 61.1%, 60.0%, and 6.7%, respectively, for the yoga, exercise, and waitlist groups (see Figure 5). Follow-up pairwise comparisons were conducted to evaluate differences among these percentages, using Holm's sequential Bonferroni method to control for Type I error (i.e.,  $\alpha = .017$ ). The proportion of participants who experienced a

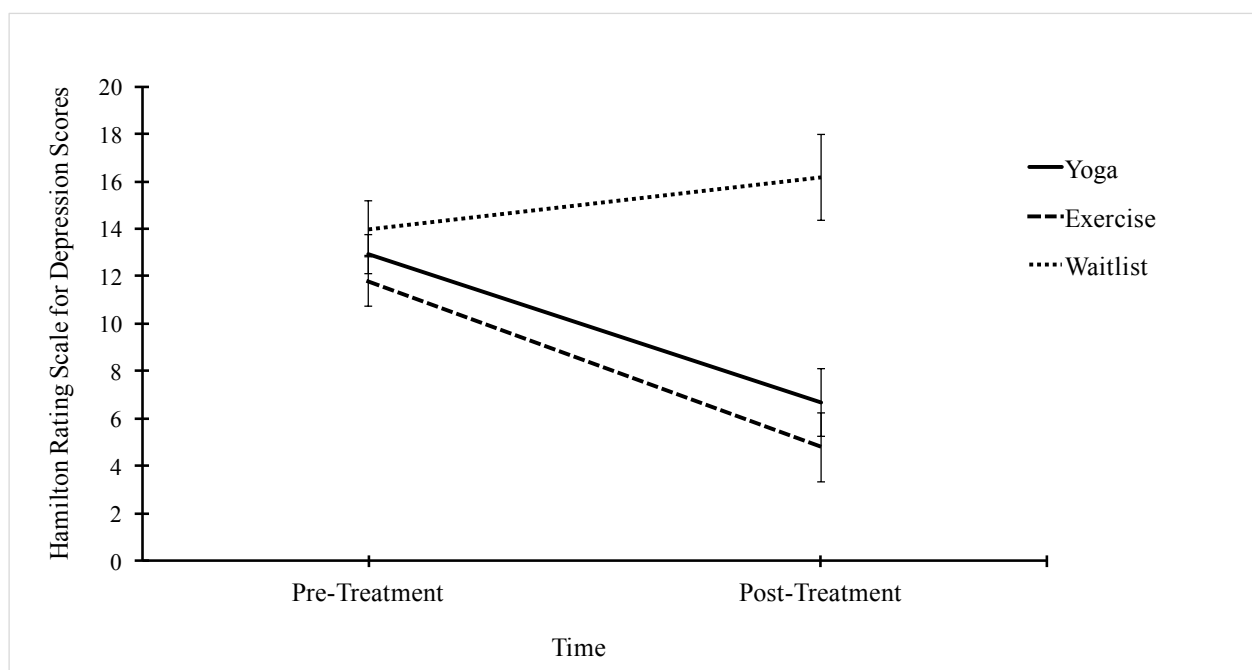
response in the yoga group was significantly greater than that of the waitlist group,  $\chi^2(1, N = 33) = 10.48, p = .001$ , Cramer's  $V = .56$ . Similarly, significantly more participants in the exercise condition experienced a response compared to the waitlist group,  $\chi^2(1, N = 35) = 10.44, p = .001$ , Cramer's  $V = .55$ . Response rates did not differ between the yoga and exercise groups,  $\chi^2(2, N = 38) = 0.01, p = .944$ , Cramer's  $V = .01$ .



**Fig. 5.** Significant differential distribution of responders and nonresponders across treatment conditions in randomized sample.

**Primary Analyses: As-Treated Sample.** To assess pre- to post-treatment changes in HAM-D scores, a repeated-measures ANCOVA was conducted, with age of initial depression onset entered as a covariate. Although a significant interaction between time and age of onset emerged, the inclusion of the covariate did not alter findings related to the goals of this investigation. Therefore, the uncontrolled analyses are presented. There was a significant

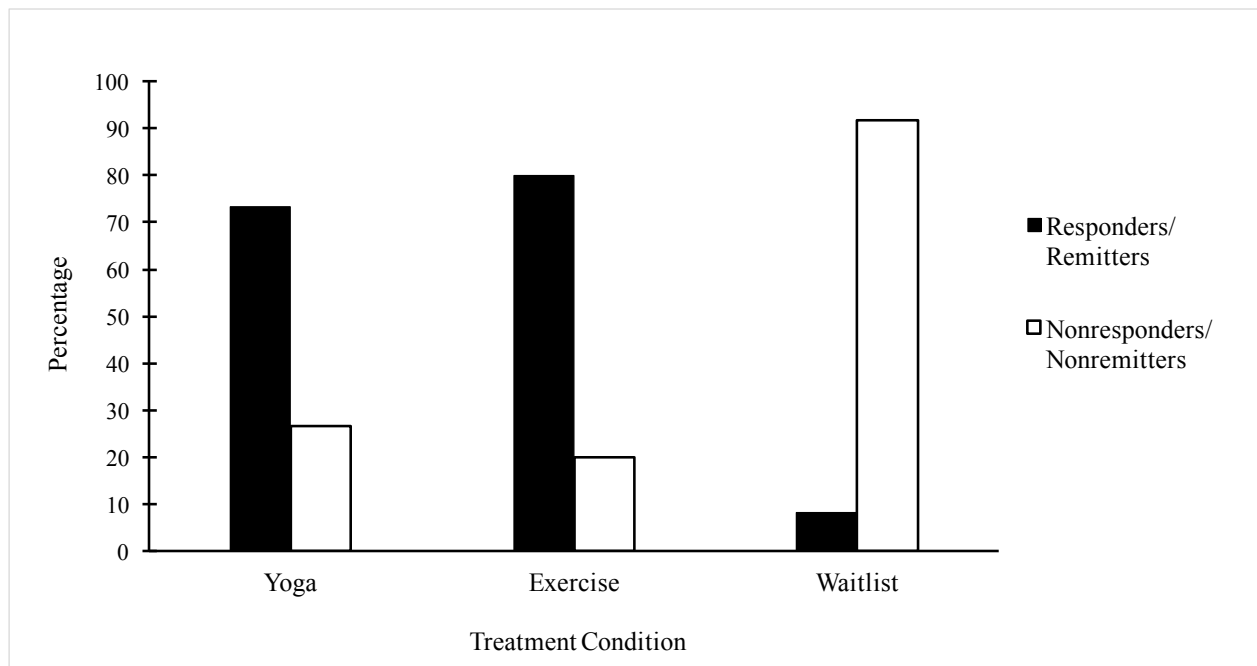
interaction between treatment condition and time,  $F(2, 39) = 12.73, p < .001$ , partial  $\eta^2 = .40$ . Post-hoc analyses revealed that HAM-D scores significantly decreased from pre- to post-treatment in both the yoga group,  $t(14) = 4.13, p = .001$  ( $M = 12.93, SE = 0.80$  vs.  $M = 6.67, SE = 1.43$ ), and the exercise group,  $t(14) = 5.33, p < .001$  ( $M = 11.80, SE = 1.07$  vs.  $M = 4.80, SE = 1.44$ ). There was no significant change in HAM-D scores among those in the waitlist group,  $t(11) = -1.87, p = .089$  ( $M = 14.00, SE = 1.19$  vs.  $M = 16.17, SE = 1.82$ ). See Figure 6.



**Fig. 6.** Significant interaction between time and treatment condition with respect to Hamilton Rating Scale for Depression scores in sample of completers.

A two-way contingency table analysis with a chi-square test was used to assess group differences in response/remission rates at post-treatment. Response/remission was differentially distributed across treatment groups,  $\chi^2(2, N = 42) = 16.48, p < .001$ , Cramer's  $V = .63$ . The percentage of participants who experienced a significant response in the sample of completers was 73.3%, 80.0%, and 8.3%, respectively, for the yoga, exercise, and waitlist groups (see

Figure 7). Follow-up pairwise comparisons to evaluate differences among these percentages demonstrated that significantly more participants in the yoga group experienced a response/remission compared to the waitlist group,  $\chi^2(1, N = 27) = 11.41, p = .001$ , Cramer's  $V = .65$ . Similarly, the response/remission rate was significantly higher for the exercise group versus the waitlist control,  $\chi^2(1, N = 27) = 13.72, p < .001$ , Cramer's  $V = .71$ . Rates did not differ significantly between the yoga and exercise groups,  $\chi^2(1, N = 30) = .186, p = .666$ , Cramer's  $V = .08$ .



**Fig. 7.** Significant differential distribution of responders/remitters and nonresponders/nonremitters across treatment conditions in sample of completers.

Since the frequency of participation in yoga or exercise classes could presumably affect the degree of improvement in depression symptoms, the relation of total number of classes to treatment outcome was examined among completers in the active treatment groups. There was no significant difference between the groups in terms of total classes attended,  $t(28) = -1.11, p =$

.275 (yoga:  $M = 12.80$ ,  $SD = 2.27$ ; exercise:  $M = 13.73$ ,  $SD = 2.31$ ). Adherence rates were 80.0% and 85.8% for the yoga and exercise groups, respectively.<sup>7</sup> The correlation between total classes and change in HAM-D scores (i.e., post-treatment minus pre-treatment) was not significant,  $r(30) = .177$ ,  $p = .350$ . Similarly, total classes did not differ significantly between those who experienced a response/remission and those who did not,  $t(28) = -0.72$ ,  $p = .478$ .

### **Mechanisms of Action Analyses**

**Preliminary Analyses: Physiological Variables.** Of the 42 completers in this study, 10 were unable to attend the post-treatment physiological assessment. Therefore, physiological stress reactivity data were collected for 32 participants. Complete HR data were available for all participants. Due to equipment malfunction, MAP data were missing for four participants at either pre- or post-treatment. Therefore, MAP analyses were conducted on the 28 participants with sufficient blood pressure data. In terms of cortisol data, one participant was missing sample 2 at pre-treatment and another participant was missing sample 2 at post-treatment. For these two participants, their sample 1 cortisol concentration was substituted as the baseline value. Due to a storage issue, one participant in the exercise group was missing all cortisol data at post-treatment. Therefore, cortisol analyses were conducted on the 31 participants with sufficient cortisol data. As displayed in Table 6, there were no significant differences between the treatment groups on the physiological variables at pre-treatment. At post-treatment, the only significant difference that emerged was for HR reactivity,  $F(2,29) = 4.99$ ,  $p = .014$ . Post-hoc comparisons using the Tukey HSD test revealed that post-treatment HR reactivity was significantly lower in the exercise group compared to the yoga group ( $p = .010$ ). It is important to note that the cell sizes in these preliminary analyses were small ( $8 \leq n \leq 13$ ) and standard deviations were relatively large.

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<sup>7</sup> Adherence rates were calculated based on the number of classes that participants signed in for at the Bikram yoga studio or the Kingston Family YMCA.

Table 6

*Physiological Variables Stratified by Group Assignment*

	Yoga	Exercise	Waitlist	<i>F</i>	<i>p</i>
Pre-T <sub>x</sub> HR baseline (bpm; <i>M/SD</i> )	61.96/9.41	68.77/16.24	68.63/6.22	1.36	.273
Pre-T <sub>x</sub> HR reactivity ( <i>M/SD</i> )	.40/.26	.25/.17	.29/.11	1.76	.190
Pre-T <sub>x</sub> MAP baseline (mm Hg; <i>M/SD</i> )	95.62/11.91	102.63/14.10	93.88/11.70	1.17	.327
Pre-T <sub>x</sub> MAP reactivity ( <i>M/SD</i> )	.19/.09	.17/.11	.23/.13	.793	.463
Pre-T <sub>x</sub> CORT baseline (μd/dL; <i>M/SD</i> )	0.14/0.06	0.17/0.14	0.21/0.17	.827	.448
Pre-T <sub>x</sub> CORT reactivity ( <i>M/SD</i> )	.01/.37	.31/.90	-.01/.23	.974	.390
Pre-T <sub>x</sub> AUC <sub>i</sub> (μd/dL; <i>M/SD</i> )	-1.24/3.93	1.99/3.93	-0.69/2.63	1.65	.210
Post-T <sub>x</sub> HR baseline (bpm; <i>M/SD</i> )	63.08/10.47	70.95/14.45	66.13/8.09	1.37	.271
Post-T <sub>x</sub> HR reactivity ( <i>M/SD</i> )	.34/.19	.14/.08	.27/.15	4.99	.014
Post-T <sub>x</sub> MAP baseline (mm Hg; <i>M/SD</i> )	85.72/13.55	95.08/16.28	88.16/13.70	1.14	.334
Post-T <sub>x</sub> MAP reactivity ( <i>M/SD</i> )	.16/.08	.11/.05	.17/.11	1.27	.297
Post-T <sub>x</sub> CORT baseline (μd/dL; <i>M/SD</i> )	0.18/0.14	0.20/0.17	0.18/0.12	.06	.943
Post-T <sub>x</sub> CORT reactivity ( <i>M/SD</i> )	-.14/.18	-.06/.15	-.08/.18	.68	.517
Post-T <sub>x</sub> AUC <sub>i</sub> (μd/dL; <i>M/SD</i> )	-4.27/6.35	-2.33/5.78	-2.76/5.49	.99	.385

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment; HR baseline = baseline heart rate; HR reactivity = heart rate reactivity; MAP baseline = baseline mean arterial pressure; MAP reactivity = mean arterial pressure reactivity; CORT baseline = baseline cortisol (sample 2); CORT reactivity = cortisol reactivity ((sample 4 – sample 2)/sample 2); AUC<sub>i</sub> = area under the curve with respect to increase. Untransformed cortisol data were used for the derivation of cortisol variables.

***Relations Among Physiological Stress Reactivity Variables.*** Bivariate correlations among the physiological stress reactivity variables at pre- and post-treatment are displayed in Table 7. Pre-treatment HR reactivity was positively correlated with pre-treatment MAP reactivity, post-treatment HR reactivity, and post-treatment CORT reactivity. Pre-treatment MAP reactivity was also positively associated with both post-treatment MAP reactivity and post-treatment CORT reactivity and negatively associated with post-treatment AUC<sub>i</sub>. Finally, negative correlations emerged between pre-treatment CORT reactivity and pre-treatment AUC<sub>i</sub> and between post-treatment CORT reactivity and post-treatment AUC<sub>i</sub>.

Table 7

*Correlations for Physiological Stress Reactivity Variables at Pre- and Post-Treatment*

	Pre-T <sub>x</sub> HR reactivity	Pre-T <sub>x</sub> MAP reactivity	Pre-T <sub>x</sub> CORT reactivity	Pre-T <sub>x</sub> AUC <sub>i</sub>	Post-T <sub>x</sub> HR reactivity	Post-T <sub>x</sub> MAP reactivity	Post-T <sub>x</sub> CORT reactivity
Pre-T <sub>x</sub> MAP reactivity	.38*						
Pre-T <sub>x</sub> CORT reactivity	.32	.03					
Pre-T <sub>x</sub> AUC <sub>i</sub>	-.31	-.05	-.85***				
Post-T <sub>x</sub> HR reactivity	.57**	.11	.31	-.11			
Post-T <sub>x</sub> MAP reactivity	.31	.40*	-.08	.08	.18		
Post-T <sub>x</sub> CORT reactivity	.43*	.43*	.31	-.24	.05	.03	
Post-T <sub>x</sub> AUC <sub>i</sub>	-.27	-.44*	-.15	.18	-.04	-.01	-.71***

*Note.* Untransformed cortisol data were used for the derivation of variables in these bivariate correlations. Pre-T<sub>x</sub> = measurement at pre-treatment;

Post-T<sub>x</sub> = measurement at post-treatment; HR reactivity = heart rate reactivity; MAP reactivity = mean arterial pressure reactivity; Cort reactivity = cortisol reactivity ((sample 4 – sample 2)/(sample 2)); AUC<sub>i</sub> = area under the curve with respect to increase.

\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

**Identification of Covariates.** Relationships among post-treatment measurements of the physiological stress reactivity variables (i.e., HR reactivity, MAP reactivity, CORT reactivity, AUC<sub>i</sub>) and demographic/clinical variables were examined in a series of bivariate correlations and independent samples *t*-tests (see Table 8). This was done to identify covariates for analyses involving group differences in the physiological stress reactivity variables, as well as analyses investigating the mediating role of these variables in the antidepressant effects of yoga and exercise. VO<sub>2</sub>max was also examined as a potential covariate, as it has been suggested that this measure of aerobic capacity may be important to consider in terms of the antidepressant effects of physical therapy approaches (e.g., Blumenthal et al., 1999). Associations between the potential covariates and the outcome variable of the mediation analyses (i.e., post-treatment HAM-D scores) were also examined.

As shown in Table 8, there was a significant negative correlation between post-treatment HR reactivity and age and a significant positive association between post-treatment MAP reactivity and total number of episodes. Therefore, age and total number of episodes were included in subsequent analyses involving post-treatment levels of HR reactivity and MAP reactivity, respectively. Post-treatment CORT reactivity was negatively associated with both age and pre-treatment BMI. As well, it differed significantly across relationship status. That is, participants who were married had significantly lower reactivity compared to those who were unmarried ( $M = .01, SD = .05$  vs.  $M = .16, SD = .24$ ). Age, pre-treatment BMI, and relationship status were entered as covariates in subsequent analyses involving CORT reactivity. AUC<sub>i</sub> was positively correlated with age, age of onset of initial depressive episode, and pre-treatment BMI. It was also significantly related to relationship status and comorbidity. That is, participants who were married had significantly greater AUC<sub>i</sub> than participants who were unmarried ( $M = -0.27,$

$SD = 6.70$  vs.  $M = -7.51$ ,  $SD = 7.75$ ). Further, those with a comorbid disorder had significantly lower  $AUC_i$  than those without a comorbid disorder ( $M = -9.62$ ,  $SD = 6.22$  vs.  $M = -2.37$ ,  $SD = 7.95$ ). Age, relationship status, age of initial onset, pre-treatment BMI, and comorbidity were, therefore, included as covariates in subsequent analyses involving  $AUC_i$ . Finally, no significant associations emerged between post-treatment HAM-D scores and any of the potential covariates ( $ps \geq .075$ ; not displayed in a table).

Table 8

*Relations Between Demographic and Clinical Characteristics and Post-Treatment Measurements of**Physiological Stress Reactivity Variables*

	Post-T <sub>x</sub> HR reactivity		Post-T <sub>x</sub> MAP reactivity		Post-T <sub>x</sub> CORT reactivity		Post-T <sub>x</sub> AUC <sub>i</sub>				
	<i>r</i>	<i>t</i>	<i>r</i>	<i>t</i>	<i>r</i>	<i>t</i>	<i>r</i>	<i>t</i>			
Age	-.39		.029		.634		.048		.37		.040
Ethnicity		-0.89		-0.91		-0.19		.848		-0.10	.924
Highest education level		0.59		-1.25		1.87		.072		-1.46	.156
Relationship status		1.80		-1.05		2.66		.014		-2.61	.014
Pre-T <sub>x</sub> BMI	-.34		.060		.937		.038		.36		.046
Age of onset	-.12		.505		.810		.164		.55		.001
Total # of episodes	-.20		.265		.049		.361		-.03		.855
Pre-T <sub>x</sub> BDI	.27		.151		.603		.627		-.14		.466
Current treatment		0.33		0.89		0.83		.413		0.61	.547
Comorbid disorder		0.89		0.76		-1.87		.071		2.61	.014
$\Delta VO_2$ max	-.16		.375		.321		.988		.15		.420

*Note.* Log transformed cortisol data were used for the derivation of variables in these analyses. Post-T<sub>x</sub> HR

reactivity = heart rate reactivity at post-treatment; Post-T<sub>x</sub> MAP reactivity = mean arterial pressure reactivity at

post-treatment; Post-T<sub>x</sub> CORT reactivity = cortisol reactivity ([sample 4 – sample 2]/sample 2) at post-

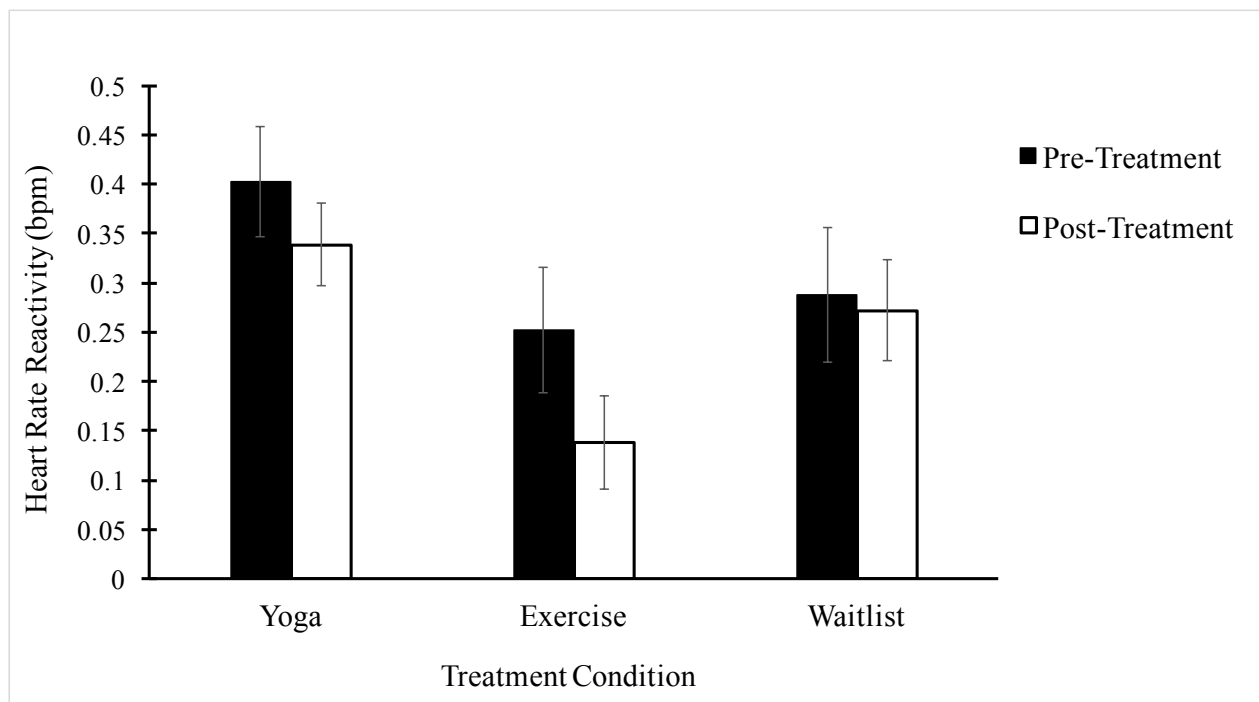
treatment; Post-T<sub>x</sub> AUC<sub>i</sub> = area under the curve with respect to increase at post-treatment; Pre-T<sub>x</sub> BMI = body

mass index at pre-treatment; Pre-T<sub>x</sub> BDI = Beck Depression Inventory-II scores at pre-treatment;  $\Delta VO_2$ max =

percent change in maximal oxygen uptake from pre- to post-treatment.

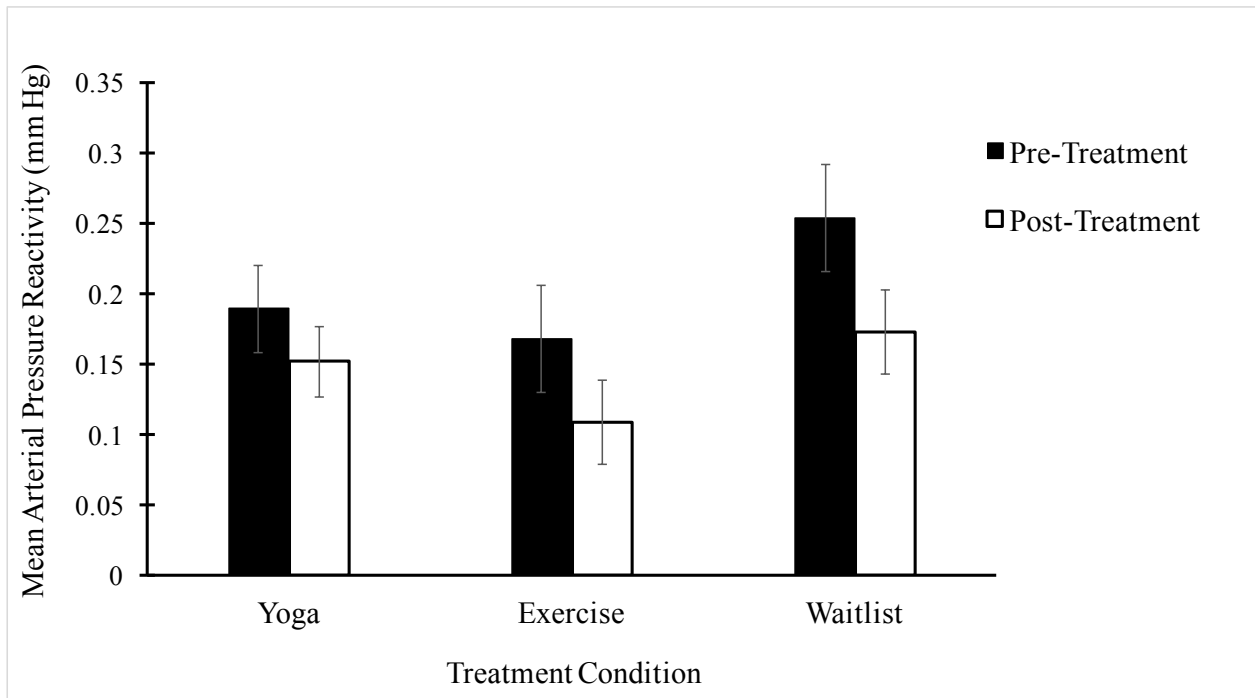
### Primary Analyses: Group Differences in Changes in Physiological Stress Reactivity

**Variables.** Pre- to post-treatment changes in the physiological stress reactivity variables were assessed with repeated-measures ANCOVAs. This allowed for the examination of the effect of treatment group (i.e., yoga vs. aerobic exercise vs. waitlist) on the dependent variable of time (i.e., pre- vs. post-treatment values of physiological variables), over and above any relevant covariates. For the analysis involving HR reactivity as the within-subjects' variables, the inclusion of age as a covariate did not change the pattern of results; therefore, the uncontrolled analysis is presented. Neither the main effect of time ( $p = .053$ ) nor the group by time interaction were significant ( $p = .508$ ).



**Fig. 8.** Mean heart rate reactivity (in bpm) by group assignment and time.

For the analysis involving MAP reactivity, the inclusion of total number of episodes did not change the pattern of results; therefore, the covariate was dropped from the model. In the uncontrolled model, the main effect of time was significant,  $F(1, 25) = 7.41, p = .012$ , partial  $\eta^2 = .229$ , such that MAP reactivity decreased from pre- to post-treatment ( $M = .20, SE = .02$  vs.  $M = .15, SE = .02$ ; see Figure 9). No significant group by time interaction emerged ( $p = .685$ ).

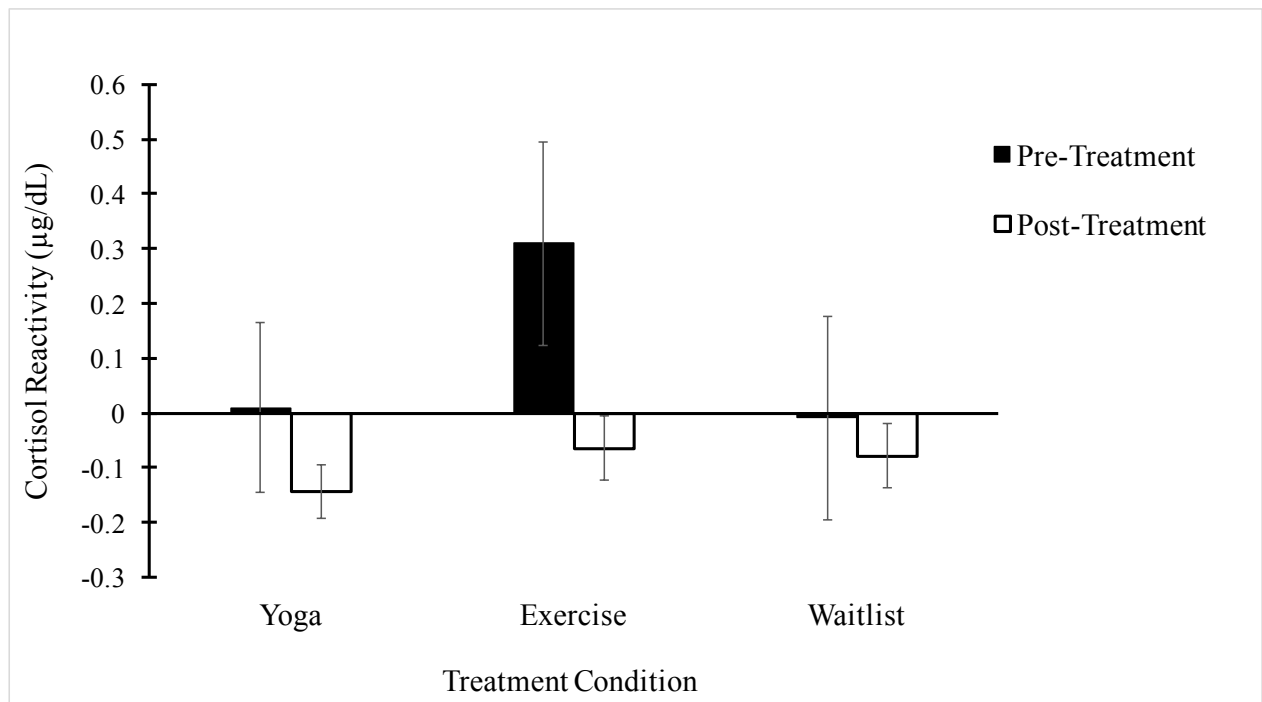


**Fig. 9.** Average mean arterial pressure reactivity (in mm Hg) by group assignment and time.

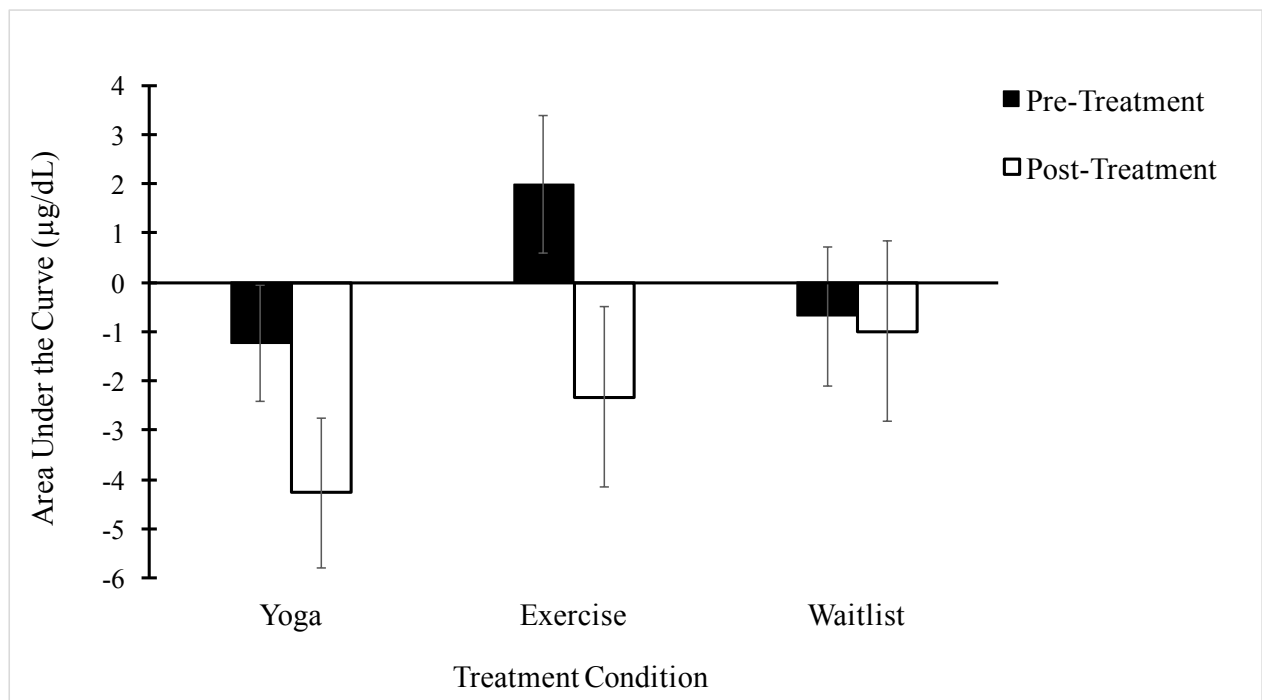
For the analyses involving pre- to post-treatment changes in CORT reactivity or  $AUC_i$ , several models were run for each cortisol variable given the number of relevant covariates. In addition to an uncontrolled model, all covariates were tested separately, as well as together in a fully controlled model. In the uncontrolled model of cortisol reactivity, there was a significant main effect of time,  $F(1, 28) = 5.96, p = .021$ , partial  $\eta^2 = .176$ . That is, CORT reactivity decreased from pre- to post-treatment ( $M = 0.10, SE = 0.10$  vs.  $M = .08, SE = .10$ ). The group by time interaction was not significant ( $p = .525$ ). See Figure 10 for the uncontrolled model's

estimated marginal means of untransformed CORT reactivity. Inclusion of either age or relationship status did not alter the pattern of results. However, when pre-treatment BMI was entered as a covariate, the main effect of time did not hold ( $p = .192$ ). Similarly, in the fully controlled model, neither the main effect of time nor the group by time interaction were significant ( $ps > .163$ ).

In the uncontrolled model of  $AUC_i$ , neither the main effect of time nor the interaction were significant ( $ps \geq .200$ ). See Figure 11 for estimated marginal means for untransformed  $AUC_i$  values in this model. The addition of the covariates (age, relationship status, pre-treatment BMI, age of initial onset, comorbidity) resulted in nonsignificant effects in terms of the group by time interaction ( $ps \geq .160$ ). However, a significant main effect of time emerged with the inclusion of either relationship status,  $F(1, 27) = 5.31, p = .029$ , partial  $\eta^2 = .164$ , or age of initial onset,  $F(1, 27) = 15.53, p = .001$ , partial  $\eta^2 = .365$ . In both models,  $AUC_i$  significantly decreased from pre- to post-treatment (relationship status:  $M = -1.66, SE = 1.67$  vs.  $M = -4.33, SE = 1.22$ ; age of initial onset:  $M = -1.60, SE = 1.61$  vs.  $M = -4.46, SE = 1.18$ ).



**Fig. 10.** Mean cortisol reactivity (in µg/dL) by group assignment and time.



**Fig. 11.** Mean cortisol exposure (in µg/dL) by group assignment and time.

**Primary Analyses: Mediation of Antidepressant Effects via Changes in Physiological Stress Reactivity Variables.** Table 9 shows the parameter estimates for separate mediation analyses involving HR reactivity and MAP reactivity. For the analysis involving HR reactivity (see top panel of Table 9), the inclusion of age as a covariate did not change the pattern of results; therefore, results from the model controlling for only pre-treatment HR reactivity and pre-treatment HAM-D scores are presented. Over and above the effects of the covariates, post-treatment HR reactivity did not differ significantly when either active treatment condition was compared to the waitlist group. Further, post-treatment HR reactivity did not significantly predict post-treatment HAM-D scores. As can be seen from the table, the indirect effect (i.e., mediating effect) of treatment group with respect to post-treatment HAM-D scores was not significant for either of the pairwise comparisons.

Similar null findings were found when MAP reactivity was entered as the mediator (see bottom panel of Table 9). The inclusion of total number of depressive episodes did not affect the pattern of results; therefore, results with the exclusion of this covariate are presented. The difference in post-treatment MAP reactivity was not significant for the comparison of either yoga or exercise relative to the waitlist group. As well, post-treatment MAP reactivity was not a significant predictor of post-treatment HAM-D scores. The indirect effects of the treatment group comparisons on post-treatment HAM-D scores were not significant.

Table 9

*Regression Coefficients, Standard Errors, and Model Summary Information for Mediation Models With Heart Rate Reactivity and Mean Arterial Pressure Reactivity*

	Post-T <sub>x</sub> HR reactivity ( <i>M</i> )			Post-T <sub>x</sub> HAM-D ( <i>Y</i> )			Indirect effects on <i>Y</i>		
	Coeff	SE	<i>p</i>	Coeff	SE	<i>p</i>	Coeff	SE	95% CI
Constant	0.12	0.11	.264	8.93	4.67	.067			
Yoga vs. waitlist ( <i>D</i> <sub>1</sub> )	0.02	0.06	.729	-7.18	2.53	.009	-0.03	0.58	-1.50, 0.96
Exercise vs. waitlist ( <i>D</i> <sub>2</sub> )	-0.11	0.06	.088	-9.84	2.84	.002	0.15	1.03	-1.61, 2.65
Pre-T <sub>x</sub> HR reactivity	0.39	0.12	.004	-4.47	6.03	.466			
Pre-T <sub>x</sub> HAM-D	0.00	0.00	.691	0.58	0.31	.071			
Post-T <sub>x</sub> HR reactivity ( <i>M</i> )				-1.32	8.08	.872			
							$R^2 = .46$		
							$F(4, 27) = 5.67, p = .002$		
							$F(5, 26) = 4.50, p = .004$		
	Post-T <sub>x</sub> MAP reactivity ( <i>M</i> )			Post-T <sub>x</sub> HAM-D ( <i>Y</i> )			Indirect effects on <i>Y</i>		
	Coeff	SE	<i>p</i>	Coeff	SE	<i>p</i>	Coeff	SE	95% CI
Constant	0.20	0.08	.021	9.30	6.13	.144			
Yoga vs. waitlist ( <i>D</i> <sub>1</sub> )	-0.00	0.04	.909	-9.19	2.61	.002	-0.03	0.87	-1.35, 2.30
Exercise vs. waitlist ( <i>D</i> <sub>2</sub> )	-0.06	0.04	.185	-10.07	3.17	.004	-0.38	1.38	-3.58, 2.25
Pre-T <sub>x</sub> MAP reactivity	0.30	0.15	.054	-13.06	11.17	.255			
Pre-T <sub>x</sub> HAM-D	-0.01	0.01	.159	0.67	0.37	.084			
Post-T <sub>x</sub> MAP reactivity ( <i>M</i> )				6.35	14.33	.662			
							$R^2 = .26$		
							$F(4, 23) = 2.06, p = .119$		
							$F(5, 22) = 4.63, p = .005$		

*Note.* *M* represents the mediator variable; *Y* represents the dependent variable; *D*<sub>1</sub> and *D*<sub>2</sub> represent dummy variables. Waitlist group was coded as reference group. Coeff = unstandardized regression coefficient; Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment; HR reactivity = heart rate reactivity; MAP reactivity = mean arterial pressure; HAM-D = Hamilton Rating Scale for Depression scores.

The mediation analysis with CORT reactivity also led to nonsignificant path coefficients and indirect effects. Additional covariates did not change the pattern of results; therefore, mediation results controlling for only pre-treatment CORT reactivity and pre-treatment HAM-D scores are presented (see top panel of Table 10). Post-treatment CORT reactivity did not differ significantly across the pairwise group comparisons, and post-treatment CORT reactivity was not significantly associated with post-treatment HAM-D scores. Consistent with this, the indirect effect of treatment group on post-treatment HAM-D scores was not significant for either of the pairwise comparisons, indicating the absence of a mediating effect.

Finally, for the mediation analysis involving  $AUC_i$ , age and relationship status emerged as covariates that slightly changed the pattern of results compared to the uncontrolled model. Therefore, results controlling for age and relationship status, as well as pre-treatment  $AUC_i$  and pre-treatment HAM-D scores, are presented (see bottom panel of Table 10). Post-treatment  $AUC_i$  values were significantly lower in the yoga group compared to the waitlist group but did not differ between the exercise and waitlist groups. The association between post-treatment  $AUC_i$  and post-treatment HAM-D scores failed to reach significance. Consistent with this, the indirect effects of the treatment group comparisons on post-treatment HAM-D scores were not significant.

Table 10

Regression Coefficients, Standard Errors, and Model Summary Information for Mediation Models with Cortisol Reactivity and Area Under the Curve with Respect to Increase

	Post-T <sub>x</sub> CORT reactivity (M)		Post-T <sub>x</sub> HAM-D (Y)		Indirect effects on Y		
	Coeff	SE	Coeff	SE	Coeff	SE	95% CI
Constant	-0.03	0.16	8.69	4.26			
Yoga vs. waitlist (D <sub>1</sub> )	0.09	0.09	-8.01	2.44	0.35	0.72	-0.65, 2.21
Exercise vs. waitlist (D <sub>2</sub> )	0.07	0.10	-11.23	2.80	0.29	0.75	-0.99, 2.07
Pre-T <sub>x</sub> CORT reactivity (C <sub>1</sub> )	0.30	0.19	-3.68	5.34			
Pre-T <sub>x</sub> HAM-D (C <sub>2</sub> )	0.01	0.01	0.45	0.31			
Post-T <sub>x</sub> CORT reactivity (M)			4.07	5.26			
		$R^2 = .14$					$R^2 = .50$
		$F(4, 26) = 1.08, p = .388$					$F(5, 25) = 4.97, p = .003$
	Post-T <sub>x</sub> AUC <sub>1</sub> (M)		Post-T <sub>x</sub> HAM-D (Y)		Indirect effects on Y		
	Coeff	SE	Coeff	SE	Coeff	SE	95% CI
Constant	-7.40	7.09	5.77	5.23			
Yoga vs. waitlist (D <sub>1</sub> )	-7.64	3.18	-9.47	2.56	2.18	1.57	-0.27, 5.79
Exercise vs. waitlist (D <sub>2</sub> )	-0.91	3.69	-11.77	2.66	0.26	1.59	-3.64, 3.02
Pre-T <sub>x</sub> AUC <sub>1</sub> (C <sub>1</sub> )	0.07	0.15	0.22	0.11			
Pre-T <sub>x</sub> HAM-D (C <sub>2</sub> )	0.19	0.39	0.53	0.29			
Age (C <sub>3</sub> )	0.04	0.17	0.05	0.12			
Relationship status (C <sub>4</sub> )	7.34	4.65	2.16	3.53			
Post-T <sub>x</sub> AUC <sub>1</sub> (M)			-0.29	0.15			
		$R^2 = .40$					$R^2 = .61$
		$F(6, 24) = 2.66, p = .040$					$F(7, 23) = 5.16, p = .001$

Note. M represents the mediator variable; Y represents the dependent variable; D<sub>1</sub> and D<sub>2</sub> represent dummy variables (waitlist coded as reference group); C variables represent covariates. Coeff = unstandardized regression coefficient; Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment; CORT reactivity = cortisol reactivity ([sample 4 – sample 2]/[sample 2]); AUC<sub>1</sub> = area under the curve with respect to at pre-treatment; HAM-D = Hamilton Rating Scale for Depression scores.

**Preliminary Analyses: Psychological Variables.** Examinations of psychological mechanisms, including changes in levels of perceived hassles, rumination, and mindfulness, were conducted on the sample of 42 completers. No data were missing for pre-treatment measurements of the psychological variables; however, some data were missing from weeks 1 to 8. This may have been partly owing to the method of data collection (i.e., collected via online questionnaires). Each week, participants were emailed a link that took them to an online battery of questionnaires that was coded by participant number. Research personnel did not check to ensure that the questionnaires had been completed each week and, therefore, did not subsequently follow-up with a participant if she had not completed them. An investigation of the pattern of missing data led to the assumption that the data were missing at random. In subsequent analyses using MLM, the presence of missing data at Level 1 was specified during model building and addressed during the running of analyses. It was not handled with any other method prior to MLM. For subsequent mediation analyses involving changes in psychological variables across the intervention period, missing data at week 8 (i.e., post-treatment;  $n = 6$ ) were addressed with the last observation carried forward method. This method was chosen over multiple imputation, as the PROCESS macro for mediation is not compatible with an imputed dataset.

As displayed in Table 11, there were no significant differences between groups on psychological variables at pre-treatment. At post-treatment, significant group differences emerged for rumination,  $F(2, 39) = 9.60, p < .001$ , and acceptance,  $F(2, 39) = 4.32, p = .020$ . Post-hoc comparisons using the Tukey HSD test revealed that compared to the waitlist group, post-treatment rumination scores were lower in both the yoga group ( $p = .028$ ), and the exercise group ( $p < .001$ ). Further, acceptance was significantly higher in the exercise group compared to the waitlist group ( $p = .015$ ).

Table 11

*Psychological Variables Stratified by Group Assignment*

	Yoga	Exercise	Waitlist	<i>F</i>	<i>p</i>
Pre-T <sub>x</sub> hassles ( <i>M/SD</i> )	61.47/30.03	52.43/25.31	63.25/24.80	0.63	.540
Pre-T <sub>x</sub> rumination ( <i>M/SD</i> )	61.60/12.10	53.93/15.10	61.42/9.01	1.76	.185
Pre-T <sub>x</sub> awareness ( <i>M/SD</i> )	36.13/4.70	35.80/6.37	36.17/7.09	0.02	.984
Pre-T <sub>x</sub> acceptance ( <i>M/SD</i> )	22.80/5.10	25.47/6.59	21.25/5.40	1.88	.166
Post-T <sub>x</sub> hassles (bpm; <i>M/SD</i> )	26.00/17.89	24.50/4.51	30.58/15.72	0.45	.644
Post-T <sub>x</sub> rumination ( <i>M/SD</i> )	44.07/13.51	36.67/8.66	55.92/13.55	9.60	.000
Post-T <sub>x</sub> awareness ( <i>M/SD</i> )	37.53/8.11	35.47/8.09	33.58/5.18	0.96	.392
Post-T <sub>x</sub> acceptance ( <i>M/SD</i> )	28.20/7.74	31.33/6.76	23.75/4.81	4.32	.020

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment; Missing data at post-treatment (*n* = 6) were addressed with the last observation carried forward method.

***Relations Among Psychological Variables.*** Bivariate correlations among the psychological variables at pre- and post-treatment are displayed in Table 12. Pre-treatment hassles scores were positively correlated with post-treatment hassles scores, pre-treatment rumination, and post-treatment awareness levels. As well, hassles scores at pre-treatment were negatively associated with pre- and post-treatment acceptance levels. Pre- and post-treatment acceptance scores were positively correlated with each other and negatively correlated with pre-treatment rumination. A negative association also emerged between post-treatment levels of rumination and acceptance. Pre-treatment scores on both rumination and awareness were positively correlated with post-treatment awareness levels. Finally, consistent with the pre-treatment association, a positive association was found between post-treatment scores on hassles and rumination.

Table 12

*Correlations for Psychological Variables at Pre- and Post-Treatment*

	Pre-T <sub>x</sub> hassles	Pre-T <sub>x</sub> rumination	Pre-T <sub>x</sub> awareness	Pre-T <sub>x</sub> acceptance	Post-T <sub>x</sub> hassles	Post-T <sub>x</sub> rumination	Post-T <sub>x</sub> awareness
Pre-T <sub>x</sub> rumination	.61***						
Pre-T <sub>x</sub> awareness	.03	.10					
Pre-T <sub>x</sub> acceptance	-.44**	-.56***	.05				
Post-T <sub>x</sub> hassles	.42**	.13	-.02	-.09			
Post-T <sub>x</sub> rumination	.06	.23	-.10	-.08	.42**		
Post-T <sub>x</sub> awareness	.36*	.36*	.41**	.01	.18	.00	
Post-T <sub>x</sub> acceptance	-.34*	-.35*	.13	.42**	-.24	-.58***	-.12

Note. Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment.

\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

***Identification of Covariates.*** Relationships among the psychological variables and demographic/clinical variables were assessed in a series of bivariate correlations and independent samples *t*-tests (see Tables 13-16). Consistent with analyses involving physiological stress reactivity variables, VO<sub>2</sub>max was also examined as a potential covariate. For covariates relevant to subsequent MLM analyses, I examined relations of the variables to both pre- and post-treatment measurements of each psychological variable. For mediation analyses, I was interested in covariates associated with the post-treatment measurement of each psychological variable, as well as those associated with the outcome variable of the mediation models (i.e., post-treatment HAM-D scores; not displayed in a table). Since the last observation carried forward method was used to address missing data prior to testing mediation models but not MLM, these preliminary analyses for their respective primary analyses were conducted on slightly different data (or subsamples) with respect to post-treatment measurements (i.e.,  $n = 42$  vs.  $n = 36$ ) and are differentiated in the tables.

As displayed in Table 13, there was a significant positive correlation between pre-treatment hassles and BDI scores. Age was positively correlated with post-treatment hassles for both subsamples. Within the subsample used for mediation analyses, post-treatment hassles scores were also positively associated with total number of depressive episodes. Therefore, pre-treatment BDI scores and age were entered in MLM models involving hassles, and age and total number of depressive episodes were entered in the mediation model.

Table 13

*Relations Between Demographic and Clinical Characteristics and Pre- and Post-Treatment Measurements of Hassles*

	Pre-T <sub>x</sub> hassles			Post-T <sub>x</sub> hassles (n = 36)			Post-T <sub>x</sub> hassles (n = 42)		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>
Age	.03		.875	.48		.007	.35		.025
Ethnicity		0.37	.715		1.31	.200		1.03	.311
Highest education level		0.70	.491		0.46	.646		0.26	.795
Relationship status		0.20	.843		-0.20	.841		-0.52	.607
Pre-T <sub>x</sub> BMI	-.03		.837	-.10		.548	.01		.954
Age of onset	-.08		.600	-.07		.692	-.12		.444
Total # of episodes	.07		.682	.22		.205	.33		.031
Pre-T <sub>x</sub> BDI	.46		.002	.17		.332	.009		.957
Current treatment		-0.28	.783		0.37	.717		0.42	.679
Comorbid disorder		-0.55	.586		0.04	.973		0.63	.532
ΔVO <sub>2</sub> max	-.01		.943	-.13		.519	-.07		.712

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment. BMI = body mass index; BDI = Beck Depression Inventory-II scores; ΔVO<sub>2</sub>max = percent change in maximal oxygen uptake from pre- to post-treatment.

Table 14 displays relationships among rumination variables and potential covariates. Pre-treatment rumination scores were negatively correlated with age, pre-treatment BDI scores, age of onset of initial depressive episode, and total number of episodes. As well, rumination scores at pre-treatment differed significantly across relationship status. Participants who were married had significantly lower initial levels of rumination compared to those who were unmarried ( $M = 50.33$ ,  $SD = 10.64$  vs.  $M = 64.35$ ,  $SD = 10.86$ ). Post-treatment rumination scores, regardless of subsample, were not significantly associated with any demographic or clinical variables. As such, age, pre-treatment BDI scores, age of onset of initial depressive episode, total number of depressive episodes, and relationship status were included in subsequent MLM analyses

involving rumination. No covariates were included in the mediation model.

Table 14

*Relations Between Demographic and Clinical Characteristics and Pre- and Post-Treatment Measurements of Rumination*

	Pre-T <sub>x</sub> rumination			Post-T <sub>x</sub> rumination (n = 36)			Post-T <sub>x</sub> rumination (n = 42)		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>
Age	-.39		.011	-.05		.759	-.08		.614
Ethnicity		-0.08	.933		1.10	.279		0.31	.762
Highest education level		2.92	.005		1.42	.164		1.36	.181
Relationship status		4.00	.000		1.25	.220		1.52	.138
Pre-T <sub>x</sub> BMI	-.11		.486	-.21		.223	-.22		.157
Age of onset	-.15		.358	-.30		.078	-.27		.088
Total # of episodes	-.31		.043	.06		.725	.07		.669
Pre-T <sub>x</sub> BDI	.64		.000	.08		.630	.17		.286
Current treatment		0.31	.758		-0.89	.379		-0.59	.560
Comorbid disorder		-1.92	.062		1.82	.077		0.98	.334
ΔVO <sub>2</sub> max	.03		.875	-.21		.289	-.25		.175

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment. BMI = body mass index; BDI = Beck Depression Inventory-II scores; ΔVO<sub>2</sub>max = percent change in maximal oxygen uptake from pre- to post-treatment.

Tables 15 and 16 display results pertaining to mindful awareness and acceptance, respectively. None of the awareness variables were significantly associated with any of the potential covariates. Similarly, post-treatment acceptance levels, regardless of subsample, were not related to any demographic or clinical variables. Pre-treatment acceptance scores, however, were positively correlated with age and negatively correlated with pre-treatment BDI scores. As well, participants who were married had significantly higher levels of acceptance than those who were not married ( $M = 25.87, SD = 5.67$  vs.  $M = 21.88, SD = 5.71$ ). Age, pre-treatment BDI scores, and relationship status were, therefore, included as covariates in MLM models of

acceptance.

Finally, post-treatment HAM-D scores were negatively correlated with age of onset of initial depressive episode,  $r(42) = -.36, p = .019$ . Therefore, age of onset was included in mediation models across all psychological variables.

Table 15

*Relations Between Demographic and Clinical Characteristics and Pre- and Post-Treatment Measurements of Awareness*

	Pre-T <sub>x</sub> awareness			Post-T <sub>x</sub> awareness ( <i>n</i> = 36)			Post-T <sub>x</sub> awareness ( <i>n</i> = 42)		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>
Age	-.08		.602	.02		.901	-.01		.936
Ethnicity		-1.95	.059		-1.58	.124		-1.38	.176
Highest education level		0.65	.519		0.98	.332		1.46	.154
Relationship status		0.56	.581		-0.11	.914		0.22	.830
Pre-T <sub>x</sub> BMI	-.09		.590	-.31		.070	-.28		.073
Age of onset	.10		.543	.20		.249	.13		.411
Total # of episodes	-.12		.444	-.17		.322	-.15		.329
Pre-T <sub>x</sub> BDI	.00		.996	.17		.311	.13		.400
Current treatment		0.75	.456		1.22	.232		1.71	.095
Comorbid disorder		0.34	.734		0.09	.926		-0.13	.898
ΔVO <sub>2</sub> max	-.11		.572	.10		.616	.12		.509

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment. BMI = body mass index; BDI = Beck Depression Inventory-II scores; ΔVO<sub>2</sub>max = percent change in maximal oxygen uptake from pre- to post-treatment.

Table 16

*Relations Between Demographic and Clinical Characteristics and Pre- and Post-Treatment Measurements of Acceptance*

	Pre-T <sub>x</sub> acceptance			Post-T <sub>x</sub> acceptance (n = 36)			Post-T <sub>x</sub> acceptance (n = 42)		
	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>	<i>r</i>	<i>t</i>	<i>p</i>
Age	.37		.017	-.16		.353	-.05		.758
Ethnicity		-1.05	.299		0.89	.378		0.46	.647
Highest education level		-1.42	.164		-0.12	.903		-0.44	.665
Relationship status		-2.16	.037		0.21	.837		-0.41	.685
Pre-T <sub>x</sub> BMI	-.09		.586	.08		.649	.11		.493
Age of onset	.17		.269	-.10		.583	-.09		.579
Total # of episodes	.16		.314	-.19		.260	-.13		.410
Pre-T <sub>x</sub> BDI	-.43		.004	-.02		.907	-.15		.359
Current treatment		-0.08	.938		0.21	.835		0.08	.933
Comorbid disorder		0.91	.368		-1.25	.220		-1.28	.209
ΔVO <sub>2</sub> max	.03		.864	.30		.125	.323		.077

*Note.* Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment. BMI = body mass index; BDI = Beck Depression Inventory-II scores; ΔVO<sub>2</sub>max = percent change in maximal oxygen uptake from pre- to post-treatment.

### **Primary Analyses: Group Differences in Psychological Variables Using Multilevel**

**Models.** See Tables 17-20 for fixed and random effect estimates of the multilevel models. Only effects from the first iteration of each model, with time coded such that the intercept of the model represented values of the psychological variable at post-treatment, are displayed in the tables.

That is, the pairwise comparisons of yoga versus waitlist and exercise versus waitlist, in terms of post-treatment intercepts and slopes, are presented. These comparisons are displayed in the tables as they were most germane to the hypotheses made. The second iteration of the model, which allowed for the comparison of yoga versus exercise, resulted in different values for the intercept of the intercept and the intercept of the slope. This is to be expected given that different dummy

variables were entered. For ease of interpretability, estimates from the comparison of yoga versus exercise from the second iteration of the model are presented in the text rather than in tables.

Further, since no group differences in the psychological variables at pre-treatment were expected, fixed effects for pre-treatment intercepts are presented in the text if they reached significance.

***Perceived Hassles.*** In the model of hassles, only age emerged as a significant covariate. Therefore, the other covariates (i.e., ethnicity, total number of episodes, pre-treatment BDI) were dropped from the model and the controlled analysis with age is presented (see Table 17). At both pre- and post-treatment, the intercept of the intercept was significant (pre-treatment: coefficient = 51.97,  $p < .001$ ; see Table 17 for post-treatment values), indicating that hassles scores at the start and end of treatment were significantly different from zero. The intercept of the slope was also significant, implying that the rate of linear change in hassles from pre- to post-treatment was significantly different from zero. In terms of group differences, participants in the exercise group had significantly lower scores at post-treatment than those in the waitlist group. Age was significant with respect to the post-treatment intercept, indicating that an older chronological age was associated with greater hassles scores at the end of treatment. At pre-treatment, there were no significant differences in intercepts across any of the pairwise comparisons ( $ps \geq .147$ ). Despite the significant post-treatment difference between exercise and the waitlist group, their slopes did not differ significantly. There were no differences in post-treatment intercepts or slopes for yoga versus waitlist (see Table 17) or for yoga versus exercise (intercept: coefficient = 5.40,  $p = .344$ ; slope: coefficient = 0.01,  $p = .997$ ). Figure 12 shows the linear trajectories estimated from the MLM stratified by treatment group.<sup>8</sup>

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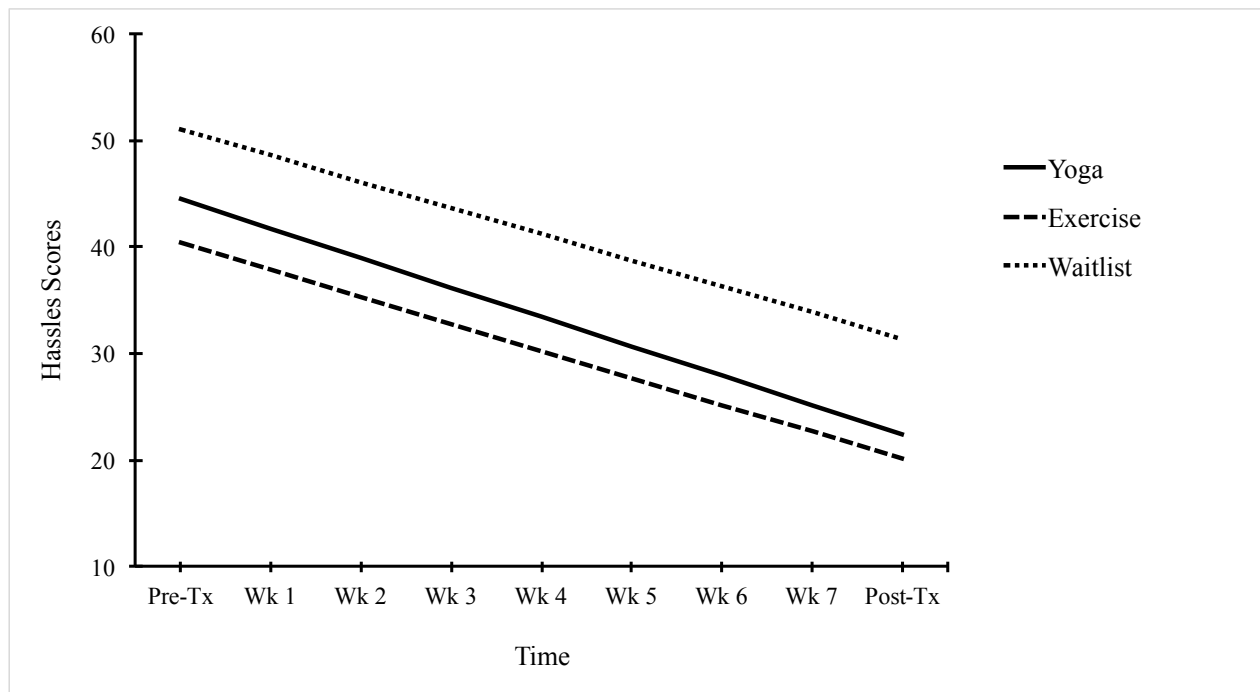
<sup>8</sup> The estimates presented in this figure, as well as subsequent figures for the other psychological variables examined with MLM, were derived from the multilevel model results. Therefore, these estimates do not reflect the actual pre- and post-treatment values, stratified by treatment group, as demonstrated in Table 11.

Table 17

*Parameter Estimates for the Multilevel Model of Hassles, Controlling for Age*

	Coefficient	SE	<i>t</i>	<i>p</i>
<b>Fixed effects</b>				
Post-T <sub>x</sub> intercept				
Intercept	33.84	4.55	7.44	<.001
Yoga vs. waitlist	-10.85	5.94	-1.83	.076
Exercise vs. waitlist	-16.24	6.23	-2.61	.013
Age	0.53	0.17	3.21	.003
Pre- to Post-T <sub>x</sub> slope				
Intercept	-2.27	0.65	-3.49	.001
Yoga vs. waitlist	-0.45	0.84	-0.54	.593
Exercise vs. waitlist	-0.45	0.90	-0.50	.618
Age	0.04	0.02	1.53	.134
	Variance component	<i>df</i>	$\chi^2$	<i>p</i>
<b>Random effects</b>				
Intercept	183.57	37	205.26	<.001
Slope	2.60	37	87.47	<.001
Within individual	148.89			

*Note.* Waitlist group was coded as reference group. Age was centered around the variable mean.



**Fig. 12.** Multilevel model estimates of hassles scores from pre- to post-treatment stratified by treatment group.

***Rumination.*** In the model of rumination, both age and pre-treatment BDI emerged as significant covariates. All other covariates (i.e., educational attainment, relationship status, total number of depressive episodes) were dropped from the model and the controlled analysis with age and pre-treatment BDI is presented (see Table 18). Over and above the effects of the covariates, the intercept of the intercept at both pre- (coefficient = 58.51,  $p < .001$ ) and post-treatment was significant, implying that rumination scores at the start and end of treatment were significantly different from zero. The intercept of the slope, however, was not significant. In terms of group differences, both the yoga and exercise groups had significantly lower rumination scores at post-treatment compared to the waitlist group. Importantly, the groups appeared to start out at similar levels of rumination, since none of the pairwise comparisons at pre-treatment were significant ( $ps \geq .381$ ). Age and BDI scores were significant with respect to the pre-treatment

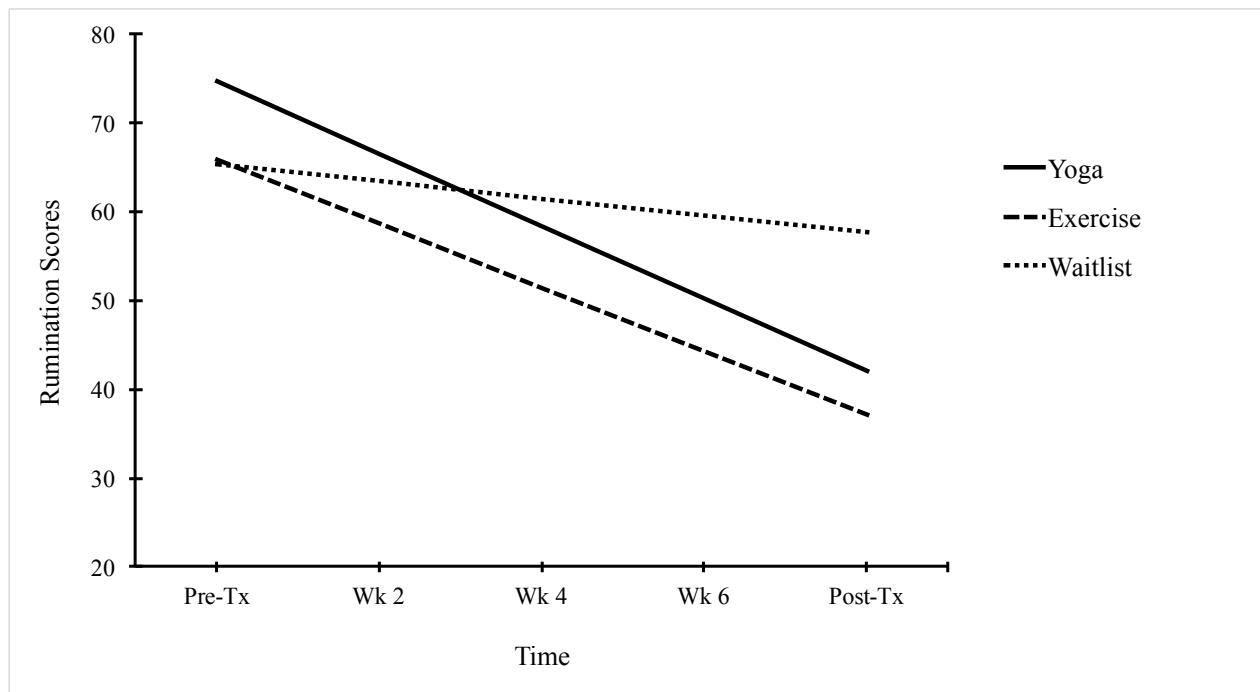
intercept. That is, an older chronological age was associated with lower rumination scores prior to treatment,  $\beta = -0.23$ ,  $SE = 0.09$ ,  $t(35) = -2.57$ ,  $p = .015$ , and higher pre-treatment BDI scores were associated with higher levels of rumination prior to treatment,  $\beta = 0.69$ ,  $SE = 0.14$ ,  $t(35) = 5.10$ ,  $p < .001$ . Consistent with the observed post-treatment group differences, both active treatment conditions had rumination slopes that were negative relative to the slope of the waitlist group. The covariates were also significantly associated with slope. That is, the rate of linear change in rumination appeared to be flatter for participants with higher pre-treatment BDI scores compared to lower pre-treatment scores and steeper for older participants relative to younger participants. When yoga and exercise were compared to each other, no significant differences in post-treatment intercept (coefficient = 5.47,  $p = .260$ ) or slope (coefficient = 1.53,  $p = .245$ ) emerged. Figure 13 shows the linear trajectories estimated from the MLM stratified by treatment group.

Table 18

*Parameter Estimates for the Multilevel Model of Rumination, Controlling for Age and Pre-Treatment BDI*

	Coefficient	SE	<i>t</i>	<i>p</i>
<b>Fixed effects</b>				
Post-T <sub>X</sub> intercept				
Intercept	58.01	3.74	15.51	<.001
Yoga vs. waitlist	-15.86	4.83	-3.28	.002
Exercise vs. waitlist	-21.33	5.25	-4.06	<.001
Age	0.09	0.14	0.62	.541
Pre-T <sub>X</sub> BDI	0.01	0.22	0.05	.959
Pre- to Post-T <sub>X</sub> slope				
Intercept	-0.12	1.02	-0.12	.904
Yoga vs. waitlist	-3.29	1.31	-2.50	.017
Exercise vs. waitlist	-4.82	1.43	-3.37	.002
Age	0.08	0.04	2.05	.048
Pre-T <sub>X</sub> BDI	-0.17	0.06	-2.90	.006
	Variance component	<i>df</i>	$\chi^2$	<i>p</i>
<b>Random effects</b>				
Intercept	114.96	35	188.53	<.001
Slope	6.02	35	80.73	<.001
Within individual	52.49			

*Note.* Waitlist group was coded as reference group. Pre-T<sub>X</sub> BDI = Beck Depression Inventory-II scores at pre-treatment. Age and Pre-T<sub>X</sub> BDI scores were centered around the variable mean.



**Fig. 13.** Multilevel model estimates of rumination scores from pre- to post-treatment stratified by treatment group.

**Mindfulness.** In the model of awareness, the inclusion of ethnicity did not change the pattern of results and ethnicity did not emerge as a significant predictor; therefore, the uncontrolled analysis is presented (see Table 19). At both pre- and post-treatment, the intercept of the intercept was significant (pre-treatment: coefficient = 35.00  $p < .001$ ), indicating that awareness scores at the start and end of treatment were significantly different from zero. The intercept of the slope was not significant. With respect to between-subjects differences, participants in the yoga group reported significantly greater awareness scores at post-treatment compared to those in the waitlist group. Importantly, there were no significant pre-treatment differences in intercepts across any of the pairwise comparisons ( $ps \geq .904$ ), suggesting that all groups started out at similar levels of mindful awareness. Consistent with the post-treatment difference between the yoga and waitlist groups, those in the former group had a significantly

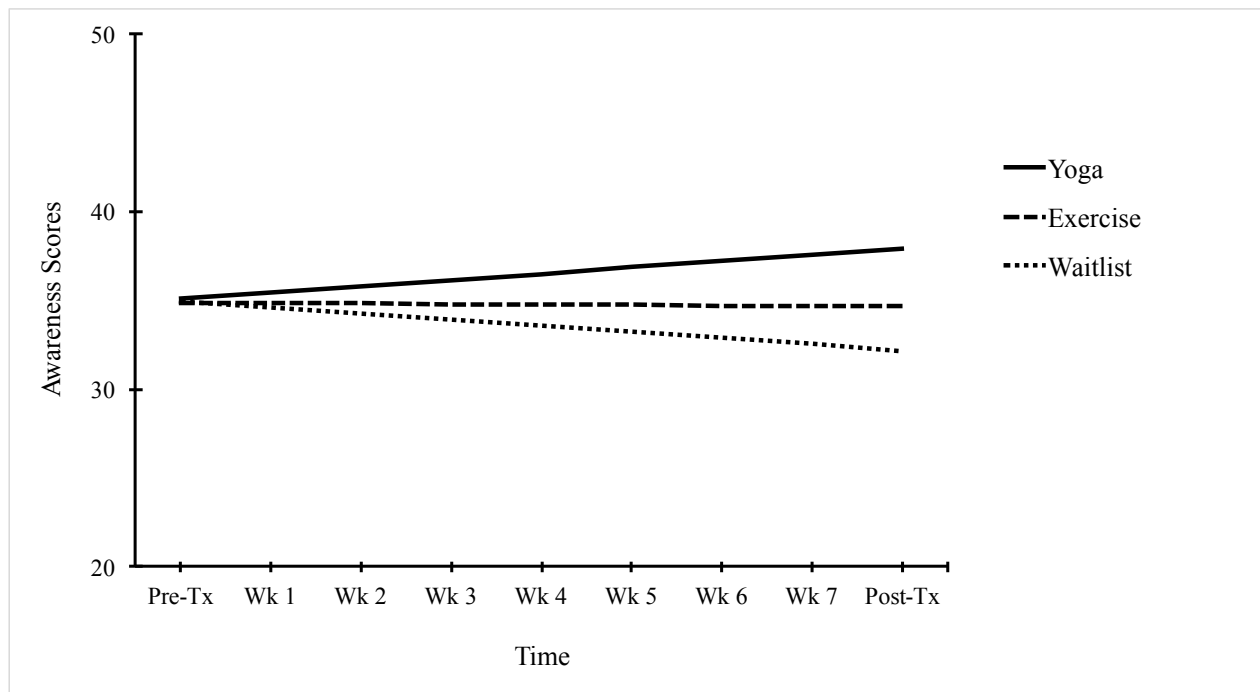
steeper awareness slope from pre- to post-treatment than those in the latter group. There were no differences in post-treatment intercepts or slopes for exercise versus waitlist (see Table 19) or for yoga versus exercise (intercept: coefficient = 3.25,  $p = .231$ ; slope: coefficient = 0.37,  $p = .245$ ). Figure 14 shows the linear trajectories estimated from the MLM stratified by treatment group.

Table 19

*Parameter Estimates for the Multilevel Model of Awareness*

	Coefficient	SE	$t$	$p$
<b>Fixed effects</b>				
Post-T <sub>x</sub> intercept				
Intercept	32.17	2.10	15.29	<.001
Yoga vs. waitlist	5.73	2.81	2.04	.048
Exercise vs. waitlist	2.48	2.85	0.87	.388
Pre- to Post-T <sub>x</sub> slope				
Intercept	-0.35	0.25	-1.41	.166
Yoga vs. waitlist	0.70	0.33	2.10	.042
Exercise vs. waitlist	0.32	0.34	0.95	.347
	Variance component	$df$	$\chi^2$	$p$
<b>Random effects</b>				
Intercept	49.04	39	830.81	<.001
Slope	0.60	39	225.46	<.001
Within individual	9.49			

*Note.* Waitlist group was coded as reference group.



**Fig. 14.** Multilevel model estimates of awareness scores from pre- to post-treatment stratified by treatment group.

In the model of acceptance, only age emerged as a significant covariate. Therefore, the other covariates (i.e., relationship status, pre-treatment BDI) were dropped from the model and the analysis controlling for age is presented (see Table 20). Over and above the effects of age, the intercept of the intercept at both pre- (coefficient = 22.47,  $p < .001$ ) and post-treatment was significant, implying that acceptance scores at the start and end of treatment were significantly different from zero. The intercept of the pre- to post-treatment slope, however, was not significant. In terms of group differences, participants in the exercise group had post-treatment acceptance scores that were significantly greater than those in the waitlist group. None of the groups differed significantly at pre-treatment ( $ps \geq .304$ ), suggesting that all groups started out at similar levels of acceptance. Age, however, was significant with respect to the pre-treatment intercept,  $\beta = 0.13$ ,  $SE = 0.06$ ,  $t(38) = 2.35$ ,  $p = .024$ , indicating that an older chronological age

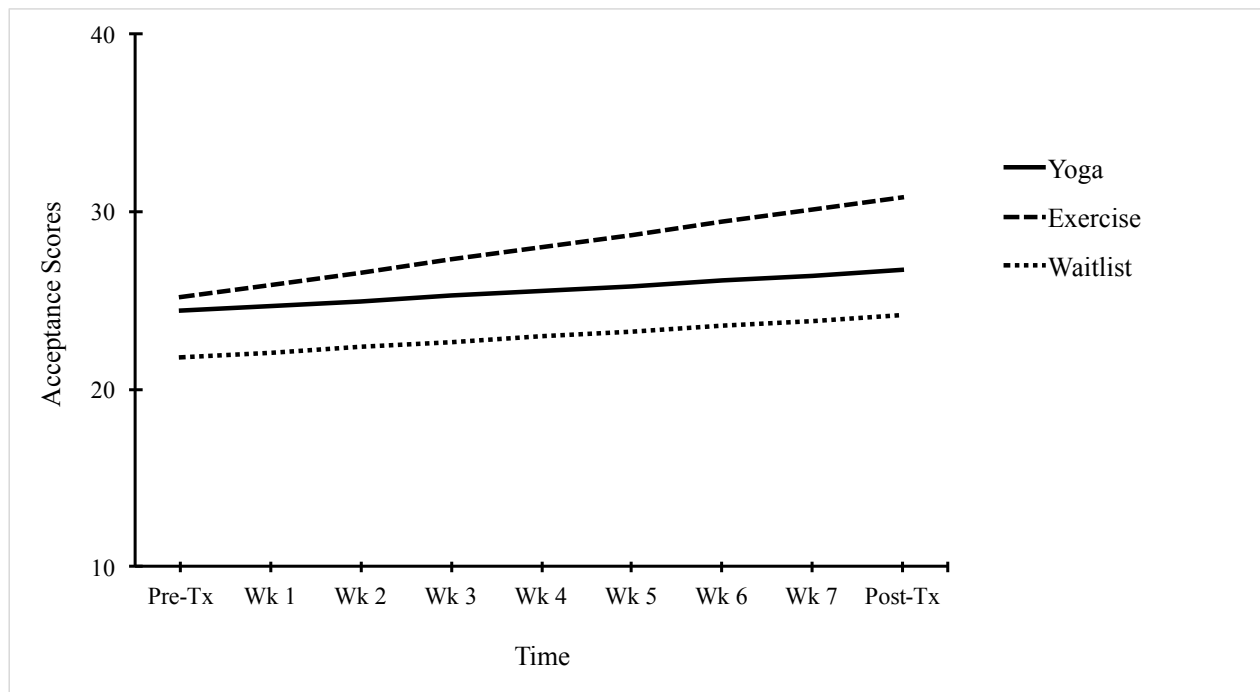
was associated with greater acceptance scores prior to treatment. Age was also negatively associated with slope, suggesting that the rate of linear change in acceptance was flatter for older participants compared to younger participants. Interestingly, despite the significant difference in post-treatment acceptance scores between the exercise and waitlist groups, their slopes were not significantly different. There were no differences in post-treatment intercepts or slopes for yoga versus waitlist (see Table 20) or for yoga versus exercise (intercept: coefficient = -4.62,  $p = .084$ ; slope: coefficient = -0.60,  $p = .114$ ). Figure 15 shows the linear trajectories estimated from the MLM stratified by treatment group.

Table 20

*Parameter Estimates for the Multilevel Model of Acceptance, Controlling for Age*

	Coefficient	SE	<i>t</i>	<i>p</i>
<b>Fixed effects</b>				
Post-T <sub>x</sub> intercept				
Intercept	23.77	2.05	11.60	<.001
Yoga vs. waitlist	2.82	2.70	1.05	.302
Exercise vs. waitlist	7.44	2.84	2.62	.013
Age	-0.08	0.08	-1.07	.291
Pre- to Post-T <sub>x</sub> slope				
Intercept	0.16	0.29	0.55	.585
Yoga vs. waitlist	0.09	0.39	0.22	.824
Exercise vs. waitlist	0.69	0.41	1.69	.100
Age	-0.03	0.01	-2.47	.018
	Variance component	<i>df</i>	$\chi^2$	<i>p</i>
<b>Random effects</b>				
Intercept	43.54	38	591.99	<.001
Slope	0.80	38	222.81	<.001
Within individual	12.17			

*Note.* Waitlist group was coded as reference group. Age was centered around the variable mean.



**Fig. 15.** Multilevel model estimates of acceptance scores from pre- to post-treatment stratified by treatment group.

**Primary Analyses: Mediation of Antidepressant Effects via Changes in Psychological Variables.**

Table 21 shows the parameter estimates for separate mediation analyses involving perceived hassles and rumination. For both analyses, the inclusion of covariates did not change the pattern of results; therefore, only pre-treatment levels of the relevant psychological variable and pre-treatment HAM-D scores were controlled for. In the model of hassles (see top panel of Table 21), although post-treatment hassles significantly predicted post-treatment HAM-D scores, post-treatment hassles scores did not differ significantly when either active treatment condition was compared to the waitlist group. The indirect effects of the treatment group comparisons on post-treatment HAM-D scores were also not significant. As such, hassles did not emerge as a significant mediator of the group differences in post-treatment HAM-D scores.

Rumination, on the other hand, emerged as a significant mediator (see bottom panel of Table 21). Post-treatment rumination scores were significantly lower in both active treatment conditions compared to the waitlist group. Post-treatment rumination scores, controlling for all other predictors, in turn significantly predicted post-treatment HAM-D scores. In terms of pre- to post-treatment *improvement* in these variables, the results indicated that for every 1 unit decrease in post-treatment rumination, post-treatment HAM-D scores also decreased by 0.26. Although the pairwise group comparisons with respect to post-treatment HAM-D scores were still significant in the full mediation model, the indirect effects of the active treatment groups versus the waitlist group were significant. This indicates that changes in rumination mediated the antidepressant effects of both yoga and exercise.

Table 21

Regression Coefficients, Standard Errors, and Model Summary Information for Mediation Models with Levels of Perceived Hassles and Rumination

	Post-T <sub>x</sub> hassles (M)		Post-T <sub>x</sub> HAM-D (Y)		Indirect effects on Y		
	Coeff	SE	Coeff	SE	Coeff	SE	95% CI
Constant	12.76	10.89	3.32	3.40			
Yoga vs. waitlist (D <sub>1</sub> )	-3.99	6.10	-8.18	1.88	-0.52	0.82	-2.19, 1.23
Exercise vs. waitlist (D <sub>2</sub> )	-3.00	6.26	-9.21	1.93	-0.39	0.91	-2.58, 1.14
Pre-T <sub>x</sub> hassles (C <sub>1</sub> )	0.25	0.10	-0.02	0.03			
Pre-T <sub>x</sub> HAM-D (C <sub>2</sub> )	0.14	0.69	0.70	.211			
Post-T <sub>x</sub> hassles (M)			0.13	0.05			
		$R^2 = .19$					$R^2 = .63$
		$F(4, 37) = 2.13, p = .097$					$F(5, 36) = 12.50, p < .001$
	Post-T <sub>x</sub> rumination (M)		Post-T <sub>x</sub> HAM-D (Y)		Indirect effects on Y		
	Coeff	SE	Coeff	SE	Coeff	SE	95% CI
Constant	47.18	11.71	-7.57	4.98			
Yoga vs. waitlist (D <sub>1</sub> )	-11.77	4.52	-5.87	1.74	-3.02	1.33	-5.67, -0.50
Exercise vs. waitlist (D <sub>2</sub> )	-17.28	4.91	-5.85	2.01	-4.43	1.34	-6.99, -1.81
Pre-T <sub>x</sub> rumination (C <sub>1</sub> )	0.12	0.15	0.03	0.05			
Pre-T <sub>x</sub> HAM-D (C <sub>2</sub> )	0.10	0.54	0.56	0.19			
Post-T <sub>x</sub> rumination (M)			0.26	0.06			
		$R^2 = .33$					$R^2 = .73$
		$F(4, 36) = 4.36, p = .006$					$F(5, 35) = 18.85, p < .001$

Note. M represents the mediator variable; Y represents the dependent variable; D<sub>1</sub> and D<sub>2</sub> represent dummy variables (waitlist coded as reference group); C variables represent covariates. Coeff = unstandardized regression coefficient; Pre-T<sub>x</sub> = measurement at pre-treatment; Post-T<sub>x</sub> = measurement at post-treatment; HAM-D = Hamilton Rating Scale for Depression scores.

Parameter estimates for separate mediation analyses involving awareness and acceptance are displayed in Table 22. For both analyses, the inclusion of age of onset of initial depressive episode did not change the pattern of results. Therefore, results from the models controlling for only pre-treatment levels of the relevant psychological variable and pre-treatment HAM-D scores are presented. Awareness did not emerge as a significant mediator (see top panel of Table 22). More specifically, the difference in post-treatment awareness scores was not significant for the comparison of either yoga or exercise relative to the waitlist group. As well, post-treatment awareness was not a significant predictor of post-treatment HAM-D scores. As can be seen from the table, the indirect effects of the treatment group comparisons with respect to post-treatment HAM-D scores were not significant.

Acceptance emerged as a significant mediator for the exercise group (see bottom panel of Table 22). Post-treatment acceptance scores were significantly higher among participants in the exercise group compared to the waitlist group. Post-treatment acceptance scores, controlling for all other predictors, in turn significantly predicted post-treatment HAM-D scores. That is, for every 1 unit increase in post-treatment acceptance, post-treatment HAM-D scores decreased by 0.42. Although the pairwise group comparisons with respect to post-treatment HAM-D scores remained significant in the full mediation model, the indirect effect of exercise versus the waitlist group was significant. These results indicate that changes in mindful acceptance mediated the antidepressant effects of exercise.



## **Chapter 6**

### **Discussion**

The current investigation was aimed at examining the efficacy and mechanisms of action of two nontraditional treatment options for major depression, yoga and exercise. Although the antidepressant effects of exercise have been consistently documented in the literature, investigations of the mood-enhancing effects of yoga are sparse in comparison. Further, numerous methodological issues have been identified among most trials of yoga for depression and among many of the exercise trials. Therefore, the first main objective of this study was to examine and compare the efficacy of yoga and exercise using a methodologically rigorous study design that minimized risk of bias. One of the most important methodological improvements made in this study was the selection of treatment groups. Bikram yoga was chosen because of its standardization, which lends itself well to empirical investigation and potential replication. In addition to the use of a waitlist control group, an aerobic exercise condition was chosen as a second active treatment group. This allowed for a comparison of yoga to a well-supported nontraditional treatment approach that is similar in terms of nonspecific aspects of the intervention. This study was also designed to examine various ways in which yoga and exercise may alleviate depression symptoms. Several physiological and psychological variables that have been found to be influenced by these approaches, and may also play a role in an individual's depressogenic response to stress, were examined as potential mechanisms of action. Findings relating to these two main objectives are discussed separately below, as well as directions for future research.

## **Treatment Outcome**

This study was the first empirical investigation to examine the antidepressant effects of Bikram yoga, as well as to compare the effects of Bikram yoga to those of aerobic exercise. The yoga and exercise conditions resulted in similarly strong (i.e., large) effects in terms of pre- to post-treatment improvement in depression symptoms, in both the ITT and as-treated samples. Among those who completed the study protocol, 73.3% and 80.0% of participants in the yoga and exercise groups, respectively, experienced a significant treatment response/remission, compared to 8.3% in the waitlist condition. These remission rates can be considered clinically meaningful given that HAM-D scores of  $\leq 7$  are associated with low relapse rates (Paykel et al., 1995). When considering pre-treatment severity of depression symptoms based on the HAM-D, these findings suggest that Bikram yoga and aerobic exercise classes are efficacious alternative treatment options for individuals with mild symptoms. Within the ITT sample, although treatment response rates were lower, a large proportion of participants in the active treatment groups experienced a significant reduction in depression symptoms; 61.1% of participants in the yoga group and 60.0% of participants in the exercise group experienced at least a 50% reduction in symptoms on the HAM-D after 8 weeks of treatment, compared to only 6.7% in the waitlist condition. In both sets of analyses (i.e., ITT and as-treated), the effect size of treatment group on response/remission was large.

These results are consistent with conclusions drawn from meta-analytic and systematic reviews, which have suggested that yoga and exercise may be effective treatment approaches for depression (e.g., Cramer et al., 2013; Cramer et al., 2017; Cooney et al., 2013; Kvam et al., 2016; Lawlor & Hopker, 2001; Schuch, Vancampfort,

Richards, et al. 2016). More specifically, relative to control conditions (e.g., no treatment, TAU, waitlist) and various comparison groups (e.g., health education, stretching, relaxation, meditation), these reviews have found yoga and exercise to be superior in terms of their antidepressant effects. In terms of how they compare to each other, only three studies have directly examined yoga versus aerobic exercise (Schuver & Lewis, 2016; Shahidi et al., 2011; Veale et al., 1992) and none found a significant difference between the two approaches in terms of post-treatment depression symptoms. Despite encouraging findings from meta-analytic and systematic reviews, most have stated that the various methodological limitations of prior studies impede the ability to definitively conclude that these alternative approaches are efficacious for treating depression (e.g., Cramer et al., 2013; Cramer et al., 2017; Cooney et al., 2013; Lawlor & Hopker, 2001; Schuch, Vancampfort, Richards, et al. 2016). One of the primary goals of this study, therefore, was to improve upon these weaknesses, such that less-biased estimates of the antidepressant effects of yoga and exercise would result. Risk of bias is crucial to consider when designing a study, as well as when evaluating results from previous investigations (Furlan, Pennick, Bombardier, & van Tulder, 2009). In the current study, risk of bias was minimized by using proper randomization procedures and blinding of outcome assessors, describing attrition rates and missing data procedures, conducting an ITT analysis, and assessing group differences at baseline in terms of important prognostic indicators (i.e., demographic and clinical variables, value of main outcome measure). When considering the widely-used Cochrane Collaboration ‘risk of bias’ tool (Furlan et al., 2009), these methodological decisions would hopefully deem the current study low risk in terms of the domains of potential bias (i.e., selection bias, performance bias, detection bias, attrition

bias, reporting bias; other bias; see Furlan et al., 2009). Several meta-analytic reviews of RCTs of yoga and exercise for depression have used the Cochrane tool to systematically assess methodological quality. Conclusions from these reviews highlight that although some good quality studies have been conducted, the quality of studies overall is quite poor. For instance, Cramer et al. (2013) concluded that only three of 12 yoga trials were low risk of bias. With respect to exercise trials, Cooney et al. (2013) categorized 11 trials as low risk, one trial as high risk, and the rest as unclear risk ( $n = 27$ ). Similarly, another meta-analysis judged four exercise trials as low risk and the remaining 21 trials as high risk (Schuch, Vancampfort, Richards, et al. 2016). These risk of bias assessments underscore the need for additional studies that carefully consider methodological issues that may affect bias and, therefore, the clinical utility of results. As such studies accumulate, this will allow for more definitive conclusions to be drawn regarding the efficacy of yoga and exercise for depression.

In addition to comparing the overall pattern of results in the current study to meta-analytic and systematic reviews, it is important to consider the degree of improvement observed relative to previous investigations that relied on similar definitions of treatment response. Overall, it appeared that rates of treatment response and remission in the current study were generally consistent with those found in other yoga and exercise trials. For instance, the use of SKY yoga was found to result in a significant response (i.e., HAM-D  $\leq 7$ ) in 67% of inpatients with MDD (Janakiramaiah et al., 2000). Butler et al. (2008) found that 77% of individuals who took part in a yoga intervention that emphasized Hatha yoga and meditation were in full remission from MDD at a 9-month follow-up. In another recent study using Hatha yoga for treatment-resistant MDD (Uebelacker, Tremont et al.,

2017), 36.2% of participants experienced a response according to their scores on the Quick Inventory of Depression Symptomatology – Clinician Rating (QIDS; Rush et al., 2003; i.e.,  $\geq 50\%$  reduction) and 29.3% achieved remission (i.e., QIDS  $\leq 5$ ). In terms of exercise trials, Blumenthal et al. (1999) found that 60.4% of older adults who underwent 16 weeks of aerobic exercise no longer met criteria for MDD. This remission rate did not differ significantly from that of the medication group (68.8%) or the combined exercise/medication group (65.5%). A subsequent study by Blumenthal et al. (2007) demonstrated remission rates of 45% and 40% for supervised group exercise and home-based exercise, respectively. Finally, Dunn et al. (2005) found response rates ranging from 19-64% and remission rates between 19-55%, depending on total energy expenditure and frequency of aerobic exercise interventions for adults with mild to moderate MDD. Although some variation inevitably exists in the literature with respect to response/remission rates, results from the current study fall within this and provide additional support for the use of yoga and exercise in the treatment of mild depression.

The finding that almost three-quarters of completers in the yoga group experienced a significant treatment response is exciting. Empirical interest in the use of yoga for depression has been on the rise in the past decade. However, the number of studies conducted in this area is scarce compared to trials of exercise for depression. Results from this study, therefore, help to extend previous investigations that have demonstrated antidepressant effects of various styles of yoga (e.g., SKY, Iyengar yoga, Sahaj yoga, variations of Hatha yoga; Janakiramaiah et al., 2000; Sharma et al., 2005; Sharma et al., 2017; Uebelacker et al., 2017). More specifically, these results underscore the use of Bikram yoga, a standardized and readily available style of yoga, in the treatment of

depression. The findings also suggest that Bikram yoga was efficacious despite various individual factors that may affect treatment response (e.g., demographic or clinical variables). Individual trials have tended toward selective study populations (e.g., prenatal women, psychiatric inpatients), which raises a question about generalizability of findings to the wider population with depression. The use of a more heterogeneous sample is, therefore, encouraging in terms of determining the scope of participants who may benefit from Bikram yoga. Nevertheless, given that this was the first trial of Bikram yoga for depression, future studies are needed to test the replicability of these findings using larger sample sizes and selection criteria that control or account for important individual factors more carefully. For instance, women in the current study ranged in age from young adulthood all the way up to the older end of middle adulthood. Although age was not associated with any of the treatment outcome variables, it often emerged as a potential covariate with respect to the mediation analyses. It may be interesting for future studies to have a more restricted age range *or* to look at age categorically (e.g., young adulthood vs. middle adulthood), as there may be natural discontinuities in the age distribution that are related to treatment response and/or mechanistic pathways. Further, although depression severity at pre-treatment was mild on average, it was moderate or severe for some participants. Preliminary analyses with the ITT sample demonstrated that individuals who achieved a response (i.e., >50% reduction in symptom severity) had significantly lower depression severity at pre-treatment than those who did not experience a response. Therefore, evaluating whether the mood-enhancing effects of Bikram yoga generalize to populations with more severe symptomatology is an important question for future research. Finally, co-intervention with conventional treatment approaches was permitted

in the current study, which may confound the mood-enhancing effects of yoga and exercise. These potential confounding effects were presumably limited by randomization and by requiring participants to have a minimum of 3 months of consistent treatment if engaged in other modalities (e.g., no change in the type or dose of antidepressant medication in the previous 3 months), as well as the continuation of consistent treatment throughout the study. Regardless, future studies of Bikram yoga may want to more carefully consider various individuals characteristics, such as engagement in other treatment modalities, that may impact treatment response. This will allow for a better understanding of the demographic and clinical profile of who may benefit most from this alternative approach.

The standardization of Bikram yoga lends itself well to addressing other empirical questions regarding the use of yoga for depression. For instance, some investigators have questioned whether there is an ideal balance to strike between the different components of yoga (e.g., breathing exercises vs. physical postures vs. meditation; Uebelacker, Epstein-Lubow, et al., 2010). Others have proposed that certain postures are particularly mood-enhancing (Gangadhar et al., 2013; Weintraub, 2004; Weintraub & Duncan, 2007; Woolery, Myers, Sternlieb, & Zeltzer, 2004) and, as such, yoga sequences have been developed specifically for use with depressed individuals (Gangadhar et al., 2013; Naveen et al., 2013; Uebelacker et al., 2017; Weintraub & Duncan, 2007). In fact, a consensus-based method to help increase consistency across yoga interventions for depression was recently published (de Manincor, Bensoussan, Smith, Fahey, & Bouchier, 2015). This method, based on “expert” opinion of 24 yoga teachers, has identified components of a yoga practice to include and exclude in the development of yoga intervention protocols for

depression (de Manincor et al., 2015). Although this method may prove to be helpful, it seems somewhat premature to declare specific postures or sequences as especially antidepressant in nature. Nevertheless, addressing the question of whether yoga can be broken down into its active ingredients is important to consider, as it may allow for a better understanding of the mechanisms by which yoga alleviates depression and the development of tailored yoga protocols. Bikram yoga may be an appropriate means to investigate this question in future studies. As previously described, it consists of an unchanging sequence of 26 postures and two breathing exercises, practiced in a heated environment and instructed through a scripted dialogue (Choudhury, 2007). Traditionally, all but the last posture (spine-twisting) are performed twice.<sup>9</sup> For research purposes, some of these variables could be manipulated while still ensuring a high degree of standardization and the ability to clearly describe study procedures. For instance, it would be possible to vary the proportion of time spent in active postures versus *savasana* (restorative, relaxation posture) by practicing some or each of the active postures only once. The unique physical environment that Bikram yoga is practiced in could also be manipulated, to determine if the yoga sequence itself is responsible for mood-enhancing benefits or whether the heat and humidity also play a role. Although this type of examination may simply lead to the conclusion that the whole is greater than the sum of its parts (Uebelacker, Epstein-Lubow, et al., 2010), the use of Bikram yoga in subsequent research would allow for such investigations.

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<sup>9</sup> Many Bikram yoga studios throughout Canada and the United States have started offering 60-min and/or 75-min classes, in addition to the traditional 90-min class. In these shortened classes, the same sequence of postures, with their respective durations, is practiced. The modification involves practicing some of the postures once instead of twice. As a result, the scripted dialogue for the second set of the relevant posture is eliminated; the dialogue is otherwise unchanged. It appears that the decision of which postures to eliminate during the shortened classes is instructor-dependent, but does not involve any of the “warm-up” sequence (half-moon, hands to feet, awkward pose, eagle pose).

Overall, findings from this study suggest that Bikram yoga and aerobic exercise are feasible and efficacious alternative treatment approaches for depression. The percentage of participants who withdrew from the study did not differ across the treatment groups, resulting in an overall attrition rate of 20.8%. This rate was slightly higher than the overall rate demonstrated in a recent meta-analysis investigating dropout rates in RCTs of exercise for depression (i.e., 15.2%; Stubbs et al., 2016) but consistent with many individual trials (e.g., Falsati et al., 2016; Kinser et al., 2014; Shapiro et al., 2007) and lower than some (e.g., Dunn et al., 2005; Naveen et al., 2013; Oeland, Laessoe, Olesen, & Munk-Jørgensen, 2010; Prathikanti et al., 2017). Adherence rates were also acceptable among the active treatment groups (yoga: 80.0%; exercise: 85.8%). These rates are actually quite encouraging, as they are similar to those reported in studies that used a higher degree of supervision in terms of yoga and exercise participation (e.g., supervision of yoga or exercise participation by research personnel; Blumenthal et al., 2007; Mota-Pereira et al., 2011; Streeter et al., 2017; Uebelacker et al., 2017). Importantly, no serious adverse events related to study participation were reported. Therefore, it can be concluded that the Bikram yoga and aerobic exercise classes offered in this study were accepted and well-tolerated by participants. Results of this study also imply that depressed individuals may benefit from attending yoga or exercise classes in real-world settings, which provides important ecological validity to this area of investigation. Group-based settings have been used in most trials of yoga (e.g., Battle et al., 2015; Janakiramaiah et al., 2000; Sharma et al., 2005; Woolery et al., 2004) and many trials of exercise (e.g., Askari et al., 2017; Blumenthal et al., 2007; Hallgren et al., 2015). However, in contrast to the current investigation, group-based classes offered in other trials have been provided exclusively in

the context of the study setting (i.e., available only to study participants). The results of the current study are therefore important as they suggest that individuals with mild depression may experience symptom improvement by attending yoga or exercise classes that are readily accessible in one's community. Given that a high degree of interest and motivation is likely required to seek out these types of classes, whether depressed individuals with more severe symptomatology would benefit from a similar approach remains to be investigated.

### **Mechanisms Underlying the Antidepressant Effects of Exercise and Yoga**

In addition to the clear link between stress and depression (Kendler et al., 2002; Kendler et al., 2006; Kessler, 1997; Mazure, 1998), exercise and yoga have been shown to influence numerous stress-related processes. This has led to suggestions that the antidepressant effects of exercise and yoga may occur via changes in one's stress response (Kinser et al., 2012; McCall, 2013; Riley & Park, 2015; Salmon, 2001; Streeter et al., 2012). Therefore, the current examination of mechanisms underlying the antidepressant effects of exercise and yoga focused on physiological and psychological variables that may be involved in how one responds to stress.

**Physiological Variables.** Given that dysregulation of the SNS and HPA axis systems in response to stress has been observed in depression (e.g., Burke et al. 2005; Heim et al., 2000; Zorn et al., 2017), pre- to post-treatment changes in several physiological stress reactivity variables were examined. It was expected that engagement in yoga or exercise over the course of the study would lead to underlying biological changes that would contribute to altered physiological reactivity to psychological stress (Sothmann, 2006) and that these alterations would, in turn, mediate the antidepressant

effects of these approaches. The results revealed that apart from HR reactivity, the physiological stress reactivity variables decreased significantly from pre- to post-treatment. This indicates that SNS and HPA axis response to the TSST was dampened at post-treatment relative to pre-treatment, which is not surprising given that participants were engaging in the TSST for a second time at their post-treatment assessment. To help ensure a degree of novelty and stressfulness of the TSST at this appointment, two variations of the task were used. Nevertheless, decreased physiological reactivity across all groups might be expected given participants' familiarity with the TSST protocol. In terms of group differences in physiological stress reactivity from pre- to post-treatment, no significant interactions emerged for any of the variables. This is contrary to hypotheses and indicates that the active treatment groups did not differ from the waitlist group in terms of changes in HR reactivity, MAP reactivity, CORT reactivity, or AUC<sub>i</sub> over the course of the study.

These findings are inconsistent with those of previous yoga and exercise trials, demonstrating decreases in physiological stress reactivity to tasks such as the TSST. In the exercise literature, two meta-analytic reviews have found significant associations between fitness or activity levels and reduced heart rate and blood pressure reactivity to acute psychological stressors (Crews & Landers, 1987; Forcier et al., 2006). Numerous trials have also concluded that higher levels of physical activity are associated with attenuated cortisol reactivity (Klaperski et al., 2013, 2014; Rimmelle et al., 2007; Zschucke et al., 2015). With respect to the effects of yoga on SNS or HPA axis reactivity to stress, relevant studies are limited and characterized by a great deal of methodological heterogeneity (e.g., varied laboratory stressors to induce a physiological response). Nevertheless, reductions in

heart rate and blood pressure reactivity (Kanojia et al., 2013; Madanmohan et al., 2004; Telles & Naveen, 2004; Vijayalakshmi et al., 2004), as well as attenuated cortisol reactivity (Hopkins et al., 2016), have been observed. Findings of exercise- and yoga-induced changes to SNS and HPA axis reactivity, however, have not been unanimous. In a meta-analytic review of the relation between fitness levels and various cardiovascular responses (e.g., heart rate, blood pressure, concentrations of epinephrine and norepinephrine) to psychological stress, Jackson and Dishman (2006) concluded that the cumulative evidence does *not* support the idea that increased fitness is related to attenuated stress reactivity. The authors found some evidence suggesting a quicker recovery among more fit individuals, but even these effects were small. Their conclusions likely differed from those of others (Crews & Landers, 1987; Forcier et al., 2006) as Jackson and Dishman more carefully examined features of study design, stressor tasks, dependent measures, and participants that were believed to be relevant to the relation of fitness and physiological stress reactivity. The authors stated that their meta-analytic approach allowed them to identify key conceptual methodological weaknesses and inconsistencies among individual studies (Jackson & Dishman, 2006). Since this review, additional trials of exercise and yoga have been published, demonstrating the absence of reduced SNS or HPA axis reactivity in response to stress (Hagins et al., 2013; Krogh et al., 2010; Sarubin et al., 2014). In line with the general rationale provided by these authors (Hagins et al., 2013; Jackson & Dishman, 2006; Krogh et al., 2010; Sarubin et al., 2014), the nonsignificant results in the current study may be owing to several methodological issues.

First, the null findings may represent a true failure of the specific yoga and exercise interventions used in this study to provide significant reductions in physiological stress reactivity. Since previous investigations of yoga and exercise have found evidence of various physiological effects, perhaps this study did not provide a “dose” of activity adequate to lead to biological alterations. Without these underlying biological alterations, physiological stress reactivity may have gone largely unaffected. This reasoning is consistent with findings from a cross-sectional study that examined HPA axis reactivity to a physiological stressor in physically inactive individuals, moderately trained runners, and highly trained runners (Luger et al., 1987). The authors found evidence of an attenuated cortisol response only among highly trained runners. The idea of an insufficient dose is also consistent with the finding that the groups in the current study did not differ with respect to changes in  $VO_2$ max. Many trials of exercise have monitored energy expenditure to help ensure that participants engage in a certain intensity, or minimum dose, of exercise (e.g., Blumenthal et al., 2007; Oeland et al., 2010; Schuch et al., 2015). This approach could have been implemented in the current study, with the use of heart rate monitors to estimate energy output. However, the use of naturalistic class settings with no supervision from research personnel, along with variability across participants and class types, would make it extremely difficult to guarantee a minimum energy output. As a result, the approach in which yoga and exercise classes were offered in the current study may have limited the hypothesized effects on physiological variables. Future investigations into mechanisms underlying the antidepressant effects of yoga and exercise may want to implement more supervision and procedures that will better control for energy expenditure.

The absence of significant group by time interactions for the physiological variables, including pre- to post-treatment changes in  $\text{VO}_2\text{max}$ , may also be explained by inadequate control of relevant extraneous factors. For example, variation in leisure-time physical activity, independent of study participation, could have influenced both fitness levels and stress reactivity variables (Jackson & Dishman, 2006; Buckworth, Dishman, & Cureton, 1994). Participants in this study were permitted to engage in non-group physical activity, contingent on maintaining their original activity levels throughout the duration of the study. Leisure-time physical activity was assessed during the screening procedure and pre-treatment assessment. However, it was not regularly monitored throughout the study, which impedes the ability to ensure consistent maintenance of original activity levels or an examination of how leisure-time physical activity may affect study variables. It has also been demonstrated that cardiovascular and respiratory responses to exercise training vary widely among individuals, even among monozygotic twins (Bouchard & Rankinen, 2001; Wolfarth et al., 2005). It has been suggested that investigations of exercise training better account for participants' adaptability to exercise and/or the influence of genetics on fitness (Jackson & Dishman, 2006). Jackson and Dishman (2006) proposed that future studies consider comparing monozygotic and dizygotic twins, or model variation in physiological adaptations to standardized exercise training. These suggestions were beyond the scope of the current investigation but remain important methodological consideration for larger-scale studies. In terms of cortisol measurements specifically, it could be argued that several extraneous variables known to affect cortisol levels were not sufficiently controlled for. Cortisol follows a circadian rhythm and can be influenced by various factors, including caffeine, smoking, antidepressant medications, oral contraceptives, and

menstrual phase (Badrick, Kirschbaum, & Kumari, 2007; Granger, Hibel, Fortunato, & Kapelewski, 2009; Kloze et al., 2007; Maki et al., 2015; Poll et al., 2007; Schwartz, Granger, Susman, Gunnar, & Laird, 1998). Although steps were taken to control for some of these factors (i.e., collection of saliva samples between 1500 and 1700 h; abstinence from smoking cigarettes and ingesting caffeine for a minimum number of hours) and assess others (i.e., antidepressant medications, oral contraceptives), it is possible that the influence of these factors contributed to the nonsignificant cortisol results. To more carefully consider these extraneous variables and ensure reliable measurement of cortisol, future studies may benefit from the use of stricter exclusion criteria (e.g., medications that affect cortisol, menopausal women) and more homogeneous samples.

As would be expected given the lack of group differences in pre- to post-treatment changes in the physiological stress reactivity variables, any changes that did occur did not mediate the antidepressant effects of yoga or exercise. These results may be interpreted as meaning that changes in heart rate, blood pressure, and cortisol reactivity were not important in terms of understanding how yoga and exercise improved depression in the current study. Nevertheless, as described above, several methodological issues may have played a role in the observed absence of physiological changes. As well, this study may have simply been underpowered in terms of its ability to identify group differences in changes in the physiological variables. These analyses were conducted on a subset of participants from an already small sample size. Therefore, rather than ruling out these variables as potential mechanistic pathways, future investigations with larger sample sizes are needed, that also incorporate the abovementioned methodological suggestions. This

will help to further examine these potential mediators while reducing the chance of Type II error.

**Psychological Variables.** Although the stress response is often thought of in terms of physiological changes that happen suddenly and seemingly automatically, cognitive appraisals and emotional reactions to stressful situations also play important roles. Because of this, when testing the hypothesis that yoga and exercise improve depression symptoms via changes in how one responds to stress, it is important to consider variables that are psychological in nature. In the current study, psychological variables that were examined included perceived hassles, rumination, and mindfulness.

**Perceived Hassles.** Participants in the exercise group reported significantly lower levels of perceived hassles at post-treatment compared to those in the waitlist group. The comparison between yoga and the waitlist group was not significant (coefficient = -10.85,  $p = .076$ ) but may have reached significance with a larger sample size and increased statistical power. With this consideration in mind, these results are generally consistent with those of previous investigations, demonstrating that trials of exercise and yoga have been associated with reductions in perceived stress and/or the severity of hassles (e.g., Askari et al., 2017; Cramer et al., 1991; Hewett et al., 2018; Michalsen et al., 2005). In the current study, exercise reduced perceptions of hassles to a greater degree than yoga, which is somewhat inconsistent with previous studies. That is, when directly compared to each other, yoga has been found to have a greater beneficial impact on perceived stress than exercise (Chattha et al., 2008; Rocha et al., 2012). This discrepancy may be explained by several differences between those studies and the current investigation, including sample size and composition, interventions (i.e., type, frequency, duration), and measurement of

perceived stress. Given such methodological heterogeneity, the question of which approach is more beneficial in terms of perceived stress requires additional examination. Nevertheless, results of this study, along with many others (e.g., Askari et al., 2017; Cramer et al., 1991; Hewett et al., 2018; Michalsen et al., 2005), are interesting because they suggest that activities that do not necessarily emphasize a change in how one thinks about stressors can, in fact, alter one's perception of stress.

It has been proposed that exercise and yoga may decrease levels of perceived stress via physiological changes, such as alterations to the HPA axis or improved autonomic functioning (Askari et al., 2017; Hewett et al., 2018; Michalsen et al., 2005). Given the lack of significant physiological changes in the current study, this explanation likely cannot explain the reductions in perceived hassles among those in the active treatment groups. Other psychological changes that may have resulted from engagement in exercise or yoga may have played a role. For instance, it is possible that enhanced self-efficacy, which was not measured in the current study but has been shown to increase with exercise and yoga (e.g., Barbour, Edenfield, & Blumenthal, 2007; Craft, 2005; Evans et al., 2009), mediated the positive effects of the active treatment groups on perceived stress. It has also been suggested that decreased rumination resulting from exercise and yoga may help to strengthen an individual against stress (Askari et al., 2017). More specifically, if engagement in unhelpful ruminative thinking patterns is reduced, an individual may feel less burdened by hassles or stressors that occur in everyday life. Consistent with this idea was the finding that perceived hassles and rumination scores in the current study were significantly and positively associated, at both pre- and post-treatment.

Linear rates of change in perceived hassles scores from pre- to post-treatment did not differ between the conditions. Perceived hassles also did not emerge as a significant mediator of the antidepressant effects of exercise and yoga. This lack of mediation may indicate that changes in perceived hassles are not important in terms of understanding the antidepressant effects of these approaches. However, given that the MLM analysis demonstrated group differences in perceived hassles at post-treatment, and the mediation analysis revealed that post-treatment hassles significantly predicted post-treatment HAM-D scores, the lack of a significant mediation effect may be better accounted for by insufficient power. Future studies with larger sample sizes are, therefore, needed to further investigate the role of perceived stress in the mood-enhancing effects of exercise and yoga. These studies may also benefit from using the more widely popular Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983) rather than the HUS (DeLongis et al., 1982; Kanner et al., 1981). The Perceived Stress Scale was designed to measure the perception of stress, in a nonspecific manner, by asking respondents how often they felt or thought a certain way in the last month. More specifically, the scale items tap into how unpredictable, uncontrollable, and overwhelmed respondents find their lives, without inquiring about specific stressful life events. This may produce a more valid estimate of an individual's *overall perception* of stress than the HUS, which assesses specific hassles and does not explicitly ask about thoughts or feelings related to them. Following this, the construct measured by the Perceived Stress Scale may be more salient to the antidepressant effects that occur with exercise and yoga. Consistent with this idea, Cohen and Williamson (1988) found higher scores on the Perceived Stress Scale to be associated with a greater vulnerability to stressor-induced depressive symptoms. Therefore, the

suggestion that was made with respect to physiological stress reactivity variables also applies here; future investigations are needed to further examine the role of perceived stress in the mental health benefits of exercise and yoga, rather than ruling it out as a potential mediator.

***Rumination.*** Consistent with hypotheses, participants in both the yoga and exercise groups reported significantly lower levels of rumination at post-treatment compared to those in the waitlist group. As well, the linear rates of change from pre- to post-treatment in the active treatment groups were significantly different (i.e., negative) relative to the control group. These results are an important addition to the relatively small body of research evidence that has examined changes in rumination following trials of yoga or exercise (Craft, 2005; Kinser, Bourguignon, Whaley, et al., 2013; Schuver & Lewis, 2016; Uebelacker, Tremont, et al., 2010). Although a strength of these studies has been their use of depressed samples, three of these studies (Craft, 2005; Schuver & Lewis, 2016; Uebelacker, Tremont et al., 2010) have important methodological issues that need to be considered when interpreting results. Schuver and Lewis (2016) compared a combined yoga and mindfulness intervention to a control condition (i.e., combined walking and health education). Although participants in the yoga/mindfulness group had significantly greater reductions in rumination than the control condition, the design of the study precludes the ability to differentiate the effects of yoga from those of mindfulness. Craft (2005) allowed participants to self-select into a trial of exercise or a control group. These groups did not differ significantly on various demographic and clinical variables, or on scores for dependent variables at study entry. However, other relevant characteristics, such as an individual's stage of change in terms of exercise behaviour (Prochaska &

DiClemente, 1983), were not assessed and may have resulted in important differences between the groups. Another issue with Craft's (2005) study was the use of a group-based exercise program and a non-group based control condition. This made it difficult to understand whether decreases in rumination among those in the exercise group were owing to the exercise itself or from participation in a group, which involves potential interaction and social support from others. Finally, in Uebelacker, Tremont, et al.'s (2010) pilot study, the small sample size ( $N = 10$ ) and lack of a control group limited the ability to draw firm conclusions regarding the effects of Vinyasa yoga on depression symptoms and rumination.

The changes in rumination observed in the current study provide additional support for the idea that yoga and exercise may be effective tools to decrease rumination. When engaged in these activities, individuals may focus their attention on the task at hand, as well as on somatic sensations that are occurring in the moment (e.g., increased breathing rate, increased heart rate, muscle contraction; Schuver & Lewis, 2016). The focus of attention in this way may serve to distract individuals from their typical thinking patterns. If an individual has the tendency to ruminate, this may mean that the opportunity to engage in such thoughts is decreased (Nolen-Hoeksema, 1991). Participation in yoga or exercise in a group setting, specifically, may further promote distraction and decrease rumination. In group settings, there is frequent instruction from class instructors, as well as other factors where attention may be directed (e.g., other people in the class). Finally, various benefits that are received through regular engagement in yoga or exercise may also help to decrease rumination. For example, over time, individuals may experience positive reinforcement as goals are met, progress is observed, and other beneficial effects

are experienced. Each of these positive aspects may serve as further sources of distraction from ruminative thoughts (Nolen-Hoeksema, 1991).

Given that rumination is a potent risk factor for the onset and maintenance of depression (Aldao et al., 2010; Just & Alloy, 1997; Nolen-Hoeksema et al., 1993), it follows that yoga- and exercise-induced changes in rumination may be an important mechanism by which these approaches alleviate depression symptoms. Consistent with hypotheses, rumination emerged as a significant mediator underlying the antidepressant effects of both yoga and exercise. The test of mediation showed that as rumination decreased from pre- to post-treatment for individuals in the active treatment groups, depression scores also decreased. These results are exciting as they represent the first test of a mediation model, looking at the role of rumination in *how* yoga and exercise improve mood. A qualitative study by Kinser, Bourguignon, Whaley, et al. (2013) demonstrated that depressed women who took part in an 8-week Hatha yoga intervention described yoga as helpful for depression because of its ability to interrupt negative thinking patterns. Results from the current study provide quantitative evidence to support this idea, and may also extend it to the domain of aerobic exercise.

***Mindfulness.*** Mindfulness in the current study was assessed with the PHLMS (Cardaciotto et al., 2008), which contains two domains that are most relevant to the definition of mindfulness – present-moment awareness and acceptance (Bishop et al., 2004; Kabat-Zinn, 1994). It was hypothesized that both yoga and exercise would lead to enhanced mindfulness; however, specific predictions relating to the two components were not made. The findings suggested that yoga had a unique effect on awareness, whereas exercise had a greater impact on acceptance. More specifically, participants in the yoga

group reported significantly greater awareness scores at post-treatment compared to those in the waitlist group. As well, the slope of change from pre- to post-treatment for the yoga group was significantly steeper relative to the control group. Post-treatment acceptance scores for participants in the exercise group were significantly greater than those in the waitlist group. However, the pre- to post-treatment slopes for these group were not significantly different.

The enhancement of mindfulness observed in this study is consistent with a growing number of trials looking at the effects of yoga on mindfulness (e.g., Battle et al., 2015; Bowden et al., 2012; Curtis et al., 2011; Falsafi, 2016; Gard et al., 2012; Hewett et al., 2011; Uebelacker, Tremont, et al., 2010), as well as the small number of trials involving exercise (de Bruin et al., 2016; Mothes et al., 2014). Of the yoga trials, most used the Five-Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2007), which produces an overall mindfulness score, as well as separate subscale scores for five domains (observing, describing, acting with awareness, nonjudging, nonreactivity). Each of these investigations demonstrated significant increases in overall mindfulness, as well as increases on many of the individual domains, including awareness. Although this may be interpreted as meaning that yoga has broad effects on the multidimensional construct of mindfulness and influences multiple components, the FFMQ has been noted to have subscales that are redundant and not necessarily reflective of core components of mindfulness (Cardaciotto et al., 2008). In their trial of exercise, de Bruin et al. (2016) used a short version of the FFMQ, which produced only an overall mindfulness score. Similarly, Mothes et al. (2014) examined mindfulness unidimensionally with the Mindfulness Attention Awareness Scale (MAAS; Brown & Ryan, 2003). This scale was

developed to measure “present-centered attention-awareness” and any items related to an attitudinal component of mindfulness (e.g., acceptance) were purposefully excluded (Brown & Ryan, 2003). Cardaciotto et al. (2008) developed the PHLMS so that the two essential components of mindfulness could be measured independently, without the redundancy that additional components may bring. The use of this measure in the current study provides an important extension of previous findings. That is, the examination of both acceptance and awareness helped to identify unique effects of yoga and exercise on the psychological construct of mindfulness.

In order to theorize why yoga had an effect on awareness, whereas exercise had an effect on acceptance, it is important to consider Cardaciotto et al.’s (2008) conceptualization of each component. Awareness is defined as “the continuous monitoring of ongoing internal and external stimuli” and acceptance is defined as “a nonjudgmental stance toward one’s experience” (p. 208). As part of the scripted dialogue, participants in a Bikram yoga class are constantly instructed to direct their attention on different stimuli, including the breath, contraction of specific muscles, and the sensations of stillness and relaxation (Choudhury, 2007). The dialogue is almost exclusively about the physicality of the postures and the proposed health benefits (Choudhury, 2007). Although instructors may provide corrective feedback to specific individuals, the dialogue is otherwise directed to the entire class and contains minimal levels of praise. With the exception of final *savasana*, Bikram yoga practitioners are instructed to keep their eyes open throughout the entire class, as this is believed to help foster presence by keeping one’s attention from wandering (Choudhury, 2007). Finally, class practitioners are not permitted to speak in class, as this may disrupt others. Given these explicit instructions, it is easy to see how a

practice such as Bikram yoga could enhance mindful awareness. It is also understandable that it may have a greater impact on awareness over acceptance, at least when it comes to a relatively short period of practice (i.e., 8-week trial). Unlike some other styles of yoga, Bikram yoga does not emphasize setting intentions, philosophical ideas, or spirituality (Choudhury, 2007). These components of yoga may be more relevant to the development of acceptance, although this remains speculative at this point and requires further investigation.

The exercise classes in the current study varied and were not instructed with standardized scripts. Therefore, it is difficult to know how different components of the classes may have influenced the development of acceptance. Nevertheless, the atmosphere of aerobic exercise classes is often upbeat, positive, and supportive. Instructors typically are not bound by standardized class protocols and instructions. Therefore, they may be more likely to provide positive feedback or encouraging comments to class participants. Further, participants may feel more comfortable speaking out in class, such as asking for clarification or making comments. This may help promote a sense of connectedness or social support within the class. A potentially important factor in the current study was that participants were permitted to attend whichever exercise classes that they wanted, from their modified schedule. This may have ensured that participants enjoyed the classes that they attended, which has been suggested to directly contribute to the psychological benefits of exercise (Wankel, 1993). Again, although speculative at this point, each of these factors may have played a role in enhancing participants' level of acceptance and nonjudgment toward experiences.

Interestingly, the mediation analyses revealed that acceptance was a significant mediator of the antidepressant effects of exercise, but awareness did not mediate the effects of yoga. As acceptance levels increased from pre- to post-treatment for those in the exercise group, depression severity scores decreased. This overall pattern of results is consistent with findings from Cardaciotto et al.'s (2008) development and validation study of the PHLMS. Using two nonclinical and three clinical samples, the authors demonstrated that higher levels of acceptance were generally associated with lower levels of depression symptoms and rumination. Similar associations between acceptance and depression have been noted (Long & Hayes, 2014), along with a link between acceptance and psychological resiliency (Thompson, Arnkoff, & Glass, 2011). There is also some support for the use of acceptance and commitment therapy for depression (e.g., A-Tjak et al., 2015; Forman, Herbert, Moitra, Yeomans, & Geller, 2007), which is a relatively new form of CBT that focuses on the acceptance of experiences (i.e., distressing thoughts, beliefs, sensations, feelings) rather than the attempt to change them. An accepting orientation, therefore, appears to foster positive psychological outcomes, possibly through emotion regulation (Thompson et al., 2011). Mindful awareness, on the other hand, has been found to either *not* significantly correlate with depression symptoms (Cardaciotto et al., 2008) or longitudinally predict an increase in symptoms (Long & Hayes, 2014). Long and Hayes (2014) suggested that heightened awareness, as measured by the PHLMS, may actually confer a vulnerability for depression as it may represent problematic hypervigilance to experiences. They proposed that if an individual possesses an accepting orientation in addition to present-moment awareness, this may transform awareness from a vulnerability to a strength. Some support for this hypothesis was found with respect to predicting

quality of life (Long & Hayes, 2014), and future investigations of mechanisms underlying the antidepressant effects of exercise and yoga may want to consider this potentially relevant interaction.

### **Strengths and Limitations**

This study had several strengths, most of which have been previously highlighted. First, the selection of treatment groups was important for evaluating the efficacy of yoga compared to both no treatment and to a well-supported alternative treatment approach for depression, aerobic exercise. The use of Bikram yoga, specifically, will allow for replication in subsequent studies and may lead to investigations into the antidepressant effects of component parts of yoga. Second, this study attempted to minimize risk of bias by using a study design that was more methodologically rigorous than some of the previous investigations of yoga and exercise for depression. Important methodological strengths included the use of standardized instruments to diagnose depression and assess symptom severity, proper randomization procedures, blinding of outcome assessors, an intention-to-treat analysis, and adequate treatment lengths. Third, this study expanded on previous trials by examining the effects of yoga and exercise on several physiological and psychological mechanisms of action, as well as the mediating role of these variables in understanding the antidepressant effects of these approaches. With an increased understanding of how yoga and exercise alleviate depression, tailored treatment approaches and identification of ideal candidates for such treatments may be possible. Finally, this study was quite unique in that real-world yoga and exercise classes were provided for a sample of depressed women drawn from the community. Most previous investigations have relied on selective study populations and offered yoga and exercise

interventions exclusively in the context of the research setting. Given the approach taken in the current study, the results provide important ecological validity to this area of investigation. The results suggest that depressed women, at least those with mild symptoms of depression, may experience mood-enhancing effects of yoga and exercise by attending classes in their communities.

Despite several important strengths, the results of this study should be considered in light of its limitations. First, since it was up to potential participants to initiate contact with research personnel, there may be important individual characteristics that differ between study participants and the wider population of individuals with depression. For instance, study participants may be more open-minded about nontraditional treatment approaches for depression and CAMs in general. This type of perspective on alternative approaches, along with potential expectations, could influence treatment outcome. Nevertheless, this is an issue that is inherent in all clinical research to some degree. Second, although this study had several strengths in terms of methodology relating to the treatment outcome objective, it had some methodological issues that may have affected physiological measurements or the ability to identify group differences in these variables. These have been previously noted and include a lack of control over extraneous factors that may have affected physiological measurements, such as leisure-time physical activity, genetics, and factors known to affect cortisol levels. As well, given that research personnel did not supervise the yoga or exercise classes, and participants were not required to wear a heart rate monitor, the level of engagement in class could not be estimated. Level of engagement in class could presumably influence change, or lack of thereof, in any of the study variables. Without knowing how much each participant engaged in a class, it is

difficult to draw conclusions regarding an optimal dose of yoga or exercise. Nevertheless, determining a dose-response relationship was not a goal of the current study and remains a valid question for subsequent investigations.

Third, although this study used a standardized style of yoga, the exercise intervention was not standardized and may have varied a great deal among individuals in this condition. The exercise intervention used in the current study was chosen because it was similar to the yoga intervention in a number of ways. That is, both conditions were group-based, took place in community settings, were facilitated by instructors who were not involved in the research project, and offered the opportunity for social interaction from both instructors and other class attendees. It was also chosen because finding a group-based exercise intervention that was standardized, had adequate options for class times, and was offered throughout the entire year proved to be an impossible task within the Kingston community. For these reasons, along with practical considerations (e.g., discounted rate offered by the Kingston Family YMCA to investigators), a decision was made to offer an exercise intervention with a variety of class options but a strong aerobic component. This lack of consistency or standardization, however, hinders the ability to better understand the presence or absence of certain effects within the exercise group.

## **Conclusion**

The current study makes several important contributions to the literature. This was the first investigation to examine the antidepressant effects of Bikram yoga. Importantly, this occurred within a study design that was more methodologically rigorous than many previous trials of yoga for depression, which presumably helped to reduce the risk of bias. The results demonstrated that engagement in Bikram yoga resulted in similar

improvements in depression symptoms as aerobic exercise. This helps extend findings of previous trials that have examined the antidepressant effects of other styles of yoga. Most of these trials, including those involving exercise for depression, have offered these interventions exclusively in the context of the research setting. Therefore, the real-world settings used in this study provide ecological validity to this area of investigation and have important clinical implications.

Yoga and exercise classes are generally easily accessible. Most medium- to large-sized cities in North America have an affiliated Bikram yoga studio, and exercise classes are widely available at gyms, specialized fitness studios, and community centers. In addition to accessibility, these approaches may be appealing for a number of other reasons (Astin, 1998; Tindle et al., 2005; Wu et al., 2007). For instance, yoga and exercise represent alternative treatment options for depression that are both cost-effective and have limited side effects. In fact, yoga and exercise have been linked to numerous benefits, both in terms of mental and physical health. Generally, there is also less stigma attached to physical activity than to conventional treatments, which may help to foster treatment seeking behavior on the part of depressed individual. As a complement to this, health care professionals, such as family physicians, may be more likely to recommend these approaches as evidence in support of their antidepressant effects continues to accumulate. Although exercise is already recommended as a first-line monotherapy for mild to moderate depression (Ravindran et al., 2016) and yoga may not be far behind, it appears that some family physicians are hesitant to recommend alternative approaches (Jarvis, Perry, Smith, Terry, & Peters, 2015). Ultimately, an increased use of yoga and exercise

may help reduce treatment delays, which could have positive effects on prognosis, and alleviate burden on mental health care professionals.

In addition to improvements in acute symptoms, the use of yoga and exercise for depression may help protect against the risk of recurrence. That is, individuals who make more permanent lifestyle changes by engaging in physical activity beyond symptom improvement may continue to experience mood-enhancing benefits. A small number of studies have conducted follow-up assessments to determine the longer-term effects of yoga and exercise and the results have been promising (Babyak et al., 2000; Hallgren et al., 2016; Kinser et al., 2014; Uebelacker et al., 2017). There is some evidence for continued benefits without continued engagement in yoga or exercise (Kinser et al., 2014); however, it may be more likely that these healthful behaviours need to be maintained to help protect against relapse (Babyak et al., 2000). Future studies are needed to investigate the longer-term effects of yoga and exercise, including an assessment of optimal dose to maintain improvements in mood.

This study is also important for its initiative in investigating potential mediators of the antidepressant effects of yoga and exercise. Numerous mechanisms of action have been proposed and some have been investigated. However, studies have often failed to conduct proper tests of mediation. The current study uncovered some relevant mediators, including changes in rumination and mindful acceptance, but the ways in which yoga and exercise alleviate depression are not well understood. Future studies that improve upon the methodological issues that may have affected physiological measurements in the current study are needed. As well, many other plausible mechanistic pathways have not been adequately examined and are deserving of empirical attention. For example, potential

physiological mechanisms involve parasympathetic activity, central nervous system neurotransmitters such as gamma-aminobutyric acid and serotonin, brain-derived neurotrophic factor, endocannabinoids, and anti-inflammatory cytokines (Conn, 2010; Kinser et al., 2012; Pascoe & Bauer, 2015; Prathikanti et al., 2017; Ströhle, 2009; Uebelacker, Epstein-Lubow, et al., 2010). Other hypothesized psychosocial mechanisms include enhanced self-efficacy, self-acceptance, sense of achievement/mastery, social connectedness, and behavioural activation (Conn, 2010; Kinser et al., 2012; Pascoe & Bauer, 2015; Prathikanti et al., 2017; Ströhle, 2009; Uebelacker, Epstein-Lubow, et al., 2010). These mechanisms are likely not mutually exclusive; therefore, in addition to further examining various physiological and psychological mediators, future studies may also want to consider interactions between these processes. Ultimately, a better understanding of *how* yoga and exercise reduce depressive symptoms, along with *who* they are best suited for (e.g., women vs. men; young adulthood vs. middle adulthood; severity and/or recency of depression symptoms), may lead to the development of tailored protocols and the identification of ideal treatment candidates.

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Appendix A

Diagram of Bikram Yoga Asanas



## Bikram Yoga Asana Names

Postures are listed in Sanskrit with English in parentheses

1. Pranayama (standing deep breathing)
2. Ardha-Chandrasana (half moon pose), Pada-hasthasana (hands to feet pose)
3. Utkatasana (awkward pose)
4. Garurasana (eagle pose)
5. Dandayamana-Janushirasana (standing head to knee pose)
6. Dandayamana-Dhanurasana (standing bow pose)
7. Tuladandasana (balancing stick pose)
8. Dandayamana-Bibhaktapada-Paschimotthanasana (standing separate leg stretching pose)
9. Trikanasana (triangle pose)
10. Dandayamana-Bibhaktapada-Janushirasana (standing separate leg head to knee pose)
11. Tadasana (tree pose)
12. Padangustasana (toe stand)
13. Savasana (dead body pose)
14. Pavanamuktasana (wind-removing pose)
15. Bhujangasana (cobra pose)
16. Salabhasana (locust pose)
17. Poorna-Salabhasana (full locust pose)
18. Dhanurasana (bow pose)
19. Supta-Vajrasana (fixed firm pose)
20. Ardha-Kurmasana (half tortoise pose)
21. Ustrasana (camel pose)
22. Sasangasana (rabbit pose)
23. Janushirasana (head to knee pose)
24. Paschimotthanasana (stretching pose)
25. Ardha-Matsyendrasana (spine-twisting pose)
26. Kapalbhathi in Vajrasana (blowing in firm pose)

## Appendix B

### **Telephone Pre-Screening Script for Potential Participants**

#### **(i) Introduction**

(For potential participants who have already emailed or called in asking to be contacted back)

*Hello could I please speak to \_\_\_\_\_? My name is \_\_\_\_\_ and I am calling from the Mood Research Lab at Queen's University. I'm calling because I am scheduled to conduct a phone screen with you for a study being conducted in our lab. This study is looking at nontraditional approaches to the treatment of depression. Is this a good time to talk about the study?*

#### **(ii) Explanation of the Study**

*This study is being conducted by the Mood Research Lab, at Queen's University, in collaboration with the Kinesiology department. We are looking at two nontraditional treatment approaches for depression, specifically Bikram yoga and aerobic exercise. The purpose of this study is to evaluate whether these approaches are effective at improving depression symptoms, and if so, **how** these approaches improve depression symptoms. That is, what are some of the mechanisms of action.*

*First, let me tell you a bit more about the two interventions. If you participate in this study, you will take part in either Bikram yoga classes or aerobic exercise classes.*

- *Are you familiar with Bikram yoga or do you know what it is?*

**If NO:** Briefly describe it

*[Bikram yoga is often referred to as hot yoga, as it is done in a heated and humid room. Each Bikram yoga class is 90 minutes long and consists of 26 postures and 2 breathing exercises. The order and timing of postures is always the same. It's a physically vigorous style of yoga.]*

**If YES:** Ask the participant to tell you what she knows about it and add in information if necessary. Then continue...

- *Bikram yoga classes will be taken at a downtown yoga studio called Feel Yoga. There are more than 20 class times to choose from each week. Participants are able to alternate the class times each week, which allows for a lot of flexibility. Exercise classes will be taken at Kingston Family YMCA, which is located on Wright Crescent, near Loblaws. Are you familiar with where that is? There are six different class types to choose from (e.g., bootcamp, zumba, step classes, sports conditioning, etc. – they all have a strong cardio component) and alternate between, each with a number of different times per week. So again, a lot of flexibility. Regardless of your assigned intervention, you will be asked to attend two classes per week, for 8 weeks, and you will be able to attend these classes free of charge. It is important to understand that the classes are ongoing group exercise activities in the community, which means that you will be participating in classes with people who are not part of the study. But keep in mind that no one will have any way of knowing that you are there as part of a study unless you disclose that to them.*
- *Do you have any questions so far, about anything I've said?*

*Participation in this study involves bit more than just participating in either Bikram yoga or aerobic exercise classes for 8 weeks. Let me briefly describe what else it entails.*

- *The very first thing you'll be asked to do, prior to any yoga or exercise classes, is to attend two in-person appointments at Queen's University. At the first appointment, which will take approximately 2 hours, you will take part in an interview about your mood, your physical health, and fill out some questionnaires. You will also be asked to take part in measurements of your weight, height, waist circumference, and blood pressure. The second appointments, which will take place within a week of the first appointment, will be approximately 3 hours. It never takes longer than this. At this appointment, you will take part in some noninvasive physiological measures, including heart rate, blood pressure, heart and blood vessel function, and cardiovascular fitness. I will not get into the details of each of these measurements, unless of course you'd like more information, but I will just highlight that these are all noninvasive and are NOT painful. At the end of this appointment, you will find out whether you have been assigned to the Bikram yoga group, the aerobic exercise group, or a waitlist group. If assigned to the waitlist, all this means is that you will not participate in yoga or exercise immediately. However, after a short waiting period of approximately 8 weeks, you will then get access to either yoga or exercise classes.*
- *Throughout the duration of the intervention period, or the waiting period for those on the waitlist, you will be asked to fill out online questionnaires on a weekly basis. All this involves in being sent a link via email, which you then click on to follow the prompts. These questionnaires have been taking participants about 15 minutes to complete each week.*
- *Following the completion of the intervention period, or the waiting period, you will be asked to attend a final in-person appointment at Queen's, which will be very similar to your other appointments but a bit shorter in length. At this appointment, we redo all of the noninvasive physiological measurements, followed by a much briefer assessment of your mood symptoms, focusing only on depression symptoms and how these symptoms may have changed over the course of the study.*
- *So overall, this study involves two initial in-person appointments, an 8-week trial of Bikram yoga or aerobic exercise, or potentially a waiting period, online questionnaires, and a final in-person appointment. You will be compensated \$50 for participating in the final in-person appointment, but you will not be compensated for participating in the initial in-person appointments or in the treatment groups themselves. Please keep in mind that your participation is completely voluntary and you are free to withdraw from the study at any time.*
- *Do you have any questions at this point?*
- *Are you still interested in potentially participating?*

[If NO: Thank her for her time]

**(iii) Inclusion/Exclusion Criteria for the study**

**If YES:** *Great! Now I would like to ask you some questions to see if you are eligible to participate. These questions will take 10-20 minutes. Do you have time now?*

**If YES:** Continue with telephone screen

**If NO:** Ask for a good time to call back at

1. *How old are you?*

**Accept:** 18 - 65 years old

2. *Have you been diagnosed with, or have you had any treatment (presently or in the past) for, any psychiatric disorder, including depression, anxiety, dependence on drugs or alcohol, or anything else?*

*If so, what was it?* \_\_\_\_\_

**\*\*Get details of treatment – especially current, past 3 months, and expectations for next several months**

**Exclude:** Participants who report a history of

- Psychotic disorder (e.g., schizophrenia)
- Bipolar disorder
- Drug/alcohol dependence (current or within the past couple of years)

If depression treatment (medication or psychotherapy) was reported:

*In the past 3 months, have there been any changes to your \_\_\_\_\_ (insert treatment name) ?* (Change may include type/dose of medication, frequency of psychotherapy sessions)

**Exclude:** Participants with a significant change in their current depression treatment in the past 3 months

*I will now ask you some questions regarding your physical health and medical history. It is very important to disclose any information relevant to these questions. Based on your physical health, it may be the case that medical clearance from your family physician is required prior to enrolling you in the study, if you are otherwise deemed eligible.*

3. *Are you currently pregnant or are you actively trying to get pregnant?*

**Exclude:** Participants who are pregnant or actively trying to get pregnant

4. *Do you have any physical conditions that make it difficult to do physical activity?*

**PAR-Q:**

*Has your doctor ever said that you have a heart condition AND that you should only do physical activity recommended by a doctor?*

*Do you feel pain in your chest when you do physical activity?*

*In the past month, have you had chest pain when you were not doing physical activity?*

*Do you lose your balance because of dizziness or do you ever lose consciousness?*

*Do you have a bone or joint problem (for example, back, knee or hip) that could be made worse by a change in your physical activity?*

*Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?*

*Do you know of any other reason why you should not do physical activity?*

**If YES (=moderate/high risk), require medical clearance from physician AND approval from Dr. Pyke, or exclude**

*Now I am going to ask you regarding different medical diagnoses that you may current have, or may have had in the past.*

**Diagnoses:**

*Have you ever been diagnosed with cardiovascular disease, such as cardiac, peripheral vascular, or cerebrovascular disease?*

*Have you ever been diagnosed with a pulmonary disease, such as chronic obstructive pulmonary disease, asthma, interstitial lung disease, or cystic fibrosis?*

*Have you ever been diagnosed with a metabolic disease, such as Type I or Type II diabetes, a thyroid disorder, renal disease, or liver disease?*

**If YES (=high risk), require medical clearance from physician AND approval from Dr. Pyke, or exclude**

*Just a few more questions about different risk factors for cardiovascular disease. Most adult women have these risk factors to at least some degree.*

**CVD Risk Factors:**

*Age? (women  $\geq$  55)*

*Do you have a family history of cardiovascular disease, occurring before 55 years of age in a male first degree relative or before 65 years of age in a female first degree relative? For example, any heart attacks, revascularization (angioplasty, bypass surgery or sudden death) in parents or siblings or children?*

*Do you currently smoke? (If previous smoker): When did you quit (was it at least 6 months ago)? Are you currently exposed to second hand smoke on a regular basis?*

*Do you currently participate in at least 30 minutes of physical activity (activity that causes substantial increases in heart rate and breathing) at least 3 days/week (for at least 3 months)?*

*What do you currently weigh? And how tall are you? (calculate BMI = weight(kg)/height(m)<sup>2</sup>; >30 = obese)*

*Do you currently have high blood pressure? Is your doctor prescribing any antihypertensive medication? (If does not know current blood pressure): When is the last time you had your blood pressure taken (within last 2-3 years)? Was your blood pressure “normal” then?*

*Have you ever been diagnosed with dyslipidemia? Or are you on any lipid-lowering medication?*

*Do you know if you currently have higher than normal blood sugar levels?*

**If YES to 2+ items (=moderate risk), require medical clearance from physician**

**NOTE: USE SCREENING FORM TO DETERMINE HOW TO PROCEED IN TERMS OF PHYSICAL HEALTH ASSESSMENT – i.e., inclusion, medical clearance from physician (with or without approval from Dr. Pyke), or exclusion**

(Continue with phone screen...)

*Now I'm going to ask you a few questions regarding any experience you may have with yoga or exercise classes.*

5. *In the past 3 months, have you practiced yoga?*

*If YES: What type? When did you begin practicing (MM/DD/YY)? How many times per week do you practice?*

*If no current practice: Have you ever had a regular yoga practice (at least once/biweekly)?*

*If YES: When was the last time you practiced?*

**Exclude:** Participants with a yoga practice within the past 3 months (2+ classes per month, on average), or those with previous practice (at least once/weekly) that ended less than 2 years ago.

**Note:** Use your judgment on this.

6. *In the past 3 months, have you participated in exercise classes?*

*If YES: What type of class? When did you begin attending these classes (MM/DD/YY)? How many times per week do you attend these classes?*

If no current participation: *Have you ever attended exercise classes on a regular basis (at least once/biweekly)?*

If YES: *When was the last time you attended these classes?*

**Exclude:** Participants with who participated in aerobic exercise classes within the past 3 months (2+ classes per month, on average), or those who previously attended classes on a regular basis (at least once/weekly) that ended less than 2 years ago.

**Note:** Use your judgment on this.

**(iv) Mood Module Screen**

*Now I would like to ask you some questions about your mood over the last couple of weeks. These questions are simply meant to give me an idea about whether or not you are eligible for the study in terms of mood symptoms.*

*“In the last two weeks....”*

<u>Question</u>	<u>Response:</u> No (N); Maybe (M); Definitely (D)
(1) <i>Have you been feeling depressed or down most of the day nearly every day? (At least some of the day, some days of the week?)</i>  If YES, <i>When did it start? How long did it last?</i> [If at least TWO WEEKS & caller is <u>currently</u> experiencing problem, circle D]	N                      M                      D
<b>“During this time....”</b>	-----
(2) <i>Have you lost interest or pleasure in doing things that you usually enjoyed? (Is there anything that you’re doing less of? Do you find you have to push yourself to do things?)</i>	N                      M                      D
(3) <i>How has your appetite been? (Have you lost or gained any weight? Are you trying to lose weight as part of a diet?)</i>	N                      M                      D
(4) <i>Any difficulties sleeping? - insomnia or hypersomnia (Any trouble falling asleep? Waking up in the middle of the night? Waking up too early in the morning and not being able to get back to sleep?)</i>	N                      M                      D
(5) <i>What is your energy like? (Tired all the time? – Distinguish between low energy and sleepiness)</i>	N                      M                      D
(6) <i>How have you been feeling about yourself in this time period? (Have you been hard on yourself? About what?; What about feeling guilty about things you have done or not done?)</i>	N                      M                      D
(7) <i>Do you have trouble thinking or concentrating? What are you having trouble thinking about or concentrating on? (Is it hard to make decisions about everyday things?)</i>	N                      M                      D
(8) <i>Have you been so fidgety or restless that you are unable to sit still? (What about the opposite, like you are talking or moving more slowly than usual? Like you’re moving through thick mud?)</i>	N                      M                      D

<p><b>[At least 3 of the above symptoms need to be coded 'D'. Discontinue as soon as these criteria are met]</b></p>	<p>-----</p>
<p>-- How many times previously in your life have you felt depressed or down most of the day nearly everyday for at least two weeks and had several of the symptoms you mentioned?</p>	<p>-----</p>

- **If the participant is not eligible (less than 3 of the symptoms were coded as 'D') based on mood symptoms:**

*Unfortunately, you are not eligible to participate in this study. Thank you for your interest and time.*

- **If the participant is eligible (3 or more symptoms were coded as 'D') based on mood symptoms AND is of LOW cardiovascular risk:**

*According to your answers regarding your mood symptoms and physical health, you are eligible to participate in this study. If you are still interested in participating, I'd like to set up appointment times for your two in-person appointments.*

- **If the participant is eligible (3 or more symptoms were coded as 'D') based on mood symptoms AND is of MODERATE cardiovascular risk:**

*According to your answers regarding your mood symptoms, you are eligible for the study. However, in terms of physical health, I believe you may be at an increased risk for participating in the study. This is because you reported... (list risk factors reported). If you are still interested in potentially participating, I need you to seek medical clearance from you physician. Is this something you would like to do? (If YES): Great! I will need to send you a form, which you will then take to your physician. It describes the nature of the study and why we are seeking medical clearance. If your physician believes that you are a good candidate for participating in the study, we can move forward and book you in for your two in-person appointments. If your physician recommends that you do not participate, we will not be able to move forward with the study. Do you have any questions about this?*

- Ask for an email address or mailing address to send "Physician Clearance for Study Participation" form

- **If the participant is eligible (3 or more symptoms were coded as 'D') based on mood symptoms AND is of HIGH cardiovascular risk:**

*According to your answers regarding your mood symptoms, you are eligible for the study. However, in terms of physical health, I believe you may be at an increased risk for participating in the study. This is because you reported... (list risk factors, sign/symptoms, diagnoses reported). If you are still interested in potentially participating, I will first need to run this by Dr. Pyke. If she gives her approval, I will then need you to seek medical clearance from you physician. Is this something you would like to do? (If YES): Great! I will speak with Dr. Pyke within the next few days, at which point I will contact you to let you know the outcome. If she gives her approval, I will need to send you a form, which you will then take to your physician. It describes the nature of the study and why we are seeking medical clearance. If your physician believes that you are a good candidate for participating in the study, we can move forward and book you in for your two in-person appointments. If your physician recommends that you do not participate, we will not be able to move forward with the study. Do you have any questions about this?*

- Ask for an email address or mailing address to send "Physician Clearance for Study Participation" form

**(v) Set an appointment**

- Check with the lab calendar and write down the scheduled times.

**(vi) Confirmation**

- Confirm the times and dates of the appointment
- Give directions for getting to the Mood Research Lab (directions to the Kinesiology building will be given at first appointment)
- Ask for an email address to send them a reminder at least 24 hours before the appointment.
- Give them contact information for the study

Email: natd@queensu.ca

Phone: 613-533-6003

## Appendix C



**Queen's**  
UNIVERSITY

### **Physician Clearance for Research Study Participation**

Attention Physician:

Your patient, \_\_\_\_\_, is considering participation in the **Nontraditional Approaches to the Treatment of Depression (NATD) Project**, a research study that is being conducted at Queen's University by the Mood Research Lab (Psychology Department, Supervisor: Dr. Kate Harkness) and the Cardiovascular Stress Response Lab (Kinesiology Department, Supervisor: Dr. Kyra Pyke). This study is investigating the antidepressant effect of Bikram yoga and exercise classes, as well as the mechanisms by which these approaches may improve depression symptoms. As a participant in this study, your patient would undergo a cardiorespiratory fitness appraisal (see "Description of Study Components", pg. 2), as well as participate in *either* yoga or exercise classes (see "Description of Study Components", pg. 2), two times per week for 8 weeks (16 classes total).

Based on our screening procedures, which adhere to guidelines of the American College of Sports Medicine (ACSM, 2013), your patient has been identified as being of moderate or high cardiovascular risk (see pg. 3 for details), which ultimately increases the risk of a cardiac event occurring during exercise. For the purposes of this research project, moderate cardiovascular risk means that an individual is asymptomatic and has not been diagnosed with any cardiovascular, metabolic, or pulmonary disease, *but has two or more risk factors for cardiovascular disease*. These risk factors include age  $\geq 55$ , family history of CVD, history of cigarette smoking, sedentary lifestyle, obesity, hypertension, and dyslipidemia (ACSM, 2013). High cardiovascular risk means that an individual is *symptomatic or has been previously diagnosed with cardiovascular, metabolic, or pulmonary disease*. We ask that you kindly read through this Physician Clearance form and provide your judgement as to whether or not your patient is a good candidate, in terms of physical health, for the NATD Project. Thank you very much for your time.

Sincerely,

A handwritten signature in cursive script, appearing to read "Kate Harkness".

## Descriptions of Study Components

*Cardiorespiratory fitness appraisal.* Participants are asked to participate in a widely-used submaximal exercise test (YMCA Submaximal Cycle Ergometer Test; described in Golding, Myers, & Sinning, 1989), which will allow for an estimate of maximal oxygen uptake ( $VO_2\text{max}$ ) based on heart rate. This test is incremental in nature (i.e., speed and resistance is monitored and adjusted), with the goal of having participants reach, *but not exceed*, 85% of their age-predicted maximum heart rate (maximum heart rate estimated as  $220 - \text{age}$ ). This test typically lasts three stages, or approximately 10-15 minutes. ACSM guidelines (2013) suggest that individuals who are considered “low” or “moderate” risk for CVD *do not* require supervision by a medical doctor during submaximal exercise testing.

*Bikram yoga classes.* Bikram yoga is style of “hot” yoga that consists of two breathing exercises and 26 postures. Classes are 90 minutes in length and take place in a heated and humid room ( $\sim 40^\circ\text{C}$  and 40% humidity). Although empirical studies have not been conducted to determine the intensity of Bikram yoga classes, the intensity likely ranges from moderate to vigorous, with certain postures feeling more “intense” than others. Yoga classes are taken at Feel Yoga Studio (80 Princess Street) and instructed by fully-certified Bikram yoga instructors.

*Exercise classes.* Exercise classes involve a number of different classes (e.g., Zumba, Sports Conditioning, Bootcamp, Step) that are taking place at the Kingston Family YMCA. Classes range in length from 50 to 90 minutes and all involve a strong cardio component. The intensity of these classes likely ranges from moderate to vigorous.

Attention Physician:

For the purposes of the NATD Project, your patient, \_\_\_\_\_, has been identified as being of \_\_\_\_\_ cardiovascular risk. Please see information below regarding specific risk factors, symptoms, and/or previous diagnoses that led to this classification.

Reported or objectively measured risk factors:

	<u>Age (&gt;55yrs old)</u>
	<u>Family History</u> (Myocardial infarction, coronary revascularization, or sudden death before 55yr in father or other male first-degree relative or before 65yr in mother or other female first-degree relative.)
	<u>Smoking Status</u> (Current cigarette smoker or those who quit within the previous 6mo or exposure to environmental tobacco smoke)
	<u>Sedentary Lifestyle</u> (Not participating in 30min of moderate intensity physical activity on at least 3d of the week for at least 3mo)
	<u>Obesity Status</u> (BMI $\geq 30\text{kg/m}^2$ , or WC > 88cm (WOMEN)) – Self-report on phone screen; objectively confirmed in lab
	<u>Hypertension</u> (Systolic blood pressure $\geq 140\text{mmHg}$ and/or diastolic $\geq 90\text{mmHg}$ , confirmed by measurements on at least two separate occasions, or on antihypertensive medication) – Self-report on phone screen; objectively confirmed in lab
	<u>Dislipidemia</u> (LDL $\geq 130\text{mg/dl}$ , or HDL < 40mg/dl, or on lipid lowering medication. If only total cholesterol available, $\geq 200\text{mg/dl}$ )
	<u>Prediabetes</u> (tick yes if unknown AND either: age > 45yrs and BMI > 25 OR age < 45 and BMI > 25 + other risk factors)
/8	Total

Reported signs/symptoms of cardiovascular disease:

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Reported cardiovascular, metabolic, or pulmonary disease diagnoses:

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Determined risk level:

\_\_\_\_\_ **Moderate Risk** - Asymptomatic and has not been diagnosed with any cardiovascular, metabolic, or pulmonary disease, but has two or more risk factors for cardiovascular disease

\_\_\_\_\_ **High Risk** - Symptomatic or has been previously diagnosed with cardiovascular, metabolic, or pulmonary disease

\_\_\_\_\_

Date: \_\_\_\_\_

Cherie La Rocque, MSc, PhD Student

**Please check  one of the following:**

Based on my knowledge of my patient's current and past physical health, it is my opinion that she is a good candidate for the NATD Project. That is, **I do not have any medical concerns** regarding her participation in the study.

Based on my knowledge of my patient's current and past physical health, it is my opinion that she is NOT a good candidate for the NATD Project. That is, **I have medical concerns** regarding her participation in the study. I recommend that she does NOT participate.

Physician's Name: \_\_\_\_\_

Physician's Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Phone Number: \_\_\_\_\_

Address:

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

**Please complete and return this page via fax to 613-533-2499, Attention: Dr. Kate Harkness**

Should you have any questions regarding the participation of your patient in this project, please contact Cherie La Rocque (PhD Student, Psychology Department, Queen's University) at natd@queensu.ca or 613-533-6003, or Dr. Kyra Pyke (co-supervisor of research project, Kinesiology Department, Queen's University) at pykek@queensu.ca or 613-533-6000 ext.79631, or Dr. Kate Harkness (co-supervisor of research project, Psychology Department, Queen's University) at harkness@queensu.ca or 613-533-2886.

**Thank you very much for your help. We hope that this study and its results will be a beneficial contribution to depression and exercise research.**

## Appendix D

### **Medical Screening Interview**

(Adapted from the Physical Activity Readiness Questionnaire)

1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?  
**YES NO**
  
2. Do you feel pain in your chest when you do physical activity?  
**YES NO**
  
3. In the past month, have you had chest pain when you were not doing physical activity?  
**YES NO**
  
4. Do you lose your balance because of dizziness or do you ever lose consciousness?  
**YES NO**
  
5. Do you have a bone or joint problem (e.g. back, knee or hip) that could be made worse by a change in your physical activity?  
**YES NO**
  
6. Is your doctor currently prescribing drugs (e.g. water pills) for your blood pressure or heart condition?  
**YES NO**
  
7. Do you know of any other reason you should not do physical activity?  
**YES NO**
  
8. Do you have, or have you ever had, problems with any of the following?

	<b>Yes</b>	<b>No</b>
<b>i. Heart or blood vessels</b>	___	___
(E.g., heart attack, stroke, heart murmur, angina, coronary artery disease, high blood pressure, high cholesterol, congenital heart disease, any heart operation, bleeding or clotting disorders)		
<b>ii. Nerves or brain</b>	___	___
<b>iii. Breathing or lungs</b>	___	___
<b>iv. Hormones, thyroid, or diabetes</b>	___	___
<b>v. Muscles, joints, or bones</b>	___	___
<b>vi. Other (please list)</b> _____		

9. Please list the diagnosis or/or briefly describe any problems identified above in question #8.

10. Are you presently taking any medications? If yes, please list.

11. Do you have any allergies to medications, adhesive tape, latex, etc.?

12. Do you currently smoke? **YES** **NO**

If yes, number of cigarettes/day \_\_\_\_\_

If *previous* smoker, date of last cigarette \_\_\_\_\_ (mm/yyyy)

## Appendix E

### TREATMENT PARTICIPATION QUESTIONNAIRE

This questionnaire asks about your participation in the study interventions (i.e., Bikram yoga or aerobic exercise) and other interventions that may be applicable to you. Please provide information on *all* interventions applicable to you.

#### 1. Bikram Yoga

Check if **not** applicable

In the **past week**, how many Bikram yoga classes did you attend? \_\_\_\_\_

For each class you attended, please estimate the number of postures you **did not participate in** (i.e., laid down, sat down, or stood still). Please remember that taking a break when needed is completely fine!

Class 1: \_\_\_\_\_ Class 2: \_\_\_\_\_

#### 2. Aerobic Exercise

Check if **not** applicable

In the **past week**, how many aerobic exercise classes did you attend? \_\_\_\_\_

For each class you attended, please estimate the portion of time you **did not participate** (i.e., laid down, sat down, or stood still). Please give this estimate in 'minutes'. Please remember that taking a break when needed is completely fine!

Class 1: \_\_\_\_\_ Class 2: \_\_\_\_\_

#### 3. Adverse Events

Check if **not** applicable

In the **past week**, did you experience any adverse events or negative side effects resulting from participation in either Bikram yoga or aerobic exercise classes? These may be minor side effects (e.g., short-term muscle soreness, stiffness) or more severe events (e.g., fainting, torn muscle) that occurred during or following a class.

If yes, please describe:

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4. Therapy/Counseling

Check if **not** applicable

In the **past week**, did you attend at least one therapy or counseling session for depression?

Yes  No

In the **past week**, how many therapy or counseling sessions did you attend? \_\_\_\_\_

Please comment briefly if you had any changes to your therapy or counseling treatment in the past week (e.g., change in frequency of sessions, change from individual to group therapy).

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5. Antidepressant Medication

Check if **not** applicable

In the **past week**, did you take medication for depression?

Yes  No

In the **past week**, did you take this medication as prescribed?

Yes  No

Please comment briefly if you had any changes to your antidepressant medication in the past week (e.g., change in dose or type).

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