THE DISSERTATION COMMITTEE FOR JOHNNA LEIGH MEDINA CERTIFIES THAT THIS IS THE APPROVED VERSION OF THE FOLLOWING DISSERTATION:

USING EXERCISE TO TARGET MAINTENANCE FACTORS OF ADDICTIVE BEHAVIORS

Committee:

Jasper Smits, Supervisor

Robert A. Josephs

Caryn L. Carlson

David Rosenfield

Michael Zvolensky

USING EXERCISE TO TARGET MAINTENANCE FACTORS OF ADDICTIVE BEHAVIORS

BY

JOHNNA LEIGH MEDINA

DISSERTATION

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

THE UNIVERSITY OF TEXAS AT AUSTIN

AUGUST 2017

ACKNOWLEDGEMENTS

Thank you to the institutions and organizations that made this research possible: The National Institute on Drug Abuse, Bikram Yoga Dallas, Practice Yoga Austin, and Pure Action Yoga. I would also like to acknowledge my mentors, colleagues, family, and friends for their love and support in helping me through this process. Several important individuals deserving mention include: my graduate advisor, Dr. Jasper Smits; my statistician mentor, Dr. David Rosenfield; my dissertation committee members; my colleague, junior mentor, and best friend, Dr. Lindsey Hopkins; the Yoga Study research assistants, especially Carly Ek, Lori Hoadley, Jennifer Lo, Tricia Triece, Maddie Pantoni, and Natalie Tunnel; the 6 magnificent ladies of my UT Austin graduate cohort and graduate friends; my Miami VA internship cohort, especially Emily (could not have finished this manuscript while on internship without your solidarity); my amazing parents for encouraging my goals despite having to help me move every few years; and my loving canine children, Ritchie and Lola.

Using Exercise to Target Maintenance Factors of Addictive Behaviors

Johnna Leigh Medina, Ph.D.

The University of Texas at Austin, 2017

Supervisor: Jasper Smits

This research is prompted by the need to improve interventions for addictive behaviors. Research has identified several key biobehavioral mechanisms involved in the risk and maintenance of addiction, which are prime targets for novel interventions. The present dissertation aims to test whether we can effectively modify several factors predictive of relapse (e.g., low distress tolerance (DT), behavioral avoidance, and hypothalamic-pituitary-adrenal (HPA)-axis dysregulation) using physical activity interventions. The rationale for employing exercise for this application is supported by (1) decades of research attesting to the capacity for exercise to beneficially tap multiple biobehavioral systems, (2) more recent research supporting the clinical utility of exercise in substance use disorder treatment, and (3) emergent evidence supporting the potential of exercise as an appealing and accessible alternative or add-on to standard care. Study 1 extends the results of recent work by our group, which demonstrated efficacy for exercise to reduce anxiety sensitivity (AS), a form of distress intolerance reflecting vulnerability to somatic arousal. The results suggest that gender may be a moderator of this

effect (Medina et al., 2014), with women responding less immediately than men. This observation underscores the need to further explore the treatment of distress-vulnerability in women, as well as potential merit in exploring alternatives to aerobic training. Accordingly, Studies 2 and 3 evaluated yoga for enhancing DT in females for whom distress vulnerability served to exacerbate maladaptive coping tendencies (e.g., smoking, overeating). Study 2 served as a proof of principle, wherein we examined the efficacy of Bikram yoga for enhancing DT in a sample of females with an elevated tendency to eat in response to stress or negative affect (i.e., conceptualized as an addictive behavior). Results were consistent with our hypothesis, showing that yoga enhanced self-reported emotional DT. Moreover, we found yoga primarily increased the absorption sub-facet of DT (defined as tendency for distress to absorb attentional resources), which, in turn, mediated reductions in self-reported emotional eating (Medina et al., 2015). In Study 3, we applied an 8-week hatha yoga (Vinyasa flow) intervention, aiming to address the contribution of elevated AS to early relapse in female smokers by targeting cortisol declines during the withdrawal phase of a quit attempt. Results did not support yoga as efficacious for altering cortisol, ameliorating subjective withdrawal, or achieving continuous abstinence post-quit. We speculate this was in part due to poor intervention adherence, highlighting the importance of including intervention components to address motivation for health behavior change. We discuss other limitations and future directions from our findings across studies.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Addictive behaviors, both substance and non-substance related, are a major global health concern. Substance use disorders (SUDs) represent the most prevalent and consequential form of behavioral addiction. These are defined excessive, prolonged patterns of alcohol, tobacco, and/or other drug use that leads to significant psychiatric distress and impairment in the daily functioning of the individual (American Psychological Association (APA), 2013). Considered a difficult-to-treat problem and leading risk factor for cardiovascular disease and early mortality (World Health Organization (WHO), 2009; Degenhardt & Hall, 2012; Whiteford et al., 2013), SUDs are one of the most costly conditions in the United States (US) and worldwide. In the US alone, SUDs have a lifetime prevalence rate of 20.8% (Kessler et al., 2005) and cost $600 billion annually (National Institute on Drug Abuse (NIDA), 2012).

A variety of evidence-based pharmacological and behavioral treatment approaches exist for SUDs and other behavioral addictions (i.e., gambling). Still, there is much room to improve their effectiveness. Most individuals with SUDs do not initiate or remain in treatment (Copeland et al., 2006; Geraghty et al., 2012; Leeman et al., 2006; MacPherson et al., 2008; US Department of Health and Human Services, 1999), and the majority of those who attempt to reduce or quit using without aid are unsuccessful (Chapman & MacKenzie, 2010; Fiore et al., 1990). Furthermore, established interventions for SUDs are associated with high rates of relapse, even among treatment completers. Approximately 40-60% of patients who complete treatment for alcohol or illicit drug abuse end up relapsing (NIDA, 2012). For tobacco smoking, the relapse rate is as high as 85% (Copeland et al., 2006; Geraghty et al., 2012; Leeman et al., 2006; MacPherson et al., 2008). Thus, there is room for improving SUD treatment approaches.

Less research has been conducted on non-substance-related behavioral addictions. However, they are receiving increasing recognition as a cause for concern (APA, 2013; Potenza, 2014; Yau & Potenza, 2015). In the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5), the category Substance-Related/Addictive Disorders was established to classify substance and non-substance related behavioral addictions on a common spectrum, given relatedness in their clinical expressions (APA, 2013). However, only Gambling Disorder was included. Other non-substance and related behavioral addictions, such as those involving maladaptive or risky patterns of Internet use, sexual behavior, and eating, were considered but ultimately excluded from the Substance-Related/Addictive Disorders category, with the DSM-5 task force advising further investigation into the phenomenology and impact of these conditions, in order to guide their future classification and treatment (Potenza, 2014).

Mechanisms Across the Addictive Behaviors: Implications for Treatment

Though further progress is needed, there is ample evidence linking SUDs to other behavioral addictions. It appears that SUDs and non-substance behavioral addictions overlap in terms of the biobehavioral factors involved in their development and course (Potenza, 2014; APA, 2013). For example, altered dopamine receptor availability has been noted in SUDs, gambling disorder, and obesity. Important to note, abnormal dopamine functioning in localized D2, D3, and D4 receptor sites is typically correlated with altered reward and punishment sensitivity, which may help to explain maladaptive decision-making tendencies observed across addictive problems (Potenza, 2014; Yau & Potenza, 2015). Relatedly, clinical research suggests that, in some cases, eating patterns may function *as* a SUD. Findings in the eating literature converge in showing that under certain conditions repeated ingestion of hyperpalatable food (i.e.,

high in fat, salt, sugar) is capable of triggering reward pathways that cause neuroendocrine and metabolic adaptations resembling those seen in drug addiction (Adam & Epel, 2007; Gearhardt, Grilo, Di Leone, Brownell, & Potenza, 2011). The context for this tendency to develop appears dependent on presence of stress coupled with biological diathesis for heightened biological stress-reactivity (Adam & Epel, 2007).

In summary, these findings underscore the complexity and interrelation between mechanisms that drive addictive processes. Beyond the scope of addiction, research on transdiagnostic mechanisms has furthered our understanding of the overlap between forms of psychopathology more broadly (Barlow et al, 2010; Dozois, Seeds, & Collins, 2009; Sauer et al., 2012). This work has suggested merit in treating addictive behaviors by targeting underlying emotional vulnerability factors. In a broad sense, emotional vulnerability refers to difficulty with respect to the ability to experience and cope with affective states leading to maladaptive consequences (Dozois, Seeds, & Collins, 2009; Leventhal & Zvolensky, 2015; Sauer-Zavala et al., 2012). In the past several decades, specialized attention, especially within the eating, anxiety/trauma, and substance use literature, has been paid to understanding the mechanisms underlying individual differences in emotional/affective vulnerability and its consequences. This has involved close examination of cognitive-affective and biological constructs implicated in emotional vulnerability (e.g., stress-reactivity, trait distress intolerance, emotion dysregulation. More recently, such factors have become subject to modification with interventions (Mansell, Harvey, Watkins, & Shafran, 2008; Sauer-Zavala et al., 2012). Indeed, this has led to several recent innovative behavioral treatments in the areas of affective disorders, personality disorders, SUDs/SUD comorbidity (Barlow et al., 2010; Mansell, Harvey, Watkins, & Shafran, 2008;

Neacsiu, Eberle, Kramer, Weismann, & Linehan, 2014). Efficacious modalities that address affective coping in their theoretical foundation, such as Dialectical Behavior Therapy (Linehan, 1993), have tended to use cognitive-behavioral and mindfulness-based approaches to help patients learn new skills to improve their ability to cope with and adaptively regulate their emotions (Barlow et al., 2010; Mansell, Harvey, Watkins, & Shafran, 2008).

Still, there is much to learn regarding the specific intervention needs of patients who present with various manifestations of affective vulnerability. In the context of addiction pathology, there are few controlled treatment studies that either directly tailor interventions for affect-vulnerable groups or evaluate lowered affective vulnerability as a mechanism of change leading to clinical improvement. First steps in advancing this research (and improving the treatment of addiction overall) will involve the identification of moderators and mechanisms of response through evaluation of easily accessible, preferred interventions with strong theoretical basis for reducing affective vulnerability through multiple biobehavioral avenues. The present dissertation evaluates behavioral health interventions for targeting two important affect-vulnerability factors implicated in addiction maintenance and relapse: distress tolerance and hypothalamic-pituitary-adrenal (HPA) axis responding.

Distress Tolerance (DT)

Distress tolerance (DT) is defined as an individual-difference trait, reflecting both the perceived and actual incapacity to withstand negative experiential states (Brown, Lejuez, Kahler, Strong, & Zvolensky, 2005; Simons & Gaher, 2005). Individuals characterized by low DT appraise distress as highly unacceptable, threatening, and distracting (Simons & Gaher, 2005). Behaviorally, these persons display urgency to avoid or escape situations that provoke distress,

evidenced by tendencies for limited goal-persistence and maladaptive self-regulatory coping strategies (e.g., binge drinking, smoking, overeating; Leyro, Zvolensky, & Bernstein, 2011). Because low DT captures the susceptibility to negative experiential states, the construct is considered transdiagnostically relevant to psychopathology.

Regarding the scope of the DT construct, Simons and Gaher (2005) have operationalized DT as facets involved in the *process* of managing and regulating non-specific emotional distress. These facets include: (1) one's general perceived *Tolerance* of negative or threatening emotions, (2) one's *Appraisal* or value judgment about feeling distressed or upset, as well as (3) the resulting *Absorption* of attention in the distress itself, and (3) the propensity for action aimed at *Regulation* or reduction of distress (Simons & Gaher, 2005). In support of this conceptualization, scores on the self-report based Distress Tolerance Scale (DTS; Simons & Gaher, 2005) have predicted symptom severity and problem behavior in a range of clinical populations (Anestis et al., 2007; Leyro et al., 2010).

Other researchers, however, have made distinctions between cognitive/affective versus physical/somatic distress vulnerabilities (Leyro, Zvolensky, & Bernstein, 2011; Zvolensky et al. 2008; Zvolensky et al., 2011), as evidenced by the array of lower-order constructs and related measures that have emerged in the study of low DT and its consequences (Leyro, Zvolensky, & Bernstein, 2011). For example, an identified risk factor for anxiety disorders is the fear of somatic arousal. Termed anxiety sensitivity (AS), this construct strongly predicts clinical anxiety disorder status and has thus become a crucial intervention target for anxiety disorders (Reiss, 1991; Reiss & McNally, 1985), as well as for tobacco smokers with comorbid anxiety (Morissette et al., 2007). Other forms of low DT implicated in risk for psychopathology include

intolerance of frustration, situations defined by ambiguity, and physical pain (Leyro, Zvolensky, & Bernstein, 2011).

Both self-report and behavioral measures have been developed to tap these various manifestations of low DT (Leyro, Zvolensky, & Bernstein, 2011). However, in line with diverse theoretical frameworks, there is no established gold standard approach to measuring DT across the distinct, related forms of psychopathology, and little evidence exists on the relative sensitivity to treatment among DT measures (McHugh & Otto, 2012; Zvolensky, Bernstein, & Vujanovic, 2011).

As summarized by Leyro et al. (2011), overall data has been somewhat inconclusive as to whether domain-specific manifestations of distress intolerance represent constructs distinct from general low emotional distress tolerance. Towards establishing consensus in the field regarding its theoretical scope and characteristics, a recent factor analysis has been conducted among self-report DT measures (McHugh & Otto, 2012). Results suggest that lower-order constructs may be subsumed under a global emotional DT construct, as scores across measures appear to most strongly load onto a general DT factor (McHugh & Otto, 2012). Still, domain-specific self-report measurements with psychometrically sound properties continue to be used given the relevance of their items for identifying clinically-specific concerns and their usefulness in establishing clinical severity norms (Leyro, Zvolensky, & Bernstein, 2011).

This literature was used to inform our approach to studying DT in the present dissertation. Depending on the research question and clinical population of interest in each of the three studies, we considered ways to address both broad DT and AS. When appropriate for

describing elevated AS as a more-specific manifestation of low DT, we used the terms "low DT" and "AS" interchangeably.

Because low DT leads to coping-oriented substance use, it is considered a maintaining factor of substance abuse and addiction. This is especially the case in individuals with comorbid psychopathology (Bonn-Miller et al., 2009; Brown, Lejuez, Kahler, & Strong, 2005; Buckner, Keough, & Schmidt, 2007; Cooper, Frone, Russell, & Mudar, 1995; Simons & Gaher; 2005; Zvolensky et al., 2009). This has been extensively studied in the context of nicotine addiction. Over the past several decades, observational, experimental, and clinical intervention studies have found that individuals low in DT, as defined by elevated AS or intolerance of frustration, classify as a difficult-to-treat subgroup of nicotine users who are particularly prone to relapse (Brown, Lejuez, Kahler, & Strong, 2005). In one study, smokers with high AS, as evidenced through heightened reactivity to a laboratory biological CO2 gas inhalation challenge, had been unable to achieve a full week of abstinence during any of their previous quit attempts (Zvolensky, Feldner, Eifert, & Brown, 2001).

Prospective studies have demonstrated similar findings for individuals with low DT. Specifically, low emotional DT predicts greater withdrawal symptom severity and shorter time to lapse following a tobacco quit attempt (Brown et al., 2005; Brown et al., 2009; Brown et al., 2008; Abrantes et al., 2008). Such tendencies for early lapse, as well as subsequent relapse, are also evidenced by low DT smokers who receive gold-standard treatment (Abrantes et al., 2008; Brown, Lejuez, Kahler, & Strong, 2005). In the context of RCTs, early post-quit lapse (i.e., that occurs on or shortly after the scheduled quit date) tends to be preceded by a sharp increase in negative affect (Abrantes et al., 2008; Brown, Lejuez, Kahler, & Strong, 2005). Given the

negative-reinforcement value of smoking, these early lapses have been understood to reflect individuals' efforts to escape the aversive sensations of acute nicotine withdrawal (Abrantes et al., 2008; Brown, Lejuez, Kahler, & Strong, 2005; Shiffman & Waters, 2004; West, Hajek, & Belcher, 1989; Zvolensky, Feldner, Eifert, & Brown, 2001). Further highlighting their pervasive behavioral avoidance tendencies, low DT smokers are also more likely to dropout from treatment. Together, these findings suggest that improving SUD treatment may require addressing low DT.

Hypothalamic-Pituitary-Adrenal (HPA) Axis Functioning

Stress plays a significant role in mental health. Most forms of psychopathology have been understood through a diathesis-stress framework, which recognizes the interactive role of biological factors (e.g., genetics, biochemistry) and environmental stressors in predicting the onset and course mental disorders (Goforth, Pham, & Carlson, 2011; Salomon & Jin, 2013; Zuckerman, 1999). Both disorder-specific and general diathesis-stress models have been proposed to explain the development of psychopathology (Salomon & Jin, 2013; Zuckerman, 1999). Common to these models is the idea that physiological stress mechanisms play a critical role in the onset and course of illness. The central component of biological stress responding is the HPA-axis, which governs the release of various neurochemicals and hormones (e.g., CRH, ACTH, and cortisol) that operate along a negative feedback loop in order to effectively regulate the release of one another (Zuckerman, 1999). Pertinent to the expression of psychopathology, HPA-axis activity is critically involved in motivated behavior, threat responding, and effective regulation of emotional stress (Zuckerman, 1999). The HPA-axis is also involved in a range of processes beyond stress perception. For example, it is critically involved in the regulation of

homeostatic mechanisms (e.g., neuroendocrine, immune, metabolic, hormonal) required for survival and overall systemic health. These systems are known to become disturbed under chronic stress, and, if not effectively managed, this disruption may result in serious health consequences including the development of chronic disease (Guilliams & Edwards, 2010).

Given the known contribution of psychosocial stress to the development, maintenance, and relapse of SUDs, as well as the pervasive involvement of HPA-axis activity in all biological systems, investigations of the underpinnings of addiction have paid special attention to the role of the HPA-axis in SUDs (Adinoff, Junghanns, Kiefer, & Krishnan-Sarin, 2005; Goeders, 2002; 2003; Stephens & Wand, 2012). Habitual substance use disrupts regulatory characteristics of the HPA-axis, resulting in physiological adaptations and potential consequences depending on the nature of the dysregulation.

One potential consequence is altered glucocorticoid receptor sensitivity, which alters cortisol stress-reactivity and recovery patterns, impacting one's ability to cope effectively, both emotionally and behaviorally, with stressful situations (Adinoff, Junghanns, Kiefer, & Krishnan-Sarin, 2005; Frederick, 1998; Koob & Mohl, 2001). Indeed, the effects of altered (especially reduced) glucocorticoid receptor sensitivity have been implicated in the onset and relapse of cocaine, nicotine, and alcohol use disorders (Adinoff, Junghanns, Kiefer, & Krishnan-Sarin, 2005; Frederick, 1998; Koob & Mohl, 2001). Altered glucocorticoid activity in the HPA-axis activity can also result in neuroplasticity in pathways that reinforce the reward potential of addictive substances, thereby exacerbating the addictive behavior (Koob & Mohl, 2001). This may be particularly salient maintenance factor for individuals driven by the negative reinforcement of their drug use. Merging schools of thought in the context of maladaptive eating,

a review by Adam & Epel (2007) on stress, eating, and the reward system suggests that the propensity for heightened biological stress reactivity, coupled with cognitive affective intention to diet, moderates the degree to which individuals engage in tendencies of emotional stress-eating (Adam & Epel, 2007).

Cortisol dysregulation also appears to be implicated in substance use relapse. In stimulant use disorders, this appears to be related to hypercortisolism caused by habitual use. In daily tobacco smokers (compared to non-smokers), for example, unstable but repeated elevations in cortisol, as well as amplified cortisol-awakening responses, are observed (Friedman et al., 1987; Steptoe & Ussher, 2006). Pointing to how this is related to relapse, on the first day following tobacco deprivation (2-24 hours post-cessation), there is a sharp plummet in cortisol concentration caused by the absence of nicotine (i.e., proposed by authors as representing a rebound effect; Cohen, al 'Abasi, & Collins, 2004; Pomerleau, Garcia, Pomerleau, & Cameron, 1992; Ussher et al., 2006). Though levels begin to increase steadily after several days, this initial drop in cortisol is associated with withdrawal symptom intensity and early relapse (al'Absi et al., 2004; Steptoe & Ussher, 2006). Efforts understand the clinical utility of targeting cortisol in order to achieve improved early abstinence outcomes are warranted.

Targeting Emotional Vulnerability Facilitates Treatment Efficacy

Initial research suggests that targeting DT and the HPA-axis facilitates treatment efficacy for addictive problems. Early-stage intervention development efforts have begun targeting DT in the context of nicotine dependence. The components of these interventions have drawn from evidence-based approaches used in other low DT-associated forms of psychopathology (e.g., personality, eating, and anxiety disorders). Brown and colleagues (2008), for example,

implemented a mindful acceptance-based augmentation to standard cognitive behavioral therapy (CBT) to target DT in smokers with a history of repeated relapse (Brown et al., 2013). Among those who completed the trial, 81% were able to remain abstinence for longer than 72 hours (43% maintained abstinence for over one month), suggesting that low-DT smokers were able to improve their cessation success with this adjunct intervention (Brown et al., 2013). Moreover, 82% of participants indicated that the skills learnt from this adjunctive module were either "very" or "extremely" useful in helping participants quit smoking, suggesting the intervention was well tolerated (Brown et al., 2008). Though these results preliminary results appear promising, the lack of a control comparison group renders our inability to determine whether the acceptance-based component was directly responsible for these outcomes, and, thus, that the mechanism of therapeutic action was indeed DT.

Meanwhile, the controlled pilot investigations that have been conducted in smokers encourage strategies using systematic distress-induction (Schmidt, Raines, Allan, & Zvolensky, 2016; Zvolensky et al., 2008). Illustratively, a recent RCT among anxiety-sensitive smokers showed that a behavioral interoceptive (i.e., internal sensation) exposure intervention aided smoking cessation through the mechanism of reduced AS (Schmidt, Raines, Allan, & Zvolensky, 2016; Zvolensky et al., 2008).

Rationale for Targeting Emotional Vulnerability with Exercise

Rationale for the application of exercise to address emotional vulnerability factors is supported by several lines of research. First, evidence establishes exercise as a stress-reducing intervention mediated by its regulatory effect on the HPA-axis (Mastorakos, Pavlatou, Diamanti-Kandarakis, & Chrousos, 2005; Ross & Thomas, 2010; Stranahan & Mattson, 2008). Second,

exercise appears to have effects on the low DT sub-construct AS (Broman-Fulks, Berman, Rabian, & Webster; Broman-Fulks & Storey, 2008; Smits et al., 2008). Third, exercise has shown benefit as a supplementary intervention to aid traditional SUD treatment (Nelson, 2013). Fourth, exercise has potential as an easily accessible modality without the stigma associated with traditional mental health treatments.

Abundant translational and experimental research has been conducted on the effects of exercise on stress in animals and humans. This work indicates that one way exercise may reverse the maladaptive effects of chronic, oxidative stress on mental health is by targeting pro-inflammatory cytokines (Mastorakos, Pavlatou, Diamanti-Kandarakis, & Chrousos, 2005; Ross & Thomas, 2010; Stranahan & Mattson, 2008). Anti-inflammatory potential has been most-supported for voluntary repeated vigorous-intensity aerobic training (Mastorakos, Pavlatou, Diamanti-Kandarakis, & Chrousos, 2005). Another path by which exercise can reduce inflammatory stress is by regulating cortisol secretion patterns in the HPA-axis. A bout of intense exercise acts as a brief systemic stressor, such that over time, repeated exercise has a lowering effect on basal cortisol and overall tonic effect on acute HPA-axis-reactivity to stress (Hamer, Taylor, & Steptoe, 2006).

A budding line of clinical research on yoga suggests the ancient practice may have similar anti-inflammatory and stress-reducing potential to aerobic exercise. Some researchers have proposed yoga is able to exerts its effects on stress via alternating between sympathetic activation (i.e., through the completing and transitioning through asana (physical postures)) and parasympathetic activation (i.e., through meditation and breathing exercises; Ross & Thomas, 2010; Sarang & Telles, 2006; Telles et al., 2013). Recent evidence suggests that both a bout of

light-intensity (i.e., stretch-based, restorative) and vigorous-intensity yoga can reduce cortisol levels in women (Sullivan et al., 2017). However, results also suggest that practitioners find vigorous intensity yoga (termed "power yoga") more enjoyable and energizing, suggestive of intense-yoga's affect regulation potential. Furthermore, initial evidence suggests that a *regular* vigorous-intensity yoga practice can effects similar to aerobic exercise on stress-reactivity. The parent trial to our Study 2 showed that an 8-week Bikram hot-yoga intervention was able to reduce cortisol reactivity to stress for women with heightened baseline stress-reactivity patterns (Hopkins et al., 2016). Further exploration into the comparison between yoga and other physical activity is warranted.

Regarding DT, numerous RCTs in the area of anxiety supports efficacy for a brief (e.g., 2-week) vigorous-intensity exercise intervention to reduce elevated AS in college students with subclinical anxiety (Smits et al., 2008; Broman-Fulks et al., 2008) and in individuals with clinical PTSD (Fetzner & Asmundson, 2015). Importantly, Smits and colleagues' (2008) study conducted a test of mediation that confirmed enhanced anxiety tolerance as a driving mechanism of clinical anxiety symptom improvement with exercise (Smits, Powers, Cho, & Telch, 2004).

Smits and colleagues have since applied these findings to smokers warranting AS reduction in their RCT that evaluated an aerobic exercise augmentation to standard group-based CBT for smoking cessation (Smits et al., 2012; 2016). Results revealed that exercise enhanced treatment effectiveness by mitigating the risk of high-AS status. Specifically, rates of point-prevalence abstinence and sustained abstinence following a target quit-date was higher for participants with higher AS at baseline randomly assigned to 15-week exercise + standard treatment (ST) (vs. a ST + wellness education control condition) at each assessment point than

for lower-AS patients (Smits et al., 2016). Furthermore, among these high-AS participants, there were also reductions in AS as the result of exercise (Smits et al., 2016).

Complementing these results, a recent pilot trial examined efficacy of a stand-alone exercise intervention (16-week gym membership) among adults with alcohol use disorders (AUD; Nelson, 2013). Findings demonstrated AS reductions at both the 8-week and 16-week follow-up for AUD patients with clinically elevated AS scores at baseline (vs. those without). Moreover, the greatest gains were seen in high-AS AUD patients who exercised for at least 150 minutes per week over the 16-week intervention period (Nelson, 2013). This finding is consistent with the results of dose-effectiveness trials on exercise for the treatment of psychopathology in depression and anxiety, which advocate for exercise practice that meets or exceeds public-health-recommended standard (Asmundson, et al., 2013; DeBoer, Powers, Utschig, Otto, & Smits, 2012; Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Stathopoulou et al., 2006; Wipfli, Rethorst, & Landers, 2008).

It is worth noting that, though the evidence on exercise in the realm of AS has been consistent, it is unclear whether exercise is able to tap other low DT facets relevant to addiction. In fact, a recent trial examining brief exercise exposure among participants with anxiety concerns showed the contrary. This RCT found that a vigorous aerobic bout of exercise reduced AS (i.e., reactivity to a post-exercise CO2 challenge), but *not* other distress vulnerabilities, emotional DT and physical discomfort intolerance (DI) (Broman-Fulks, Kelso, & Zawilinski, 2015). The inconclusive nature of these findings warrants additional research attention. Future research calls for studies to examine patient-characteristic moderators in the exercise-DT relation, and, more

specifically, to evaluate exercise to treat various facets of low DT and in the context of various SUDs.

Despite these mixed results from the DT literature, researching consistently documents exercise as beneficial to SUDs, suggesting that it may aid in SUD recovery through a variety of mechanisms (both related and unrelated to low DT). Findings of several smoking cessation RCTs (Marcus et al., 1999, 2013, 2015), for example, parallel the results of Smits et al. (2016) by showing CBT-enhancement with vigorous-intensity exercise. Importantly, Marcus and colleagues also gathered initial support for yoga, a mind-body alternative to aerobic training. Her research group first evaluated a 12-week CBT-adjunctive aerobic exercise intervention (Marcus, et al., 1999) and next, an 8-week CBT-adjunctive hatha yoga intervention (Marcus et al., 2013, 2015). Their results demonstrated comparable augmentative potential for both forms of exercise. As a particularly pertinent component of their results to relapse-vulnerable smokers with low-DT, they also found that adjunct physical activity attenuated participants' nicotine withdrawal (Marcus et al., 1999; 2013, 2015). These findings may reflect a dose-response effect of exercise. This is substantiated by emerging data suggesting that acute *vigorous*-intensity aerobic exercise or yoga may be required to target the biobehavioral mediators (e.g., cortisol levels, craving) of nicotine withdrawal (Taylor, Ussher, & Faulkner, 2007; Ussher, Taylor, & Faulker, 2012).

Furthermore, beyond the area of nicotine dependence, regular physical activity can treat comorbid mental health problems of inpatients with alcohol and illicit substance use disorders (Linke & Ussher, 2014; Zschucke, Heinz, & Strohle, 2011). Encouraging its capacity to address emotional distress-vulnerability specifically, exercise is especially known to reduce SUD-concomitant anxiety and depression (Palmer, Vacc, & Epstein, 1988; Zschucke, Heinz, &

Strohle, 2011). The general health benefits of exercise in SUDs have also encouraged its application. Indeed, a recent review paper concluded that regular exercise training enhances quality of life and facilitates health-risk reduction from substance use disorders (Linke & Ussher, 2014). As a final practical note, exercise is a readily available practice that lacks the association with stigma of traditional therapies. Accordingly, in addition to aiding in SUD-recovery, it may serve as a particularly appealing behavioral health alternative for individuals who cannot access conventional treatments or avoid these for other reasons (i.e., low DT).

In summary, previous research calls for improving the effectiveness, feasibility, and tolerability of treatments for SUDs. Novel interventions are particularly warranted that can address the contribution of low DT to SUD maintenance, relapse, and treatment attrition. Treatments for enhancing DT in psychopathology to date have involved mindful acceptance and behavioral exposure; and so far, these techniques appear effective in low DT substance users with tobacco addiction. Exercise (especially of the aerobic type) emerges as another efficacious behavioral candidate for addressing low DT. In addition, exercise holds practical and health-promoting potential for addressing public health burden of SUDs.

Evidence of the clinical utility for exercise to target low DT *directly* has been demonstrated among high-AS tobacco smokers. Given the nature and timing of relapse within for smokers with low DT, application of high-intensity (vigorous) exercise is particularly encouraged by its capacity to attenuate putative mechanisms of nicotine withdrawal. Still, knowledge regarding the exercise-DT relation is limited, especially in the context of SUDs. In patients with subclinical anxiety, acute aerobic exercise appears capable of reducing AS but not general emotional DT or other-related domain-specific facets (e.g., intolerance of discomfort). In

conclusion, additional research testing whether multi-modal acute and regular exercise can tap facets of DT is needed, especially in relapse-vulnerable SUDs patients.

Conclusion and Overview of Dissertation Studies

Clearly needed are treatments with potential for addressing the dynamic interplay of biobehavioral risk and maintaining factors implicated in addiction pathology, while addressing effectiveness limitations (e.g., accessibility, attrition). Through three separate RCTs, we evaluate aerobic exercise and yoga for targeting affect-vulnerability factors associated with addictive-behavior maintenance and relapse (i.e., low distress tolerance (DT), hypothalamic-pituitary-adrenal (HPA)-axis dysregulation). The long-term objective of this initial line of research is to better understand the role of exercise in mental health treatment. By uncovering mechanisms of treatment response with exercise, we hope to promote its utility for the appropriate clinical groups who may benefit from integrating exercise as either a stand-alone or augmentative treatment for addiction.

Study 1. Does the efficacy of a brief aerobic exercise intervention for reducing anxiety sensitivity vary as a function of gender?

A moderate-to vigorous-intensity exercise program is emerging as a promising strategy for reducing AS. Identifying determinants of response will further elucidate the potential utility of exercise as treatment for populations with elevated AS. Prior literature suggests that the effects of exercise on mental health may vary as a function of gender, with men benefitting more than women (Elliot et al., 2012; Bhui & Fletcher, 2000; Hunt-Shanks, Blanchard, & Reid, 2009). The present study tested the hypothesis that the effect of exercise on AS would vary as a function of gender, such that the effect would be stronger for men than for women. We tested this

hypothesis using the data from our group's previous study (Smits et al., 2008, cited above) in 60 participants with elevated levels of AS who were randomly assigned to a two-week exercise intervention [EX] or a waitlist control condition [WL].

Study 2. Can the practice of alternative, mind-body yoga enhance emotional distress tolerance in distress-vulnerable women with addictive coping tendencies?

Decades of research devoted to the study of transdiagnostic affect intolerance identify low affective distress tolerance (DT) and related (e.g., anxiety sensitivity (AS), discomfort intolerance) as explanatory mechanisms for the maintenance of and interrelation between anxiety, depressed mood, and substance use pathology (Leventhal & Zvolensky, 2015). Hatha yoga encourages one to implement experiential tolerance and acceptance (i.e., one of the goals of mindfulness) and non-reaction in the face of physical and psychological discomfort. It therefore, emerges as a potential strategy for increasing DT. To test whether a hatha yoga intervention can enhance DT this study randomly assigned females high in emotional eating in response to stress ($N = 52$) either to an 8-week, twice-weekly hatha (Bikram) yoga intervention or to a waitlist control condition. Self-reported DT scores and emotional eating urges were measured at baseline, weekly during treatment, and 1-week post-treatment and compared across time between groups. Moreover, we examined DT as a potential mechanism of change accounting for reductions in an index of stress and addiction-related psychopathology (emotional eating).

Study 3. Can a yoga practice aid in smoking cessation by way of targeting biobehavioral nicotine withdrawal?

The call for the development of specialized interventions for smokers at heightened risk for relapse is guided by the selection hypothesis of smoking prevalence, which posits that

smokers who are not able to quit successfully are “burdened” by specific characteristics that make it more challenging to quit (Hughes & Brandon, 2003).

Accordingly, Study 3 is informed by results from Studies 1 and 2, as well as by basic experimental research on the putative biobehavioral processes underlying smoking relapse in at risk populations. This study randomly assigned 50 female smokers low in DT (i.e., elevated AS) to either an 8-week yoga intervention [YOGA] or a waitlist control [WL] prior to undergoing a self-guided quit attempt. Our primary aim was to investigate the effect of yoga on cortisol. We hypothesized participants assigned to the yoga condition (relative to waitlist) would evidence greater reductions in salivary cortisol levels form pre-to-post intervention (ad-libitum). Furthermore, during the initial 12-hrs of a post-intervention quit attempt, we hypothesized yoga participants would self-report lower withdrawal symptom severity and evidence slighter declines in salivary cortisol (relative to the previous day). Our secondary aim was to evaluate the efficacy of yoga for smoking cessation. Measuring quit-success at 1-week follow-up, we hypothesized YOGA would evidence lengthier abstinence duration (in days) than WL.

STUDY 1 - Gender Moderates the Effect of Exercise on Anxiety Sensitivity

Accruing empirical evidence supports exercise as a therapeutic strategy for improving mood and anxiety disorders (Asmundson et al., 2013; DeBoer, Powers, Utschig, Otto, & Smits, 2012), especially for mild to moderate major depressive disorder (MDD; Dunn, Trivedi, Kampert, Clark, & Chambliss, 2005; Singh, Stavrinos, Scarbek, et al., 2005; Veale, Le Fevre, Pantelis, et al., 1992). A meta-analysis aggregating the results of randomized, controlled trials for MDD revealed a large effect (d = 1.42; Stathopoulou et al., 2006) supporting the overall effectiveness of exercise interventions for improving clinical depression.

Though less extensively studied, exercise has also shown initial efficacy for treating anxiety disorders (Petruzello et al., 1991; O'Connor, Raglin, & Martinsen, 2000; Stathopoulou et al., 2006; Wipfli, Rethorst, & Landers, 2008). A recent quantitative review evaluated the effectiveness of exercise for anxiety in both clinical and non-clinical adult samples. The 49 RCTs included exercise interventions at the moderate-to-vigorous intensity ranging from an acute bout to five times per week for a duration of 30 to 90 minutes per session. Results showed exercisers to fare significantly better than those in no-treatment control groups (*Hedge's g* = -0.48), and either comparable to or better than those in other active treatments commonly used to treat anxiety (*Hedge's g* = -0.19), such as cognitive behavioral therapy (CBT), relaxation therapies (e.g., meditation, light exercise, yoga), group psychotherapy, and stress management education. Moreover, their results indicated that exercise can yield outcomes comparable to medication (Wipfli, Rethorst, & Landers, 2008).

Study published in peer reviewed journal: Medina, J. L., Hopkins, L. B., Powers, M. B., Baird, S. O., & Smits, J. A. J. (2015). The effects of a hatha yoga intervention on facets of distress tolerance. *Cognitive Behaviour Therapy, 44,* 288-300. I served as primary author for this work.

Similarly, because exercise can induce somatic arousal in a repeated, systematic, and prolonged fashion, it may effectively serve as fear extinction training. Indeed, within standard evidence-based cognitive-behavioral interventions for panic disorder (PD), this type of interoceptive exposure appears to be critical for symptom improvement (Smits, Powers, Cho, & Telch, 2004), likely by way of reducing anxiety sensitivity (AS; fear of anxiety sensations and their consequences; McNally, 2002; Smits, Julian, Rosenfield & Powers, 2012; Smits, Berry, Tart, & Powers, 2008; Smits et al., 2007). Given the identified role of AS as a cognitive-affective risk and maintenance factor for anxiety disorders (e.g., panic disorder; McNally, 2002; Olatunji & Wolitzky-Taylor, 2009) as well as for related problems characterized by maladaptive coping behaviors and poor emotion regulation (e.g., substance use, binge eating, PTSD; Taylor, 1999), a moderate-to vigorous-intensity exercise program may prove beneficial, not only for those with a PD diagnosis, but also for reducing AS in at-risk populations more broadly.

Our group extended previous work by Broman-Fulks et al. (2004) by demonstrating that a brief (2-week) moderate-intensity aerobic exercise intervention in adults with elevated scores ($\geq$ 25 indicating possible clinical problems; Peterson & Plehn, 1999, p. 70) on the Anxiety Sensitivity Index (ASI; Reiss & McNally, 1985) led to clinically significant changes in AS from pretreatment through 3-week follow-up (Smits et al., 2008). Indeed, clinically significant change (requiring reduction of scores $\geq$ two standard deviations below the baseline sample mean) was observed in 88% of exercising participants (Smits et al., 2008), with mean ASI decreasing from 33 at pretreatment to 14.5 at posttreatment and to 11.5 by 3-week follow-up. Beyond building additional support for a brief exercise regimen for reducing AS, we showed that these clinically meaningful reductions in AS resulting from exercise mediated subsequent improvements in self-

reported depressive and anxiety symptoms (see Smits et al., 2008). This trial was the first to directly evaluate altered-AS as a causal mechanism of the anxiolytic and antidepressant effects of exercise. Identifying moderators of exercise's efficacy for reducing AS may further elucidate the nature of the AS-exercise relation, and thus, the potential utility of exercise as treatment for anxiety disorders and related aforementioned problems associated with elevated AS.

Prior evidence from outside the AS literature suggest that the effects of exercise on mental health may vary as a function of gender, with men benefitting more than women (Elliot et al., 2012; Bhui & Fletcher, 2000; Hunt-Shanks, Blanchard, & Reid, 2009). For example, a recent investigation revealed a stronger inverse relation for males more than for females between physical activity frequency and frequency of depressive symptoms and consideration of suicide (Elliot et al., 2012). In addition, the meta-analysis by Wipfli and colleagues (2008) revealed significant effect sizes in mixed-gender and male-only samples, but not in female-only samples, suggesting that there may be meaningful gender differences in the efficacy of exercise interventions for reducing anxiety symptoms. Such differences could have important implications for clinical practice (e.g., matching strategies, need for additional strategies) and help guide research on the understanding of the mechanisms of action of exercise for mental health conditions.

Building upon the aforementioned work, the present study tested the hypothesis that the effect of exercise on AS would vary as a function of gender, such that the effect would be stronger for men than for women. We tested this hypothesis using data from our previously published study (Smits et al., 2008). In this study, participants with elevated levels of anxiety sensitivity ($N = 60$) were randomly assigned to a 2-week exercise intervention [EX] or a waitlist

control condition [WL]. Because Smits and colleagues (2008) found no significant difference between the two slightly different exercise conditions in reductions of AS (with both showing greater decreases in ASI scores from pretreatment to follow-up compared to WL), we collapsed across exercise conditions to form a single EX group for the present study. Using this data set, we investigated whether there were gender differences in the effects of exercise on AS in response to a brief, 2-week programmed exercise. More specifically, we predicted a significant 3-way interaction, such that the change in ASI over time in EX relative to WL would be greater for males than for females.

Method

Participants

Study participants (N = 60; 45 Female; M_{Age} = 20.68, SD = 5.80) consisted of (1) undergraduate students at a medium-sized private university in the Southwest (N = 50; 38 Female; M_{Age} = 20.40, SD = 5.03) and (2) community individuals in the Boston area (N = 10; 7 Female; M_{Age} = 22.10, SD = 8.95). Undergraduate participants were recruited from classroom survey screenings in introductory psychology courses. In the Southwest sample, 182 of the 286 potentially eligible participants (i.e., with surveys indicating clinically elevated AS ≥25) indicated interest in participating and were contacted by study staff to complete a phone interview. Of the 91 deemed eligible, 50 participants enrolled, and were given course credit for participation. Participants from the Boston area site were recruited from community advertisements near a large public university. Of the 91 surveyed at the Boston site, 30 completed phone interview, and 10 interested participants were enrolled (9 students and 1 person from larger community area; see Smits et al., 2008).

All participants met the following entry criteria: elevated anxiety sensitivity (indexed by ASI score ≥ 25; Peterson & Reiss, 1992); absence of physical conditions that could be exacerbated by exercise; body mass index < 35; no current involvement in an exercise program (i.e., ≤ one aerobic exercise session per week); no recent change in psychotropic medications (e.g., stabilized for at least four weeks for antidepressants and two weeks for benzodiazepines); and no current psychotherapy. The study sample consisted primarily of students (98%) who were Caucasian (71%). Only 1 participant reported taking current psychotropic medication (prescribed Adderall for ADHD symptoms).

Measures

Demographics. Following study enrollment and one week prior to the intervention (i.e., pre-treatment), self-reported demographic information was collected from each participant.

Anxiety Sensitivity. The Anxiety Sensitivity Index (ASI) is a 16-item validated measure of anxiety sensitivity, defined as the fear of anxiety-related sensations and their consequences (Peterson & Reiss, 1992). On the ASI, respondents indicate on a 5-point Likert-type scale (0 = very little to 4 = very much) the degree to which anxiety symptoms are distressing (e.g., "It scares me when my heart beats rapidly") and the concern about negative consequences of anxiety symptoms (e.g., "When I notice that my heart is beating rapidly, I worry that I might have a heart attack"). Normative studies indicate that scores above 25 indicate possible clinical problems (Peterson & Plehn, 1999). The ASI has sound psychometric properties in both clinical and nonclinical samples, including adequate construct validity (McNally & Lorenz, 1987; Reiss, Peterson, Gursky, & McNally, 1986; Taylor, Koch, & McNally, 1992; Telch, Shermis, & Lucas, 1989). The ASI was administered to all participants at four separate time points: pretreatment,

mid-treatment (1 week after exercise initiation), posttreatment (end of 2-week exercise program), and 3-week follow-up (i.e., three weeks following completion of exercise intervention).

Intervention Procedures

Exercise [EX]. The exercise dose for this intervention was guided by previous meta-analyses, which documented that moderate-to-high-intensity exercise (e.g., 60-80% of maximum age-predicted heart rate) superior to low-intensity exercise (Wipfli et al., 2008). Accordingly, the intervention consisted of thrice-weekly 20-minute moderate intensity aerobic exercise sessions over two weeks (six sessions total), which were designed to elicit sensations of physiological arousal as a type of interoceptive exposure targeting their anxiety-related fears. Along with direct verbal instruction from the experimenter for the participant to attend to the sensations experienced, participants were asked by the protocol therapist to rate their level of subjective distress (assessed on a scale of "0 = not intense at all" to "100 = extremely intense") every three minutes during exercise. At the first session, participants were provided with the rationale behind exercise for anxiety (Smits et al., 2008). Exercise was completed and supervised by CPR-certified study personnel at the laboratory in a room furnished with treadmills and appropriate safety equipment (e.g., defibrillator); the exercise room featured a computer-controlled exercise training management system (Smooth® 7.1 HR Pro, InternetFitness.com, Inc., Mt. Laurel, NJ). The system allows for input of relevant data for each participant (resting and maximal heart rate, target heart rate, and session duration). The computer receives a heart rate (HR) signal from a Polar® transmitter (chest strap), allowing the experimenter to adjust speed and incline of the treadmill to target specific levels of effort as assessed by HR. Exercise intensity was pre-set at the high-moderate level, which was determined by the standard calculation (70% of HR_{max} [(220-

age) * .70]). Supervising staff were responsible for checking the computerized HR feedback system every five minutes per-session in order to verifying participants were exercising within their target HR zone. Additional elements included the review of session procedures and accomplishments at the end of each session.

Waitlist [WL]. Participants assigned to the WL condition completed assessments at the same time intervals as the two active conditions, but did not participate in exercise interventions.

Data Analysis Strategy

We performed a repeated-measures ANOVA using mixed-effects models (MRMs) in SPSS 21.0. The MRM approach to repeated measures ANOVA is advantageous because it allows inclusion of all participants regardless of missing data (which improves power and generalizability), can model the covariance matrix of the repeated measures more flexibly than ANCOVA, and is the recommended method for longitudinal data analysis (Hamer & Simpson, 2009). The independent variables in our 2 x 2 x 4 mixed-effects ANOVA were Gender, Treatment Condition (EX vs. WL), and Time (pre-treatment, mid-treatment, post-treatment, and the three week follow-up). We treated Time as a categorical variable in an ANOVA model rather than as a continuous variable in a growth curve model because it allows the change over time to be free of constraints that would be required in a functional growth curve model. This approach is recommended when one performs multiple between-group comparisons over a small number of assessment points (Blackwell, Mendes De Leon, & Miller, 2006).

Pattern mixture modeling (Hedeker & Gibbons, 2006) was used to test the effects of missing data on the model. In pattern mixture modeling one investigates whether missing data patterns moderate the results. Accordingly, we created a variable coding each participant's

dropout status (i.e., identifying each participant as either a dropout [coded 1] or completer [coded 0]). This variable was then entered as a moderator of the effects in our model (Hedeker & Gibbons, 2006). Analyses included all randomized individuals ($N = 60$; 45 Female[1]).

Results

Baseline Equivalence and Attrition

As can be seen in **Table 1.1** below, the study conditions (EX [$n = 40$], WL [$n = 20$]) did not differ on any demographic or clinical (i.e., ASI) measures at pre-treatment, suggesting that random assignment produced groups with comparable demographic and clinical characteristics (Smits et al., 2008). Further, a one-way ANOVA revealed that pre-treatment ASI scores did not vary as a function of Gender ($F(1,58) = .18$, $p = .67$). One-way ANOVAs also indicated neither mean participant age ($F(1,58) = .71$, $p = .40$) or mean pre-treatment ASI ($F(1,58) = .66$, $p = .42$) differed significantly between the two study sites. Our study had a dropout rate of 21.7% (n=13; 10 in EX and 3 in WL), although all participants were included in the mixed effects analysis. Chi-square analyses revealed that there was not a significant difference between study condition ($\chi^2(1) = .78$, $p = .51$), gender ($\chi^2(1) = .33$, $p = .56$), or study site ($\chi^2(1) = .29$, $p = .59$) in dropout rate. Lastly, a one-way ANOVA revealed that there was no difference between dropouts and completers, $F(1,58) = .92$, $p = .34$, on pre-treatment ASI scores.

	Exercise Condition ($N = 40$)		Waitlist Condition ($N = 20$)	
Variable	*M*	*SD*	*M*	*SD*
Age	19.7	2.3	22.7	9.4
ASI	33.0	6.4	34.6	6.6
ASI by Gender				
Male	31.0	5.7	35.0	8.4
Female	33.4	6.5	34.3	5.8
	n	*%*	*n*	*%*
Gender				
Male	8	20.0	7	35.0
Female	32	80.0	13	65.0
Race				
White	20	50.0	16	80.0
African American	4	10.0	0	0.0
Asian	3	7.5	0	0.0
Other	2	5.0	1	0.0
Missing/Not reported	11	27.5	3	15.0
Hispanic or Latino ethnicity	2	5.0	1	5.0

TABLE 1.1 BASELINE CHARACTERISTICS

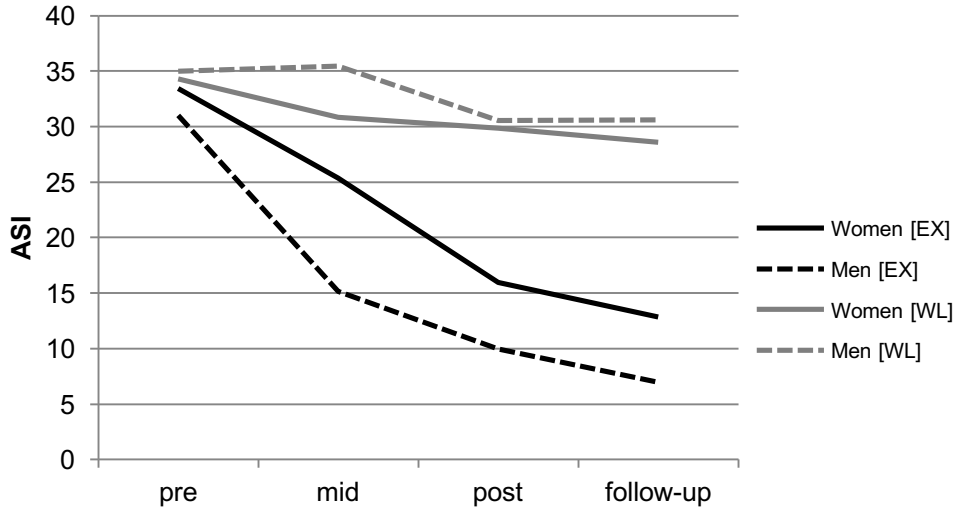
Hypothesis Testing

Pattern mixture modeling was used to test the effects of dropout status on outcome (ASI). Results showed the dropout variables did not affect outcome (i.e., $p \geq .20$ for all dropout main effects and interactions). Thus, dropout variables and their interactions were removed from the final model. In our final model, we observed a significant main effect for Time, $F(3,87) = 50.21$, $p = .000$, and Treatment Condition, $F(1,55) = 46.19$, $p = .000$, indicating a general improvement over time and lower scores in EX vs. WL, respectively. These main effects were qualified by a significant Time x Treatment Condition interaction, $F(3,87) = 20.67$, $p = .000$, suggesting greater improvement in AS for those in EX compared to WL. Additionally, we found a significant

Gender x Treatment Condition interaction, $F(1,55) = 4.53$, $p = .04$, such that, collapsed across time points, in EX compared to WL, men evidenced lower mean ASI than women.

Finally, consistent with our hypothesis, we observed a significant Time x Treatment Condition x Gender interaction, $F(3,87) = 3.37$, $p = .02$, such that the relative improvement over Time in EX compared to WL was different for males than for females (see **Figure 1.1**). To further understand this three-way interaction, we decomposed the Time variable, which consisted of 4 levels (hence 3 degrees of freedom), into three simple contrasts: the change from pre- to mid-treatment, from pre- to post-treatment, and from pre to follow up.

We then investigated whether these contrasts interacted with Treatment Condition and Gender. These analyses showed that the change from pre- and mid-treatment interacted with Treatment Condition and Gender, $b = -11.61$, $t(125) = -2.99$, $p = .003$, such that the relative improvement in Exercise compared to WL was greater for men than for women (see **Figure 1.1**). The other two contrasts (pre-to-post and pre-to-follow-up changes) were not moderated by Treatment Condition and Gender (p's $\geq .30$), contrary to our prediction. In particular, the lack of a significant Treatment Condition x Gender x pre- to post-treatment contrast ($b = -3.56$, $t(98) = -.80$, $p = .43$) suggests that, at post-treatment, the overall improvement in EX vs. WL in response to an exercise intervention was not different for men and women.



Note, AS Reduction is depicted as a function of the interaction between gender and exercise self-reported levels of as measured using the anxiety sensitivity index (ASI) assessed at four time points—pre-intervention (pre), mid-intervention week 1 (mid), post-intervention week 2 (post), and at 2 weeks following the intervention (follow-up).

FIGURE 1.1. ANXIETY SENSITIVITY (AS) REDUCTION OVER TIME

Discussion

Overall, our findings add to the growing body of literature indicating that the effects of exercise on anxiety-related constructs may be stronger for males than for females. Additionally, our study expands previous work by finding that gender also moderates the effects of a brief exercise intervention on AS, an anxiety vulnerability trait. Specifically, our findings demonstrated that two weeks of moderate intensity exercise can effectively reduce ASI across gender. However, as indicated by a significant gender by time by treatment condition interaction, the relative improvement over time in EX compared to WL was different for males than for females. This was driven by greater relative ASI reduction for men between pre- and mid-

treatment. Despite their more-robust early treatment gains, however, men did not show greater relative improvements in EX compared WL than women at post-treatment nor at follow-up.

Although speculative, we offer one potential mechanism accounting for greater AS reductions observed in men relative to women over the first week of exercise that can be drawn from the broader AS and exercise physiology literature. Namely, gender differences in physiological response to exercise appear to contribute to differing degrees of comfort during, and in-response-to, exercise performance. Specifically, women exhibit differential metabolic, pulmonary, and cardiovascular patterns compared to men of comparable fitness, including greater indices of physiological stress and autonomic arousal (Harms et al., 1998; Harms 2006; Tarnopolsky et al., 1990; Spina et al., 1993). For example, during moderate-intensity long-duration exercise, while males utilize lipids and metabolize carbohydrates more efficiently than females, females exhibit lower insulin and higher epinephrine concentrations (Tarnopolsky et al., 1990). Indeed, these data parallel women's reporting greater stress and exhaustion following exercise (Gavin, Sequin, & McBrearty, 2006). This suggests a potential for more aversive somatic responses to exercise in women, which among inactive women with elevated AS, is likely to be particularly pronounced within the beginning stage of initiating an exercise regimen.

A number of limitations deserve mention. First, although individuals with elevated AS are at risk for clinical anxiety disorders, our use of a relatively small sample of young at-risk students, as opposed to a large treatment-seeking sample, limits the generalizability of our results. For example, we cannot infer that the effects of exercise on AS is moderated by gender in older or clinical anxiety-disordered samples. The small number of males in our sample also limits generalizability and reduces our power to detect gender differences. However, a post-hoc

Monte Carlo study suggests that we have sufficient power (greater than .80) to a detect medium effect size for our gender x study condition x pre- to post-treatment (and pre- to follow-up) interactions. Replication of gender differences in AS reduction in response to aerobic exercise by future studies must be evidenced before firm conclusions can be drawn.

As another limitation, our intervention was only two weeks in length and was compared only to a waitlist control condition. Further, because we did not assess exercise continuation of participants after the assessment period, we cannot speak to gender differences in response to long-term exercise. Additionally, evaluating the effects of aerobic exercise on rates of AS relative to other brief active control conditions (e.g., strength training, mind-body exercise, health education course) may yield differing between-gender comparisons. Though we speculate the smaller AS-reduction observed in women by the end of the first week of exercise to reflect elevated perceived distress relative to men, we cannot confirm this with the given data. Though participants were cued by experimenters to provide subjective distress ratings during exercise, this procedure was intended solely as a clinical exposure technique (i.e., attention manipulation); in future studies, such ratings should be formally recorded to evaluate their role in the effectiveness of exercise.

In conclusion, our findings point to the possibility that responses to exercise interventions for anxiety pathology vary by gender. This may have implications for the delivery of these interventions and highlight the possibility that the mechanisms of change of exercise interventions, at least as it relates to anxiety reduction, may be different in women than men. We hope that this finding encourages further research aimed at understanding differences between men and women in terms of their responding to exercise interventions. In addition to considering

mechanisms at multiple levels (e.g., psychological, physiological), studies that compare types of exercise modalities (e.g., yoga, resistance training) and doses (e.g., intensities, frequencies, and duration) may yield findings that can help refine the knowledge needed to develop individually tailored exercise interventions.

STUDY 2 - The Effects of a Hatha Yoga Intervention on Facets of Distress Tolerance

Individuals with low distress or affective tolerance experience negative emotions as particularly threatening and are highly motivated to alter such experiential states (Simons & Gaher, 2005). As a result of their intolerance of distress, these individuals tend to engage in coping strategies that pose mental and physical health risks, such as cigarette smoking (Brown, Lejuez, Kahler, Strong, & Zvolensky, 2005; Buckner, Keough, & Schmidt, 2007; Bujarski, Norberg, & Copeland, 2012), and binge eating and purging (Anestis, Selby, Fink, & Joiner, 2007), as a means to reduce or avoid emotional distress. Accordingly, distress intolerance has been implicated as a transdiagnostic risk and maintenance factor for psychopathology (Zvolensky, Bernstein, & Vujanovic, 2011), particularly in disorders characterized by heightened emotional reactivity and avoidance, such as substance use, anxiety, eating, and personality disorders (Leyro, Zvolensky, & Bernstein, 2010; Zvolensky et al., 2011).

Extant research has conceptualized and approached measurement of affective intolerance in diverse ways and among heterogeneous samples (Bernstein, Zvolensky, Vujanovic, & Moos, 2009; McHugh & Otto, 2012). This has resulted in the emergence of various domain-specific affective intolerance sub-constructs that can be challenging to integrate (Bernstein et al., 2009).

Study published in peer reviewed journal. Medina, J. L., Hopkins, L. B., Powers, M. B., Baird, S. O., & Smits, J. A. J. (2015). The effects of a hatha yoga intervention on facets of distress tolerance. *Cognitive Behaviour Therapy, 44,* 288-300. I served as primary author involved in the study design, data analysis and manuscript writing.

For example, “intolerance of uncertainty,” particularly relevant to pathology of generalized anxiety (Dugas, Buhr, & Ladouceur, 2004) and obsessive-compulsive disorders (Holaway, Heimberg, & Coles, 2006; Tolin, Abramowitz, Brigidi, & Foa, 2003), reflects a cognitive-affective intolerance for uncertain outcomes. In comparison, “discomfort intolerance” (DI; Schmidt, Richey, & Fitzpatrick, 2006) and “anxiety sensitivity” (AS; Maller & Reiss, 1992) include aversion to somatic sensations of autonomic arousal, which are cornerstone to panic disorder psychopathology.

Deviating from a specific distress domain in their operationalization of the construct, Simons & Gaher (2005) define “distress tolerance” (DT) by facets involved in the process of managing and regulating subjective emotional distress. These include: (1) one’s general perceived Tolerance of negative or threatening emotions, (2) one’s Appraisal or value judgment about feeling distressed or upset, as well as (3) the resulting Absorption of attention in the distress itself, and (3) the propensity for action aimed at Regulation or reduction of distress (Simons & Gaher, 2005). In support of this conceptualization, scores on the self-report based Distress Tolerance Scale (DTS; Simons & Gaher, 2005) have predicted symptom severity and problem behavior in a range of clinical populations (Anestis et al., 2007; Leyro et al., 2010).

Studies examining the psychometric properties of various affective intolerance assessments also evidence support for the existence of a common, domain-general emotional intolerance construct. For example, a factor analysis (McHugh & Otto, 2012) of different self-report assessments of the construct yielded a single-factor latent structure of affective intolerance captured by the Discomfort Intolerance Scale (Schmidt et al., 2006), Anxiety Sensitivity Index (Reiss, Peterson, Gursky, & McNally, 1986), and DTS (Simons & Gaher, 2005). The authors

concluded that these measures likely tap a common underlying core trait of affective intolerance, which is most-directly assessed by the DTS (McHugh & Otto, 2012). Thus, distress tolerance DT, as measured by the DTS, appears to be a good option for investigations examining the relationship of affect intolerance to psychopathology and intervention effects.

Because DT is a pervasive contributor to psychopathology, several existing evidence-based treatments specifically aim to target DT. Promisingly, initial intervention research demonstrates that DT can be enhanced and that increases in DT correspond to improvements in symptom severity (Brown et al., 2008; Leyro et al., 2010). These interventions have typically taken a mindfulness-based and/or exposure-based, cognitive-behavioral approach. Dialectical behavior therapy (Linehan, 1993), for example, is an integrative approach that includes a DT skills training component for reducing emotional reactivity, and it has shown efficacy for treating borderline personality (Linehan, 1993; Linehan, 1987; Neacsiu, Rizvi, & Linehan, 2010), eating pathology (Telch, Stewart, & Linehan, 2001; Telch et al., 2001), and substance use disorders (Dimeff & Linehan, 2008). Brown and colleagues have recently developed a novel, combined mindful acceptance/CBT intervention targeting DT for smoking cessation in adults who have previously failed cessation attempts (Brown et al., 2008). By enhancing resilience to distress during critical early abstinence periods, such as the withdrawal phase, this treatment has shown efficacy for difficult-to-treat smokers (Brown et al., 2013).

The mind-body practice of yoga, which is conceptually akin to the interventions just described, may hold similar promise for enhancing DT. Hatha yoga is a branch of yoga described as "moving meditation," a physical practice of yoga (Iyengar & Menuhin, 1995). Hatha yoga requires one to focus attention on interoceptive cues and breath (pranayama) during and while

transitioning to challenging, potentially uncomfortable physical postures called asanas (Hewitt, 1990; Iyengar & Menuhin, 1995). From the Eastern philosophical tradition of mindfulness, hatha yoga encourages one to implement present-centered awareness, non-reaction, and non-judgmental acceptance of one's present state despite physical or psychological discomfort. In combination with promotion of mindful awareness and acceptance, hatha yoga, especially when practiced at moderate to vigorous intensities, may promote habituation to distress in low-DT persons. Indeed, exposure-based methods of behavioral therapy, including programmed aerobic exercise interventions, have proved effective for reducing sensitivity to autonomic arousal in anxious populations (Broman-Fulks & Storey, 2008; Smits et al., 2008).

Furthermore, evidence from a number of sources has accumulated for the beneficial effects of yoga on mental health problems, including anxiety (Dunn, 2009; Kirkwood, Rampes, Tuffrey, Richardson, & Pilkington, 2005; Smith, Hancock, Blake-Mortimer, & Eckert, 2007), depression (Shapiro et al., 2007; Uebelacker et al., 2010), disordered eating (Carei, Fyfe-Johnson, Breuner, & Brown, 2010; McIver, O'Halloran, & McGartland, 2009), and psychological distress secondary to medical conditions (Curtis, Osadchuk, & Katz, 2011; Shapiro et al., 2007). Yoga also has received support for reducing perceived stress and enhancing overall well-being in sub-clinical populations (Brisbon & Lowery, 2011; Granath, Ingvarsson, von Thiele, & Lundberg, 2006; Huang, Chien, & Chung, 2013; Smith et al., 2007; Uebelacker et al., 2010).

Despite the promise for improving psychological health in distress-sensitive persons, there have been no published reports of the efficacy of yoga for increasing DT. In addition to the theoretical promise of using yoga to improve DT, the importance of this research is further

underscored by the increasing popularity of yoga in Western culture as an alternative approach to stress management and psychological wellbeing (Barnes, Bloom, & Nahin, 2008). The positive reputation of yoga only enhances its potential to become an acceptable and accessible intervention for many people.

In this study, we test the hypothesis that practicing hatha yoga can increase DT. This hypothesis was tested using data collected as part of a larger investigation examining the feasibility, acceptability, and efficacy of a hatha yoga intervention for targeting physiological stress reactivity in women high in affective eating and risk for obesity (Hopkins-DeBoer, Medina, Baird, & Smits, 2016). The parent trial draws rationale for testing its hypothesis from the obesity and eating disorder literatures, which describe emotional or stress-induced eating as a major contributor to clinically diagnosable eating disorders, such as binge eating disorder, as well as to rates of obesity, particularly among females (Adam & Epel, 2007). The need to enhance affective coping capacity in this population provides rationale for the present investigation's examination of DT as an avenue by which yoga may reduce disordered eating behavior.

Accordingly, under this parent study, we randomized 52 females at risk for eating disorders and obesity to either an 8-week hatha yoga intervention (YOGA) or a waitlist control condition (WL). Self-reported emotional eating and DT were measured at baseline, weekly during treatment, and 1-week post-treatment. Our second aim was to examine increases in DT as a mechanism of change accounting for reduced behavioral symptoms of psychopathology resulting from the yoga intervention. Given the sample recruited for the parent study, we examined increases in DT as a mediator of the intervention effects on emotional eating. We

hypothesized that, relative to waitlist participants, those in the yoga condition would report greater increases in DT over the course of the intervention, and that these increases in DT would mediate the effects of yoga on emotional eating.

Method

Participants

Participants included adult females from the Dallas community who reported elevated levels of perceived stress, emotional eating, and dietary restraint. Eligibility criteria included score of ≥ 2.06 on the emotional eating subscale (DEES) of the Dutch Eating Behavior Questionnaire (DEBQ; van Strien, Frijters, Bergers, & Defares, 1986), score of ≥ 15 on the Restraint Scale (Polivy, Herman, & Howard, 1988), and elevated perceived stress, as defined by scoring ≥ 0.50 SD above the community mean on the Perceived Stress Questionnaire (Levenstein et al., 1993). Eligibility also required sufficient command of the English language and providing written physician medical clearance to participate in yoga practice.

Exclusion criteria included: having regularly practiced (i.e., once a week or more) yoga or other mind-body practices (e.g., tai chi, meditation) within the last year; a significant change to physical activity pattern in the past 3 months; current severe depression or substance dependence; lifetime history of anorexia nervosa or severe mental illness (i.e., bipolar or psychotic disorder of any type); pregnancy; medical conditions that could be aggravated by yoga; body mass index ≥ 40; cognitive dysfunctions or organic brain syndrome that could interfere with capacity to perform study protocol; receiving inpatient psychiatric hospitalization

within the past year; or receiving concurrent psychiatric treatment, including both psychotherapy and psychotropic medication.

Procedures

Participants will be recruited through advertisements in local newspapers and flyers that included a link to a secured online eligibility prescreen survey. Respondents who appeared eligible based on their prescreen will be scheduled for a baseline visit one week prior to the start of the yoga program. During this visit participants will be randomized to one of the two conditions (YOGA or WL) using a computerized random number generator. Participants will then be oriented to the program (depending on condition assignment) and scheduled to come

Those randomized to the yoga condition were asked to attend twice-weekly, 90-minute Bikram yoga-style classes at a local yoga studio. Each session consisted of the same series of 26 hatha yoga postures, two breathing exercises, and two savasanas (i.e., a resting/relaxation posture), in a room heated to 104 degrees Fahrenheit, which aids in safe muscle stretching. We selected this type of yoga because it is considered suitable for practitioners of various physical capabilities and, due to its consistent series of postures, is ideal for a standardized intervention protocol. In addition, the hot temperature would provide an opportunity to learn to become confortable with the bodily sensations associated with heat exposure (i.e., increase tolerance of physical distress). At the end of each week of the intervention period, as well as at post-intervention (week 9), all participants (both those assigned to YOGA and WL) were prompted by email to complete a 15-20 minute online survey containing self-report measures of DT, emotional eating, stress, and mood. Following their completion of the week 9 assessment, WL participants were provided the equivalent 2-month yoga membership at no cost.

Measures

Distress tolerance. The Distress Tolerance Scale (DTS; Simons & Gaher, 2005) is a 15-item self-report scale measuring four facets involved in the expectation of, evaluation of, and reaction to distressing states. In addition to a total DT score, the DTS produces four subscale scores measuring: (1) distress Tolerance (i.e., perceived tolerability and aversiveness of distressing feelings; e.g., "I can't handle feeling distressed or upset"); (2) Appraisal of distress (i.e., acceptability of having the distress; e.g., "My feelings of distress are not acceptable"); (3) Absorption (i.e., tendency for distress to disrupt attention and interfere with in-the-moment functioning; e.g., "My feelings of distress are so intense that they completely take over"); and (4) Regulation (i.e., the strength of one's propensity to immediately avoid or attenuate the distress; e.g., "I'll do anything to avoid feeling distressed or upset"). Participants responded to items on a 5-point Likert-type scale, with ratings ranging from strongly agree (1) to strongly disagree (5). The DTS has exhibited 6-month temporal stability and internal consistency, evidencing good reliability (Simons & Gaher, 2005). Total DTS scores, as well as each of its subscales have demonstrated adequate construct validity (Bernstein et al., 2009; Leyro, Bernstein, Vujanovic, McLeish, & Zvolensky, 2011; Simons & Gaher, 2005). In the present sample, internal consistency (Chronbach's alpha) for the DTS total score at baseline was 0.87. Alpha coefficient for the DTS subscales, Tolerance, Absorption, Appraisal, and Regulation were .72, .77, .72, and .70, respectively.

Emotional eating. The Dutch Eating Behavior Questionnaire (DEBQ; van Strien, Frijters, Bergers, & Defares, 1986) is a widely used and validated 33-item measure that assesses restrained eating, emotional eating, and eating in response to external cues (van Strien, Frijters,

van Staveren, Defares, & Deurenberg, 1986). Each item is rated on a 5-point scale from 1 (never) to 5 (very often). The emotional eating scale (DEES) of the DEBQ, which measures tendency to eat in response to negative emotions, was used to screen for emotional eating, with a score ≥ 2.06 indicative of significantly elevated distress-induced eating tendencies. In the present sample, internal consistency (Chronbach's alpha) for the DEES at baseline was 0.92.

Data Analytic Strategy

In order to analyze changes in self-reported DT and emotional eating assessed over the intervention period, we used mixed effects multilevel modeling (MLM) in SPSS® Version 20, which allows for the analysis of longitudinal data both within and between subjects (S. Raudenbush, Bryk, Cheong, & Congdon, 2004; Singer & Willet, 2003). MLM has several advantages over other strategies commonly used to analyze longitudinal data (MacKinnon, 2008; Singer & Willet, 2003; Zhang, Zyphur, & Preacher, 2009). For example, as a form of intent to treat analysis (ITT), MLM allows for the inclusion of subjects with missing data, whereby it is able to estimate a longitudinal change trajectory for each subject using the number of completed assessments available. Additionally, MLM allows for modeling of the error covariance within-subjects, which was modeled as autoregressive [AR(1)] in the present study.

In line with standard guidelines for MLM (Singer & Willet, 2003), we tested a series of 2-level models to measure rates of improvement (Level 1) in self-reported levels of distress tolerance (DTS) and emotional eating (DEES) as a function of study condition (Level 2). Level 1 of the MLM model estimates outcome as a function of time within individual (i.e., Outcomeij = b0i + b1i * Timeij +εij, where i represents each individual subject and j represents each assessment point). Level 2 of the model allows for between-individual characteristics (i.e., study

condition [COND], coded "0 = Yoga", "1 = WL") to influence outcome. The equations for Level 2 are b0i = 00 + 01*CONDi + u0i, and b1i = 10 + 01*CONDi + u1i. Level 2 is nested into the Level 1 equation, forming a composite 2-level model with the equation, Outcomeij = γ00 + γ10*Time + γ01* COND + γ11* COND *Time + (εij + u0i + u1i*TIME).

In order to determine the most accurate MLM model reflective of changes over time in our main outcomes (DTS, DEES), we compared linear, quadratic, and logarithmic growth curves for each outcome based on their deviance statistics (Bayesian Information Criterion [BIC]). For both DTS and DEES outcomes, the logarithmic growth curve was found to be the best fit to the data. Therefore, the logarithmic transformation of time [ln(Time)] was used in all tests analyzing these measures longitudinally.

Guidelines for estimating power to detect polynomial change using MLM in longitudinal studies have been published by Raudenbush and Xiao-Feng (2001), taking into account study duration, assessment frequency, and sample size. For our purpose of measuring weekly change in our outcomes over a 10-week period, a sample of $N \geq 44$ was predicted to be adequate for achieving $\geq 80\%$ power to be able to detect a large effect (Raudenbush & Xiao-Feng, 2001).

Mediation analyses. Establishing mediation in randomized trials requires demonstrating that the change in the mediator causes a change in the outcome. Enhancing the causal interpretation of our mediation test, we used a multi-level (MLM) cross-lagged panel analysis to test the mediating effect of DTS on subsequent reductions in DEES (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001; Kraemer, Wilson, Fairburn, & Agras, 2002). To test the size and significance of the proposed mediator, DTS, we employed MacKinnon and colleagues' asymmetric distribution of products test (Fritz & MacKinnon, 2007; MacKinnon, Fairchild, &

Fritz, 2007; MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002). Significance of a proposed indirect mediated pathway is determined based on confidence intervals for the product of the indirect paths of coefficients A*B. If the 95% confidence interval for the A*B product does not include 0, the mediated effect is considered significant (MacKinnon et al., 2004). The coefficient for the interaction term (i.e., COND*Time effect on DTS_j) represents the A Path of our model (labeled A3 in **Figure 2.2**). In order to control for temporal order of effects between mediator and outcome using a cross-lagged panel strategy, we lag-transformed the original variable DEES by one time point ($DEES_{j+1}$). Thus, the B Path of our mediation model represents the coefficient for the effect of DTS_j on $DEES_{j+1}$ controlling for $DEES_j$ (i.e., levels of the mediator DTS predicting future levels of the outcome DEES; see **Figure 2.2**).

Size of the mediated effect. In order to estimate the proportion mediated by the proposed mediator (PM; Shrout & Bolger, 2002), an effect size was calculated using the formula (A3* B)/C. The PM represents the proportion of the total effect of the hatha yoga intervention on emotional eating (i.e., the C Path) that was mediated by distress tolerance.

Results

Sample Characteristics

We aimed to recruit a sample of women at-risk for obesity due to high levels of emotional/stress-induced eating. Out of 650 individuals who filled out the online prescreen survey of demographics, eating behavior, perceived stress, depression, and body mass index (BMI), 573 did not meet initial eligibility criteria, and 25 declined participation. Seventy-three of the remaining women completed the diagnostic screening visit. Fifty-two eligible women attended the baseline orientation visit, where 27 were randomized to YOGA and 25 to WL.

Our final sample of 52 women (*M* age = 33.52, SD = 6.43) had an average BMI within the overweight range at baseline. Prescreen emotional eating (DEES) scores for those randomized were approximately 2 SDs above normative scores for both obese and non-obese women (Ouwens, van Strien, & van der Staak, 2003; van Strien, Frijters, Bergers, et al., 1986; van Strien & Ouwens, 2003). The sample consisted primarily of non-Hispanic White participants (75%, n = 39). Ten (19.2%) of participants identified as Hispanic/Latina. Participants were well-educated and predominantly middle to upper-middle class with 60% reporting an annual household income of below $75,000. All but one participant reported receiving either a college degree or some college, and 100% reported completing high school. See Table 1 for specific baseline descriptive statistics.

The study conditions did not differ at baseline on BMI, race/ethnicity, or annual income, nor were there differences in baseline assessments of DTS or DEES (p's > .14). Conditions differed by age, with the YOGA group being significantly younger ($F(1,50) = 5.96$, $p = .02$). We therefore controlled for age in all analyses. Overall, 17% (n = 9) of our sample dropped out of the intervention (i.e., missed both post-treatment laboratory visit and survey). Seven (26%) YOGA participants dropped out, whereas only two (8%) WL participants dropped out. However, chi-square analyses revealed that attrition did not differ significantly between conditions ($\chi 2 = 2.91$, $p = .09$). Study completers did not differ from the 10 dropouts in baseline levels of BMI, age, or DEES and DTS scores.

Average weekly yoga attendance for the 27 participants randomized to yoga ranged from 0.13 to 3.25 sessions per week (M = 1.56, SD = 0.82). Ten (27%) participants met (n = 3) or exceeded (n = 7) the prescribed two classes per week. On average, yoga participants completed

60% of the 16 prescribed yoga sessions, and sixteen (84%) completed at least 75% (12 of 16 classes) of the intervention.

	Yoga (N = 27)		Waitlist (N = 25)		Total (N = 52)	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*
Age	31.52	5.47	35.68	6.80	33.60	6.09
BMI	28.38	4.08	26.60	5.94	27.4	5.09
DTS	3.22	0.68	3.30	0.85	3.26	0.75
DEES	3.60	0.81	3.44	0.68	3.52	0.74

TABLE 2.1. BASELINE CLINICAL AND DEMOGRAPHIC CHARACTERISTICS

Variable Name	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
1. DTS Total	-	.86**	.85**	.80**	.78**	.39**	-.40**	-.02	-.05
2. DTS Tolerance	-	-	.70**	.60**	.53**	.36	-.47**	-.15	-.08
3. DTS Absorption	-	-	-	.57**	.47**	.49**	-.40**	.02	.00
4. DTS Appraisal	-	-	-	-	.56**	.32*	-.24	.14	.04
5. DTS Regulation	-	-	-	-	-	.10	-.17	-.04	-.16
6. FFMQ	-	-	-	-	-	-	-.41**	.03	-.16
7. DEES	-	-	-	-	-	-	-	.03	.11
8. BMI	-	-	-	-	-	-	-	-	.26
9. Condition	-	-	-	-	-	-	-	-	-

Note. * $p < .05$; ** $p < .0$

TABLE 2.2. DESCRIPTIVE DATA AND ZERO-ORDER RELATIONS AMONG PREDICTOR AND CRITERION VARIABLES

Hypothesis Testing

Intervention effects on distress tolerance. As hypothesized, the Condition-by-Time interaction was significant (b = -0.168, $t(128)$ = -2.014, p = 0.046), revealing that the loglinear rate of increase in DT was significantly greater in YOGA than WL (**Figure 2.1**). We calculated a Cohen's d effect size for the between-group effect using the approach recommended by Raudenbush and Xiao-Feng (2001) in multilevel mixed effects models. This yielded a standardized effect size (Cohen's d) of .82, suggesting that the between-group effect on slope of improvement in DTS was large. This suggests that the average YOGA-treated participant fared better than 79% of those in WL on DT enhancement.

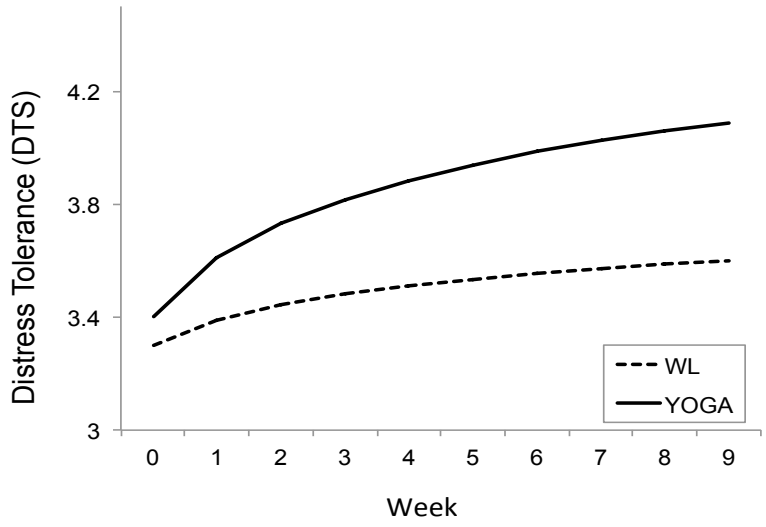


FIGURE 2.1. CHANGES IN DISTRESS TOLERANCE LEVELS (DISTRESS TOLERANCE SCALE - DTS) OVER TIME (PRE-TO-POST INTERVENTION) BY STUDY CONDITION.

Intervention effects on DTS subscales. Additional analyses were conducted to examine between-group differences in the slopes of change for each of the DTS subscales (i.e., Tolerance, Appraisal, Absorption, and/or Regulation). When testing the same model for each of the four

subscales, between-group differences were present for Tolerance (b = 0.226, t(149) = 2.154, p = .033; d = .89) and Absorption (b = 0.260, t(136) = 2.544, p = .012; d = .97), but not for Appraisal (b = 0.076, t(139) = 0.977, p = .330) or Regulation (b = 0.107, t(120) = 0.918, p = .361).

Intervention effects on emotional eating. As hypothesized, there was a significant Condition-by-Time interaction on DEES (b = 0.218, t(104) = 2.519, p = .013), suggesting that the rate of loglinear reduction in emotional eating was greater for YOGA than WL (**Figure 2.3**). This effect was large (Cohen's d = .92), indicating that the average YOGA participant fared better than 82% of those in WL on emotional eating.

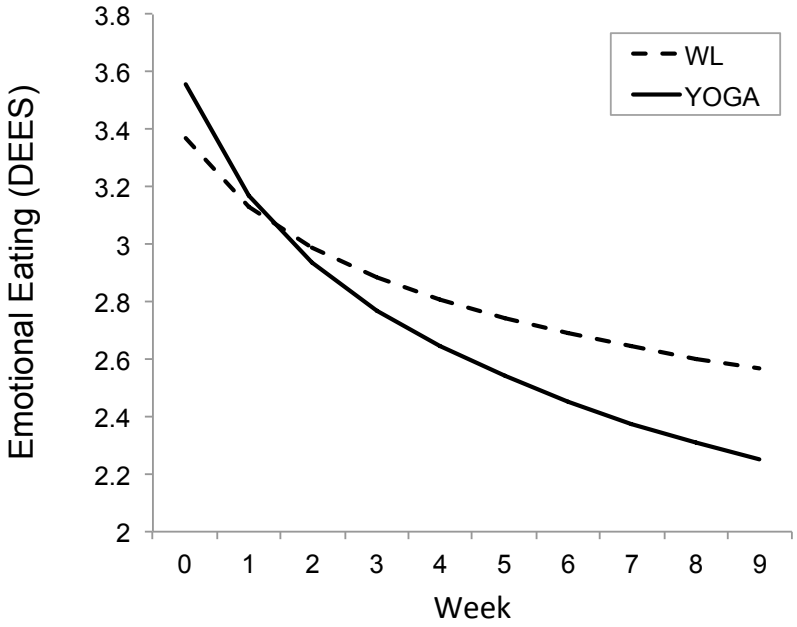
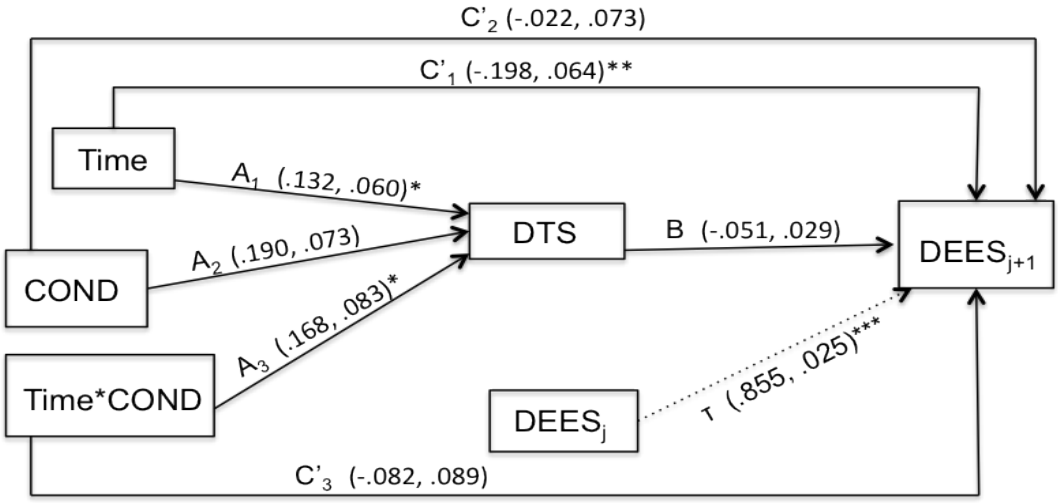


FIGURE 2.2. CHANGES IN EMOTIONAL EATING (DEES) OVER TIME BY CONDITION.

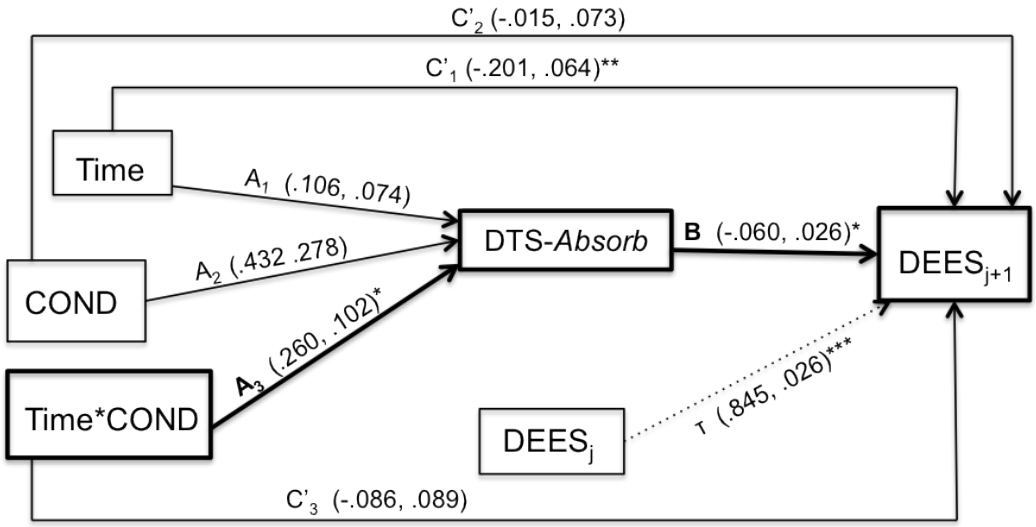
Mediation. The 95% confidence interval for the mediated effect for DTS score was (-.025, .002). Thus, mediation was not supported for the DTS total score (see **Figure 2.2** for A3 and B path coefficients). We replicated these analyses using the DTS subscales. These analyses yielded no mediation for any of the subscales except for DTS-Absorption (95% confidence

interval for the mediated effect of (-.07, .01); see **Figure 2.4** for A3 and B path coefficients). Percent of the effect of hatha yoga on emotional eating mediated by DTS-Absorption was 15%.



Note. (Coefficient *b*, std. error); $p < .001$***, $p < .01$**, $p < .05$*.

FIGURE 2.3. CROSS-LAGGED MEDIATION MODEL FOR DTS.



Note. (Coefficient *b*, std. error); $p < .001$***, $p < .01$**, $p < .05$*.

FIGURE 2.4. CROSS-LAGGED MEDIATION MODEL FOR DTS-ABSORPTION.

Discussion

The primary aim of this study was to test the effects of an 8-week hatha yoga intervention on DT. This investigation was conducted as a secondary aim of its parent trial examining a hatha yoga intervention for physiological stress reactivity and affective eating, a risk factor for disordered eating and obesity. Results showed that, in comparison to a WL control group, an intervention involving twice-weekly hot hatha (Bikram) yoga for 8 weeks resulted in greater improvements in DT (as measured by the DTS) and greater reductions in emotional eating (as measured by the DEES subscale of the DEBQ). Indeed, by week 9 post-intervention assessment, yoga had produced large and clinically meaningful effects, proving to be approximately 80% more effective than WL for improving both DT and emotional eating.

The yoga intervention's effect on self-reported DT is consistent with results from previous studies showing increases DT resulting from mindfulness and exposure-based behavioral interventions (Baer, 2009; Brown et al., 2008). Our findings for DT suggest potential for yoga interventions to improve affective tolerance in a host of psychological disorders. In addition, our finding that yoga also reduced emotional eating echoes findings from previous studies that provided initial support of yoga in the treatment of eating disorder symptoms (Carei et al., 2010; McIver et al., 2009). Moreover, we expanded on the results of these previous trials by demonstrating efficacy of yoga for treating subclinical disordered eating problems and related distress, suggesting its clinical utility as a prevention strategy for females at-risk for future obesity and other adverse health effects caused by dysregulated eating patterns.

Our finding that yoga directly enhanced DTS subscales, Tolerance (i.e., meta-cognitions about capacity to handle distress) and Absorption (i.e., attentional interference during distress),

suggests that 8 weeks of Bikram yoga practice particularly impacted cognitive components involved in distress processing, rather than those involved in emotional and behavioral distress reactivity (i.e., Appraisal or Regulation). That we found significant between-condition effects over time on these subscales is also consistent with previous studies showing that regular mind-body practice is associated with enhanced capacity to sustain attention while completing a task. One study found that experienced practitioners of yogic meditation performed better on cognitive tasks of attention than non-meditators (Prakash et al., 2010). Another showed that brief mindfulness training beneficially modified attention among alcohol dependent persons with no previous background in mindfulness (Garland, Gaylord, Boettiger, & Howard, 2010).

As our second aim, we examined increased DT as a mechanism underlying the effects of yoga on a relevant mental health outcome, namely improvements in emotional eating. Results of the mediation analyses showed that improvements in DTS-Absorption scores mediated the yoga intervention's positive effect on self-reported emotional eating. Improved Absorption explained 15% of the improvements in emotional eating caused by the yoga intervention. Thus, one way yoga reduces emotional eating, at least in this at-risk sample, appears to be by restoring the ability to concentrate and think clearly (i.e., enhanced cognitive capacity) during times of distress. Although yoga reduced DT in general (i.e., DTS total scores), it is interesting that it was only reductions in the Absorption subscale that drove improvements in emotional eating.

We can offer only speculation concerning the mixed findings among DTS subscales, given the paucity of literature providing context in which to interpret our findings. Little empirical attention has been paid to the relative clinical relevance and malleability of the individual DTS subscales in response to intervention (McHugh & Otto, 2012). One possibility is

that each of the DT facets change at different times or at different rates in response to intervention. Though our analyses cannot account for this idea, it may be that an 8-week yoga intervention can enhance general self-efficacy for handling distress (i.e., perceived Tolerance), which, in turn, makes the distress less salient in-the-moment, thus improving one's ability to approach distress with greater cognitive flexibility (i.e., decreased Absorption). Longer interventions and additional follow-up assessments should be used in future research to examine this hyposthesis.

The conjecture that yoga enhances one's ability to shift attention beyond the sensation of discomfort, toward other stimuli in the immediate environment, is supported by the mindfulness literature (Baer, 2009; Gard et al., 2012; Garland et al., 2010). For example, Garland and colleagues found that a mindfulness intervention for alcohol-dependent participants resulted in improved ability to shift attention away from visual alcohol cues, as well as decreased reliance on thought-suppression strategies, a form of experiential avoidance. Although this study lacked a control condition, it provides preliminary support for the use of mindfulness interventions for preventing stress-induced alcohol relapse (Garland et al., 2010). We speculate that ultimately, with greater capacity to sustain attention mindfully (i.e., reduced distress absorption), individuals become able to endure or cope healthfully with distress, rather than turning to food to dampen their feelings. Replication and extension of our findings will help more fully explain the relationship between yoga, mindfulness, absorption, and emotional eating.

We would like to note that we only focused on one of several potential psychological therapeutic mechanisms (i.e., DT) in this study, and cannot rule out the possibility that changes in DT are merely a byproduct of a change in some other perhaps more critical mechanism. Some

alternative mechanisms for the effects of yoga may be related to the physiological impact of exercise, such as peripheral and/or central nervous system stimulation (Broman-Fulks & Storey, 2008; Smits et al., 2008; Stoller, Greuel, Cimini, Fowler, & Koomar, 2012) or modulating cortisol reactivity to stress (Berger & Owen, 1988; Schell, Ollolio, & Schoneke, 1993). In one study, moderate-intensity physical activity, which induces repeated autonomic arousal, was negatively associated with frequency of binge eating among individuals who were fearful of such autonomic sensations (i.e., high AS, a construct related to DT) and had a tendency to eat as a means of coping with negative affect (DeBoer et al., 2012).

There are several limitations to our study that are worth noting and that can guide future investigations. First, our limited sample size and, thus, statistical power may explain our mixed findings among DTS subscales. Though power estimates for determining our sample size were gathered using published guidelines (Raudenbush & Xiao-Feng, 2001), a greater number of participants and/or more-frequent assessments could have enhanced power for detecting clinically meaningful condition differences.

Second, using additional behavioral measures of DT would have corroborated our findings using self-reported DTS. Measuring broad DT, or general affect intolerance is difficult at this time, however. Current laboratory behavioral measures of DT (e.g., breath holding challenge, computerized frustration tasks) tend to tap only domain-specific types of distress (e.g., physical discomfort, frustration) and, consequently, have been poorly correlated with each other and with other self-report measures (Leyro et al., 2010; McHugh & Otto, 2012). This problem calls for development of additional behavioral DT measurement methods that can assess both the overarching construct of emotional DT, as in the DTS, as well as its subcomponents.

Without the inclusion of additional active study conditions, our study cannot make conclusions regarding the comparative effects of yoga to traditional exercise, to psychotherapy, or to a contact control intervention. We also cannot ascertain whether yoga is better suited as a stand-alone or adjunctive treatment. That is, yoga may best serve as a complimentary intervention to established cognitive-behavioral interventions for emotional and binge eating that also emphasize broader emotion regulation skills. In short, we are limited in our ability to draw conclusions concerning the specificity of the effects of a yoga practice. Attrition represents a related limitation, as 25% of the yoga treatment condition prematurely terminated the study. Thus, we cannot confirm the effects found here to be a result of intended "dose" of yoga. Future studies should assess reasons for yoga dropout and dose underperformance to guide further yoga implementation strategies.

Further research is needed to investigate how and for whom yoga interventions will be most useful. It is possible that some groups require integrative treatment strategies to reduce their avoidant coping behaviors. One study showed that low DT and poor use of emotion regulation strategies were additively predictive of experiential avoidance (McHugh, Reynolds, Leyro, & Otto, 2013). This has application to our results, suggesting that enhanced cognitive capacity for handling distress (i.e., reduced Absorption) through yoga may be less relevant for emotional eaters who do not have available alternative emotion regulation strategies. For these individuals, yoga may be more useful as an adjunct to other cognitive and behavioral skills training.

This study offers preliminary evidence for the benefits of yoga interventions for problems characterized by elevated stress and poor affect regulation. First, our findings underscore the promise of hatha yoga practice for increasing DT and reducing emotional eating tendencies.

Second, our mediation analyses revealed a particular component of the cognitive processing of distress – Absorption – mediated the effects of yoga on disordered eating. Interventions that aid in affect modulation and enhanced coping are crucial for reducing the public health burden of an array of psychological disorders, and this study provides support for further development of specialized, mind-body interventions for those low in DT.

Study 3 – Biobehavioral Mechanisms Underlying Effects of Yoga on Nicotine Withdrawal

The need for evidence-based clinical intervention for smoking remains a major health care priority in the United States (US). As the leading cause of preventable death in the US, smoking accounts for the loss of an estimated 480,000 lives each year (United States Department of Health and Human Services [USDHHS], 2014). Additionally, an estimated 8.6 million individuals live with chronic diseases caused by tobacco use, such as lung cancer, heart disease, and COPD (Center for Disease Control [CDC], 2008; Danei et al., 2009). Consequently, at least 6-8% of total US personal health expenditures can be attributed to caring for these medical conditions (Warner, Hodgson, & Carroll, 1999). Importantly, despite increasing development of efficacious behavioral and pharmacological smoking cessation interventions (Rigotti, 2001), 19% of Americans continue to smoke (CDC, 2012). Among daily smokers, rates of heavy smoking (i.e., smoking ≥30 cigarettes per day) decreased between 2005 and 2011, while rates of light-moderate smoking (1-9 cigarettes per day) significantly increased (CDC, 2012). These rates infer the need for more-effective interventions for both groups, while calling particularly for strategies to address the increasing trend noted in less severe daily smokers.

Though 70% of smokers report the intention to quit to their doctors, the vast majority of smokers attempt to quit without aid with a less than 10% success rate (Chapman & MacKenzie, 2010; Fiore et al., 1990). Additionally, established behavioral interventions for smoking cessation are associated with high relapse rates (up to 85% within a year) and attrition (Copeland et al., 2006; Geraghty et al., 2012; Leeman et al., 2006; MacPherson et al., 2008). In order to increase the effectiveness of smoking cessation interventions and reduce the public health impact

of smoking, specialized treatments for at-risk smokers may be necessary (USDHHS, 2003). The call for the development of specialized interventions for smokers at heightened risk for relapse is guided by the selection hypothesis of smoking prevalence, which posits that smokers who are not able to quit successfully are "burdened" by specific characteristics that make it more challenging to quit (Hughes & Brandon, 2003). The development of specialized interventions is best guided by basic experimental research on the putative biobehavioral processes underlying smoking relapse in at risk populations.

Acute symptoms of nicotine withdrawal, which include irritability, frustration or anger; anxiety; difficulty concentrating; increased appetite; restlessness; depressed mood; and insomnia (DSM-5; APA, 2013), are viewed as a temporary disturbance in internal homeostasis resulting from absence or reduction of nicotine. These symptoms, which often cause severe distress and/or impairment, either remit when homeostasis is restored in a matter of days or weeks, or can be quickly relieved by smoking resumption (Hughes, Higgins, & Bickel, 1994; Hughes, Higgins, & Hatsukami, 1990; Shiffman, West, & Gilbert, 2004). Interestingly, there exists considerable variability in the nicotine withdrawal-relapse relation (Piasecki, Jorenby, Smith, Fiore, & Baker, 2003; Weinberger, Desai, & McKee, 2010), suggesting that targeting nicotine withdrawal to achieve cessation success may be critical for some but less important for others.

It has been noted that smokers with comorbid psychopathology in the form of affective disorders and SUDs may be more likely than their nicotine-dependent counterparts to experience withdrawal more intensely and subsequently relapse during the early quit phase (Weinberger, Desai, & McKee, 2010). Theoretically, this may be due to tendencies implicated in these conditions related to motivation to escape and avoid negative affect (Baker, Piper, McCarthy,

Majeskie, & Fiore, 2004). Research on the affect-vulnerability construct, low distress tolerance (DT), may be key to understanding individual difference variability in withdrawal-induced relapse (Brown et al., 2001; Brown et al., 2005; Brown et al., 2009). Specifically, persons with low DT exhibit limited ability to endure and persist through negative affective states (Brown et al., 2005), and thus are theoretically more likely to lapse and subsequently relapse when experiencing nicotine withdrawal. Indeed, studies have shown that low DT is associated with number of past failed quit attempts, early treatment dropout, higher withdrawal symptom severity and greater withdrawal-related negative affect, and immediacy to smoking lapse (Brown et al., 2005; Brown et al., 2009; Brown et al., 2008; Abrantes et al., 2008). Further, results of a cognitive-behavioral smoking cessation intervention trial revealed that 45% of quit-day lapsers exhibited low DT (Abrantes et al., 2008). Also, as predicted, low DT smokers in this sample reported significantly more negative affect on quit day relative to high DT smokers, accounting for their higher lapse rates. Together, these findings support the development and evaluation of strategies for reducing nicotine withdrawal specialized for smokers low in DT.

Experimental research indicates that changes in glucocorticoid activity may be involved in withdrawal-related relapse, suggesting the hypothalamic-pituitary-adrenocortical (HPA) axis may be a crucial intervention target in low DT smokers. Consistent with empirically documented dysregulatory effects of stimulant use on glucocorticoid production, habitual smokers exhibit elevated levels of basal cortisol as well as amplified cortisol-awakening responses compared to non-smokers (Friedman et al., 1987; Steptoe & Ussher, 2006). Within the first day following tobacco deprivation (4-24 hours), there is a sharp decline in cortisol concentrations theorized as representing a rebound effect caused by the absence of nicotine and other tobacco chemicals

from the system (Cohen, al ‘Abasi, & Collins, 2004; Pomerleau, Garcia, Pomerleau, & Cameron, 1992; Ussher et al., 2006). Though the initial plummet in cortisol begins to increase steadily after 24-hours, a significant decrease in cortisol concentration has been shown to persist through 6 weeks after quit (al’Absi et al., 2004; Steptoe & Ussher, 2006). Importantly, more pronounced cortisol declines following a quit attempt have been associated with greater experiential distress, withdrawal symptom intensity, and rates of early lapse (Cohen, al ‘Abasi, & Collins, 2004; Frederick et al., 1998; Ussher et al., 2006).

This association between post-quit cortisol declines and withdrawal symptom intensity has been replicated (Cohen, al ‘Abasi, & Collins, 2004; Frederick et al., 1998; Ussher et al., 2006), though the nature of the relation has been debated (Steptoe & Ussher, 2006; Ussher et al., 2006). There have been discrepancies in the research as to whether altered-cortisol secretion during a quit attempt is considered an effect of nicotine withdrawal, a putative mechanism underlying it, or neither. A few studies find that withdrawal symptoms and detectable cortisol declines persist in the event of nicotine replacement therapy (NRT), suggesting nicotine deprivation is not sufficient to explain withdrawal-related phenomenon (Steptoe & Ussher, 2006; Teneggi et al., 2002).

Still, there is relatively strong evidence from basic research in animal and human models to support the possibility that withdrawal symptoms as the result of nicotine deprivation may be mediated, at least in part, by cortisol. As summarized in Frederick et al. (1998), habitual smoking disrupts feedback loops involved in HPA-axis regulation. More specifically, nicotine reduces glucocorticoid receptor sensitivity by way of repeatedly stimulating cortisol and adrenaline release (this finding may explain tobacco drug tolerance). As such, the HPA-axis activity

patterns that are observed during nicotine deprivation contrasts that which are seen during regular smoking. Removal of nicotine (and therefore, its HPA-stimulatory effects), in turn, results in lower cortisol levels, and rebound receptor sensitivity heightening adrenergic activity, which may underlie withdrawal-related distress (Frederick et al., 1998; Ussher et al., 2006). This work suggests it is worthwhile to investigate whether targeting cortisol through intervention strategies would be beneficial. It is possible that interventions that can effectively prevent cortisol drops prior to the quit attempt may help protect withdrawal-symptom-vulnerable smokers from the detrimental cortisol declines that possibly contribute to relapse.

Yoga emerges as a promising candidate to aid smoking cessation in low DT smokers for several reasons. First, the application of yoga is supported by its conceptual rationale. Defined as a mindfulness-based form of physical exercise, yoga inherently combines two empirically supported strategies (i.e., acceptance/mindfulness and physical exercise) for increasing DT and for smoking cessation (Bock et al., 1999; Brewer et al., 2011; Brown et al., 2008; Marlatt & Chawla, 2007; Smits et al., 2012; Ussher, Nunziata, Cropley, & West, 2001; Ussher, Taylor, & Faulkner, 2008). Specifically, yoga encourages individuals to focus on the present moment and to use breath (pranayama) as a means toward acceptance and non-reaction through a series of potentially uncomfortable and challenging physical postures (asanas; Hewitt, 1977). Consistent with this model, initial data from a pilot study from our group shows that an 8-week hatha yoga protocol indeed yields significant increases in DT (Medina at al., 2015). Second, initial findings indicate that acute and regular yoga practice can reduce nicotine withdrawal and craving (Elibero, Van Rensburg, & Drobes, 2011). In one study, this effect was associated with greater short-term cessation success (Bock et al., 2010). Third, yoga interventions have shown to

effectively reduce perceived stress and regulate cortisol secretion patterns in several disorders associated with HPA dysregulation, such as fibromyalgia, cancer, and depression (Arora & Bhattacharjee, 2008; Curtis, Osadchuk, & Katz, 2011; Raghavendra et al., 2009; Sternlieb & Zeltzer, 2004; Woolery, Myers, Michalsen et al., 2005). Important for those with heightened propensity for relapse in response to withdrawal-induced distress, these changes in cortisol have been correlated with enhanced positive affect (West et al., 2004). Research suggests that a yoga practice may have to be in the vigorous-intensity range (i.e., hot Bikram yoga) to engender the effects on cortisol required to reduce withdrawal. Specifically, Scerbo and colleagues reported that an acute bout of vigorous aerobic exercise can effectively attenuate cortisol declines and reduce associated craving in abstaining smokers (Scerbo, Faulkner, Taylor, & Thomas, 2009). Finally, yoga is the fastest growing sport in the US, showing an increase in practitioners from 4.3 million in 2001 to 10.1 million in 2007, supporting acceptability of the use of yoga for smoking cessation.

Together, these findings promote the hypothesis that yoga is a feasible and effective specialized intervention to aid smoking cessation in individuals low in DT. Moreover, research suggests programmed yoga may be able to do so by way of targeting an important biobehavioral mechanism related to tobacco withdrawal, namely cortisol in the HPA-axis. At this time, it is unclear whether regular yoga practice can alter cortisol levels in smokers (ad-libitum) as a means to attenuating during-withdrawal subjective distress and cortisol declines during the initial stage of a self-guided quit attempt.

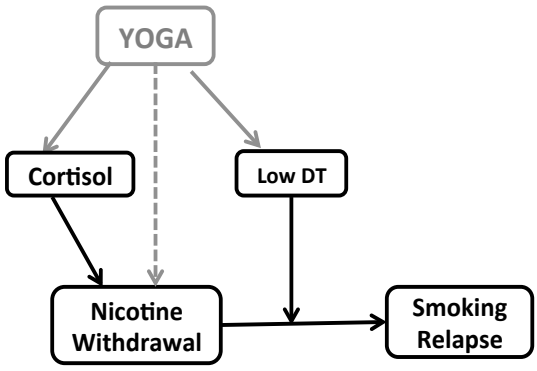


FIGURE 3.1. PROPOSED MODEL OF CAPACITY FOR YOGA TO ENHANCE SMOKING CESSATION BY CO-TARGETING LOW DT AND WITHDRAWAL.

Specific Aims and Hypotheses

To fill the noted gaps in the literature, the proposed study represents an RCT testing the efficacy of a yoga intervention for achieving targeting cortisol, subjective withdrawal, and smoking cessation success. We assigned women low in DT (i.e., illustrating elevated AS) to randomly receive either an 8-week *Vinyasa*-style yoga intervention consisting of two weekly sessions lasting 60 minutes each [YOGA] or waitlist [WL] prior to a self-guided quit attempt. Assessments were completed at baseline, during the intervention, on Quit Day and at 1-week following the quit attempt. The primary outcome measures were diurnal salivary cortisol concentrations, self-reported withdrawal severity, and self-reported abstinence status (verified by biological CO breath exhalation).

In examining the effect of yoga on ad-libitum cortisol levels in female daily smokers, we hypothesized that women assigned to YOGA would exhibit greater reductions in salivary cortisol between Baseline and post-intervention (week 9) than those assigned to a waitlist (WL) control group. The second part of this aim was to test capacity for YOGA to attenuate drops in cortisol during nicotine deprivation. We hypothesized that YOGA would achieve slighter declines in

salivary cortisol than WL during the initial 12 hours of a post-intervention quit attempt (slighter cortisol reduction between pre-quit Day 1 and Quit Day 2). In addition, we expect that the YOGA group would report lower withdrawal symptom severity than WL the evening of Quit Day (i.e., 12-hrs post-quit). Our final aim was to evaluate the clinical utility of yoga for smoking cessation. Accordingly, we obtained initial effect sizes of the advantage of YOGA over WL for achieving abstinence. We hypothesized that YOGA would evidence lengthier abstinence duration post-quit than WL.

Method

Participants

Participants included 50 adult female cigarette smokers (*M* Age = 29.40; *SD* = 8.30) from the Austin, Texas community, randomly assigned to receive either an 8-week yoga intervention (*n* = 33) or waitlist placement (*n* = 17) prior to initiating a self-guided smoking quit attempt. Participants between the ages of 18 and 65 were considered eligible if they reported consuming ≥ 8 cigarettes per day for the past year; elevated anxiety sensitivity (i.e., scored ≥20 on the Anxiety Sensitivity Index (ASI; Reiss, 1991)); at least a 5 out of 10 possible motivation to quit smoking; and interest in making a serious quit attempt within the next 2 months (Zvolensky et al., 2008). We chose the measure of ASI as our DT index because it best identifies distress-related concerns as they pertain to smokers at-risk for relapse (i.e., classified by high fear of interoceptive states, such as withdrawal symptoms; Brown et al., 2001; Hughes et al., 1990; Zvolensky et al., 2001). Moreover, factor analysis among distress intolerance self-report measures including ASI suggests separate measures may likely be tapping a latent general DT factor (McHugh & Otto, 2012).

Exclusion criteria included having practiced yoga or engaged in other mind-body practices (e.g., tai chi, meditation) regularly (i.e., once a week or more) within the last year; use of other tobacco products besides cigarettes; current severe depression, pregnancy, or any medical conditions that could potentially be aggravated by yoga; body mass index ≥ 40 (classified as obese); possessing cognitive dysfunctions or organic brain syndrome that could interfere with their capacity to perform study protocol; receiving concurrent psychotherapy of any kind or concomitant medications known to alter HPA-axis functioning; and history of a serious mental illness (e.g., psychotic disorder).

Procedures

Overview. See visual depiction of study procedures in **Figure 3.2**.

Recruitment. Participants were recruited through variety of sources including, but not limited to, advertisements in local newspapers and flyers in the Austin community.

Initial Eligibility Screening. Individuals who found out about the study via these recruitment methods indicated their interest in participating by completing an online prescreen survey, which assessed basic eligibility criteria (e.g., distress tolerance, daily smoking, motivation to quit). Those who met any of our exclusion criteria were sent an ineligibility email; those who reported severe, untreated psychopathology were offered the additional option of a psychotherapy referral list. Those who appeared potentially eligible from the prescreen phase were phoned by research personnel and asked whether they were willing/able to commit to the frequency of clinic visits were asked to come to the university research laboratory for a 2-hr, in-person Diagnostic Screen Visit.

The Diagnostic Screen Visit consisted of informed consent procedures, followed by administration of the Mini International Neuropsychiatric Interview for DSM-IV (MINI; Sheehan et al., 1999) and self-report questionnaires. In addition to evaluating psychiatric inclusion and exclusion criteria, these interviews will allow for assessment of primary and secondary diagnoses if applicable. Participants then completed the timeline follow back calendar (TLFB; past-week) and carbon monoxide (CO) analysis of breath sample (≥8ppm cutoff; Jarvis et al., 1987), evidencing daily smoking status. Those who met criteria and verbally agreed to comply with the protocol transitioned to the Baseline portion of the visit, where they were randomized and provided additional information regarding their study condition. To account for potential confounds to cortisol measurement due sex hormones, the study design also required scheduling the combined Screen/BL visit during the luteal phase (~17 days following start-date of most-recent period) of participants' menstrual cycle (Kudielka et al., 2012).

Randomization. Participants were randomized using a random number generator program; we employed block-randomized based on hormonal contraceptive use.

Baseline (BL). Baseline consisted of randomization, a program orientation, and additional lab assessments. BL assessments included of a self-report survey (administered through Qualtrics secured software) and hormone (cortisol biomarker) sample collection through participant saliva. Since adequate assessment of resting salivary cortisol required a 12-hr ad libitum (i.e., still smoking) monitoring period, participant completed saliva samples at home the day *following* their BL visit. Thus, at the close of the BL visit, participants were provided with saliva collection materials (2 Salivettes, plastic vials with cotton dental rolls inside; Sarstedt, Rommelsdorf, Germany) and were instructed by the experimenter on how to complete (1 after

waking, 1 at bedtime) and store them at home over the next 12 hours (al' Absi et al., 2004). At the close of this visit participants also scheduled their smoking Quit Day, which was 9 weeks following the BL visit. The evening of BL, the study experimenter called each participant to confirm these procedures and address any general program questions/concerns. Upon their completion of all baseline procedures (including the return of salivary cortisol samples to the lab), participants were compensated $25 for their time and allowed to enter the intervention phase of the study.

Yoga Intervention. The 8-week hatha yoga intervention prescription consisted of twice-weekly, 60-minute yoga sessions (i.e., 16 classes total) practiced at a local yoga studio in Austin, Texas (located ~2 miles from the study site). This studio features a spacious practice space, lobby, and storage cubbies; is kept clean and well maintained; offers single-occupant restrooms; and provides complimentary filtered water. The studio offered an array of hatha classes (primarily of the vinyasa style) throughout the week, taught by Yoga Alliance-certified instructors. To meet their prescribed weekly "dose", participants were allowed to attend any two "Vinyasa" or "Align" classes featured on studio's the schedule each week. Vinyasa is a dynamic class involving "flow" sequences (i.e., holding and transitioning through postures synced with breath); Align involves similar components, but with a greater focus on holding postures with proper alignment. Both Vinyasa and Align are considered all-levels-appropriate classes that allowed participants to achieve a moderate-to-vigorous intensity workout. Participants were encouraged both by the PI and yoga instructors to complete the entire 60 minutes of each yoga session, but urged to do only what is comfortable and not push themselves beyond their physical limits. To assess for adverse events and maintain clinical rapport/accountability with

participants, our study team conducted a weekly 10-minute phone check-in with each participant enrolled in the YOGA condition to discuss progress and address potential barriers to yoga practice.

Waitlist (WL). Participants randomized to the WL control condition at baseline completed the same weekly assessment/check-in, Quit Day, and follow-up procedures as YOGA. They were compensated for each laboratory visit the same amount as YOGA. At the 1-week brief follow-up visit, WL participants were given a voucher to attend 8-weeks of yoga classes at the partnering yoga studio.

Weekly Check-In. At the end of each week of the intervention, all participants (i.e., whether enrolled in YOGA or WL) received a weekly call from the study team to gather Timeline Followback (TLFB) information (daily cigarette intake) and to assess for any adverse events.

Post-Intervention (Week 9). The week following the end of the intervention (week 9) coincided with the week of the smoking quit attempt. During this week, participants performed *two* 12-hr salivary cortisol-monitoring periods—one pre-quit and one *on* Quit Day (see **Figure 3.2**).

*Day 1 (*pre-quit). The day prior to Quit Day, participants collected 2 salivary cortisol samples (a.m., p.m.), replicating the baseline-monitoring period at home. This was necessary to determine the effects of the yoga intervention on average daily salivary cortisol concentrations.

Day 2 (Quit Day). This included a 12-hr salivary cortisol-monitoring period that replicated Day 1 and BL procedures; however, Day 2 (Quit Day) collection was unique in that it assessed cortisol changes that occurred during acute nicotine withdrawal the first day of a self-

guided quit attempt. On this day, participants were asked to initiate their smoking quit attempt upon waking (and complete first Salivette). That evening, participants physically reported to the lab to (1) return saliva samples from Day 1 and Day 2 a.m.; (2) complete their final p.m. Salivette; (3) complete self-report questionnaires assessing withdrawal, subjective distress and affective state; (4) provide another hair sample; and (5) provide CO (ppm) readings & self-reported smoking prevalence for abstinence status. Participants were compensated following this Quit Day appointment.

Self-Aided Quit Attempt. This was a voluntary, unaided nicotine quit attempt (Zvolensky et al., 2008), where enrolled participants (i.e., smokers who indicated motivation ≥ 5 out of 10 to quit smoking) made their best efforts at cessation upon waking on scheduled Quit Day (week 9).

Follow-up Assessment Period. Participants were assessed for 1 week following quit to assess smoking abstinence, monitor safety, and document any adverse events. Participants reported to the lab 7 days after their quit day (week 10) to provide self-reported (point-prevalence) and biological indices of smoking abstinence (TLFB & CO readings). At the close of this visit WL participants were provided information about the yoga studio, a voucher for two months of free, twice-weekly yoga, and a new yoga mat.

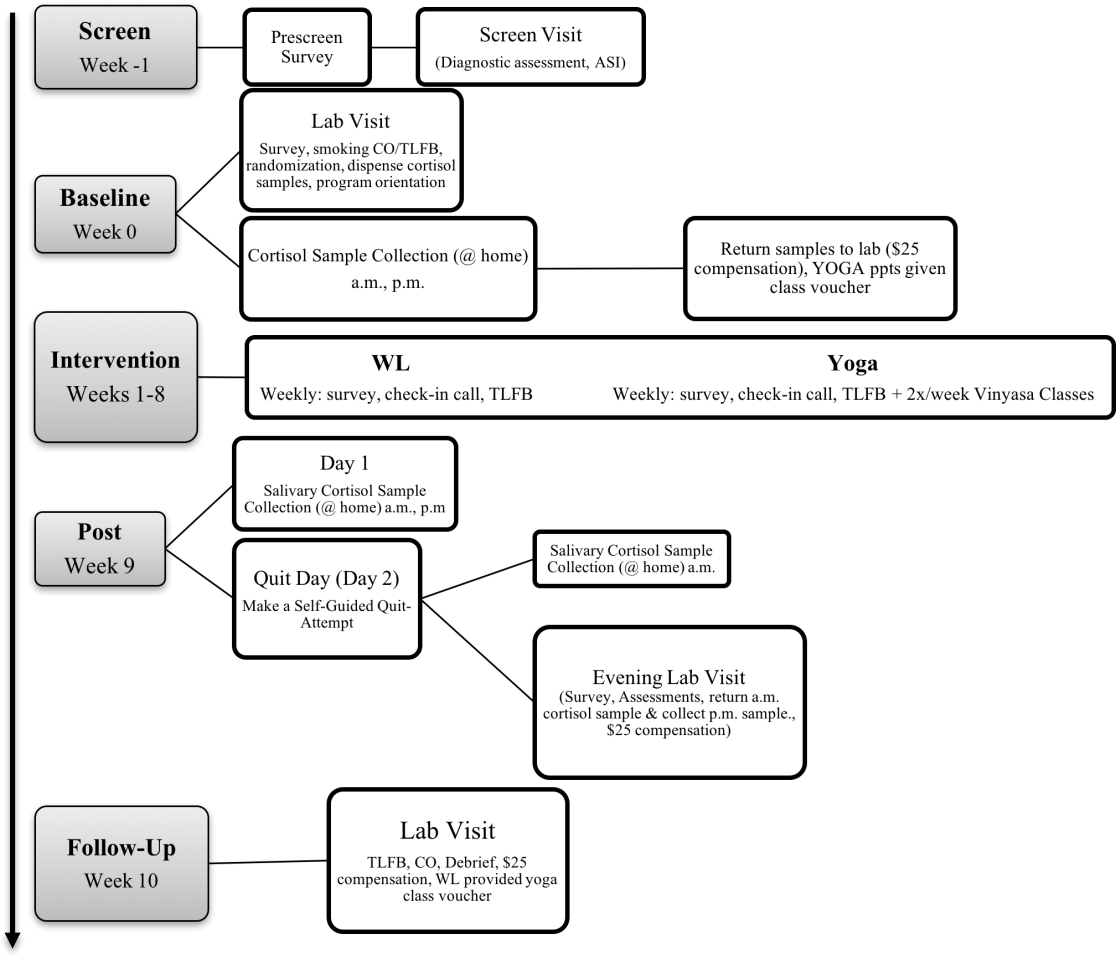


FIGURE 3.2. PROCEDURES.

Measures

Mental Health Screen. The Mini International Neuropsychiatric Interview (MINI); Sheehan et al., 1998) assessed diagnostic status at Diagnostic Screen Visit. It is a structured interview and can be safely and swiftly conducted on the phone to enable accurate diagnosis of a broad variety of mental illnesses, for screening of exclusionary/inclusionary criteria.

Urine Pregnancy Test. This was conducted for each participant at the screening visit.

Anxiety Sensitivity. The 16-item Anxiety Sensitivity Index (ASI; Reiss et al., 1986) measures sensitivity to physical (autonomic arousal) sensations. ASI was used to determine elevated AS as a screening criterion (eligible participants scored ≥ 20 on the ASI). ASI was re-assessed at Baseline to ensure that participants maintained their eligibility by the time of enrollment. The ASI has good internal consistency and excellent convergent validity with other established measures. Chronbach alpha for Baseline ASI in the present sample was 0.864.

Daily Cigarette Consumption and Continuous Abstinence. The Timeline Followback (TLFB) calendar assessed participants' daily cigarette count at baseline and across the 10-week study period. TLFB has demonstrated good reliability and validity in substance use disorders, and researchers have recently validated the TLFB for the assessment of adult cigarette use and to measure smoking among high AS persons over time (McLeish, Zvolensky, & Bucossi, 2007). TLFB was also employed as a measure of self-reported daily smoking abstinence on quit-day and during 1-week follow-up. To index initial efficacy of yoga for smoking cessation, we compared groups based on the number of days self-reported abstinence was sustained (0–7) in the first week following Quit Day. Perkins (2014) argued that this outcome of early quit success is ideal for determining pilot efficacy in the context of smoking cessation trials that may be underpowered to detect group differences on a binary measure of smoking abstinence.

Biochemical Verification. The Vitalograph Breathco Carbon Monoxide (CO) monitor (Jarvis et al., 1987) was used to assess expired CO. Detected values ≥8 ppm are considered indicative of tobacco smoking within the past 24 hrs. Participants were tested during ad libitum (screen) and deprivation stages (Quit Day, 1-week follow-up) to verify smoking status.

Salivary Cortisol Concentrations. A total of 6 salivary cortisol samples were collected from participants over 3 separate 12-hr collection periods, during which morning and evening (i.e., diurnal) cortisol was assessed. Saliva samples were collected with Salivettes (Sarstedt, Rommelsdorf, Germany), plastic vials with cotton dental rolls inside. Once the samples were collected and returned to the lab, they were stored at – 80 degrees Celsius for future processing. They were sent to Salimetrics laboratory for extraction, processing, and analysis. To extract saliva the samples were centrifuged at 4 degrees Celsius for 5 minutes at 2000xg; samples were assayed with an enzyme immunoassay, using an ELISA commercial kit (Diagnostic Products Corporation, Los Angeles, CA).

Salivary cortisol was chosen given its specific temporal utility of assessing cortisol in intervention research (McCarthy, 2012) and its ability to capture daily patterns in HPA-axis responsivity (McCarthy, 2012). Salivary cortisol samples are scheduled at times anticipating for variations in the diurnal pattern (Bailey & Heitkemper, 1991; Kudielka et al., 2012; Weitzman et al., 1971). We chose to measure morning cortisol 30-minutes after waking and evening cortisol 12-hrs following this assessment to reflect the highest and lowest expected cortisol levels for each person.

Minnesota Nicotine Withdrawal Scale-Revised (MNWS-R 79). The MNWS-R (Hughes & Hatsukami, 1986) is a validated self-report measure of withdrawal severity rated on a 5-point Likert scale (0 “none” to 4 “severe”). MNWS-R assesses DSM-IV symptoms of nicotine withdrawal. The initial 9 items of the MNWS-R cover primary DSM symptoms of tobacco withdrawal—anger, irritability, and frustration; anxiety and nervousness; depressed mood and dysphoria; craving to smoke; concentration difficulty; increased appetite, hunger, and weight

gain; insomnia and sleep disturbance; and restlessness/impatience (Hughes, 2007). The final 6 experimental items assess somatic symptoms related to tobacco deprivation, such as constipation, dizziness, coughing, dreams or nightmares, nausea, and sore throat (Hughes, 2007). The most recent version is the 15-item MNWS, and empirical evidence supports its validity and internal consistency (Etter & Hughes, 2006; Hughes, 2007; Weinberger et al., 2007). We compared the 15-item total scores between experimental groups to examine differences in withdrawal severity on Quit Day. Chronbach alpha for MNWS-R in the present sample was 0.875.

Measure	Screen	BL	Yoga Intervention								Post	Follow-up
* = on Quit Day	**Wk -1**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Consent	X											
Adverse Events/ Check-in			X	X	X	X	X	X	X	X	X	
Pregnancy Test	X											
BMI	X											
ASI	X	X	X	X	X	X	X	X	X	X	X	
Suicide Scrn.	X											
Demographic	X											
TLFB		X	X	X	X	X	X	X	X	X	X	X
CO (ppm)		X									X	X
12-hr Salivary Cortisol		X									X X*	
FTND		X			X			X			X	
MNWS-R											X*	
Debrief/Exit interview												X

TABLE 3.1. ASSESSMENT SCHEDULE.

Data Analytic Strategy

Effect of Yoga on Cortisol. In order to analyze changes in 12-hr cortisol as the result of yoga from pre-to-post intervention and from post-intervention to Quit Day (i.e., during withdrawal), we used mixed effects multilevel modeling (MLM) in SPSS® Version 24. There are several advantages of this approach over other strategies for evaluating longitudinal data, including the capacity to include subjects regardless of missing data. The natural log transformation was applied to our cortisol outcome variable to reduce skewness. We employed the Diagonal error covariance matrix based on goodness of fit determined by information criterion, AIC/BIC.

We used a single, 2-level MLM to test our hypotheses. Our MLM included assessment-day (see next paragraph) and time of day [TIME_OF_DAY] as level 1 predictors of outcome, and study condition [COND, coded "0 = Yoga", "1 = WL"] as a level 2 predictor (moderator) of our outcome. Given that withdrawal-related cortisol declines should theoretically be contingent on nicotine deprivation, we also factored participants' success at achieving a 12-hr abstinence on Quit Day into our analysis. Accordingly, our final model also included the additional level 2 grouping variable for quit-attempt status [QUIT_ATTEMPT, coded dichotomously as "attempter = 0", "lapser = 1"]. Age, BMI, and baseline FTND and ASI were included as covariates in our MLM, but were dropped from the final model, as they were not significant.

Since assessment day was a categorical variable (not a continuous variable) and was comprised of 3 levels (BL, POST, and QUIT day), the effect of day was examined using 2 dummy variables. In dummy variable coding of a categorical variable, one category (in this case, POST) is designated as the "reference" category. Then dummy variables are created for the other 2 categories (D_{BL} and D_{Quit}). When following this coding strategy, the effects of each dummy

variable represents the difference between the category that the dummy variable represents (either BL or QUIT day) and the reference category (POST). Accordingly, we included two Level 2 dummy variables [D_{BL} and D_{Quit}] in our model to test the difference in cortisol concentration between post-treatment Day 1 and each of the other two days. TIME_OF_DAY was centered at the midpoint of morning and evening (coded as "a.m. = -0.5" and "p.m. = 0.5") in order to interpret the main effect for each dummy (D_{quit}, D_{BL}) as the difference in diurnal cortisol average between that day and the reference day. The interaction between TIME_OF_DAY and each dummy reflected the change in diurnal slope between D_{quit} or D_{BL} and the reference day.

Our final MLM composite model for predicting salivary cortisol concentrations included the main effect of each Level 1 and 2 predictor (D_{quit}, D_{BL}, TIME_OF_DAY, QUIT_ATTEMPT, COND), in addition to the various combinations for modeling two-, three-, and four-way interactions between each dummy-coded day (D_{quit}, D_{BL}) and each other predictor (with the exception that QUIT_ATTEMPT did not interact with D_{BL} or its interactions). Significance of the coefficient for the two-way D_{BL} x COND interaction reflected group differences in average diurnal cortisol between BL and post-intervention. Significance of the coefficients for either the three-way (D_{QUIT} x COND x QUIT_ATTEMPT) interaction (modeling condition differences in the change diurnal cortisol levels between post-intervention and Quit Day) or four-way (D_{QUIT} x COND x QUIT_ATTEMPT x TIME_OF_DAY) interaction (modeling condition differences in the change in diurnal cortisol *slope* between post-intervention and Quit Day based on quit status) were used to test effects of yoga during withdrawal.

Effect of Yoga on Subjective Withdrawal. We employed ANCOVA to test the quit-status-moderated effect of study condition (i.e., COND x QUIT_ATTEMPT interaction) on subjective withdrawal symptom severity (MNWS-R-15) on Quit Day. Baseline FTND and ASI were entered in the model as covariates.

Initial Efficacy of Yoga for Smoking Cessation. A Poisson regression with a log link function, controlling for baseline FTND and ASI, was run to predict the effect of COND on the count distribution for the number of days (0-7) until relapse following a quit-attempt. Days abstinent was determined based on values reported on the TLFB for the 7 days between Quit Day and 1-week Follow-Up (0 days of abstinence were counted Quit Day lapsers). We examined this relation both among the entire sample (i.e., intent-to-treat (ITT)) and second, among study completers only (i.e., excluding dropouts). For study dropouts using ITT, lapse was assumed (i.e., 0 days of abstinence were counted).

Results

Participant Characteristics

Our final sample consisted of 50 female smokers, ranging in age from 19 to 53 (M = 29.40, SD = 8.30), randomized to either YOGA (n = 33) or WL (n = 17). Randomized participants reported smoking on average 11.25 cigarettes per day (SD = 11.26) at baseline; scored a mean of 3.56 (SD = 2.43) on the FTND (indicative of low to moderate nicotine dependence; Pomerleau, Majchrezak, & Pomerleau, 1989); and reported an average motivation to quit of 6 out of 10. ASI at baseline (M = 24.16, SD = 10.10) for the total sample approached clinical norm for individuals diagnosed with anxiety disorders (Peterson & Reiss, 1992). Body

mass index (BMI) for the total sample was in the normal range (M = 23.15, SD = 4.95) (see **Table 3.2** for descriptive statistics divided by group).

	Yoga (N = 33)		Waitlist (N = 17)		Total (N = 50)	
Variable	*M*	*SD*	*M*	*SD*	*M*	*SD*
Age	30.58	7.88	27.12	8.85	29.40	8.30
BMI	23.81	5.74	21.99	3.06	23.15	4.95
ASI	23.42	9.27	25.59	11.73	24.16	10.10
FTND	3.64	2.43	3.41	2.48	3.56	2.43
CO (ppm)	16.06	13.17	12.06	11.11	14.70	12.54
Avg. Cigs/Day	11.55	4.65	10.74	5.34	11.25	4.86

TABLE 3.2. BASELINE SMOKING AND CLINICAL CHARACTERISTICS.

The sample consisted primarily of young, urban, non-Hispanic White (80%, n = 40) female adults. Of the 5 (10%) participants who identified ethnically as Hispanic/Latina, 4 identified racially as White, and 1 identified as Native American. Among non-Hispanic participants, 45 (90%) identified their race as White, 2 identified as Asian/Asian American (4%), 2 identified as Native American, and 1 identified as Black/African American (2%). Majority (94%; n = 47) of our total sample was unmarried (i.e., either single (66%), living with a partner (20%), divorced (6%), or widowed (2%)). Regarding education, all but one participant gained at least a high school degree, and 48% were college graduates or higher (12% reported attaining a graduate degree). Regarding SES, 44% reported earning an annual household income of below $25,000. See **Table 3.3**, for additional participant demographic statistics.

Total Sample *N* = 50	*n*	*%*
Race		
White	46	92
Black/African American	1	2
Asian	2	4
Native American	3	6
Ethnicity		
Hispanic/Latino	5	10
Household Income		
<$25,000	22	44
$25,000-$49,000	17	34
$50,000-$74,000	5	10
>$75,000	1	2
Missing/not reported	5	10
Occupational Status		
Employed Full Time	28	56
Employed (Part-Time)	14	28
Dependent - spouse/student	1	2
Dependent - public/private aid	1	2
N/A or not reported	6	12

TABLE 3.3. PARTICIPANT DEMOGRAPHICS.

Randomization and Group Baseline Equivalence

Our attempt at randomization yielded unequal group sizes (33 = YOGA, 17 = WL). MANOVA was used to examine condition differences at Baseline in demographic and clinical characteristics. Results showed that WL and YOGA did not differ in baseline characteristics of BMI, age, nicotine dependence (FTND), reported average daily cigarette count, or ASI (p's > 0.17). Refer to **Table 3.2** for baseline descriptive statistics on AS and smoking-related variables.

In addition, the model revealed no differences between study conditions in baseline salivary cortisol parameters (p's > 0.22). Out of 50 enrolled participants, 49 provided a.m./p.m. Salivette pairs at Baseline (i.e., 98 samples collected in total). Two of the 98 samples collected were below the detectable range for salivary cortisol analysis. Outliers were removed if they were ≥ 3 SDs above the mean for their respective data points, resulting in two outliers being removed (final salivary cortisol n = 46). (see **Table 3.4**).

	Cortisol (μg/dL)		Yoga	Waitlist	Total
Baseline					
	Morning				
		M	0.429	0.437	0.432
		SD	0.255	0.228	0.244
		n	31	16	47
	Evening				
		M	0.236	0.142	0.203
		SD	0.485	0.2	0.409
		n	30	16	46
Post (Pre-Quit)					
	Morning				
		M	0.41	0.399	0.406
		SD	0.215	0.203	0.207
		n	18	12	30
	Evening				
		M	0.095	0.099	0.097
		SD	0.0726	0.104	0.085
		n	18	12	30
Quit Day					
	Morning				
		M	0.38	0.274	0.336
		SD	0.187	0.153	0.179
		n	17	12	29
	Evening				
		M	0.088	0.115	0.098
		SD	0.059	0.053	0.057
		n	19	12	31

TABLE 3.4. SALIVARY CORTISOL CONCENTRATIONS (μg/dL) SEPARATED BY DAY, TIME OF DAY, AND STUDY CONDITION.

Retention and Dropout

Participant flow and dropout are depicted in the CONSORT diagram below (**Figure 3.3)**. The 31 participants (YOGA = 19, WL = 12) who attended the Quit Day visit and completed post-intervention survey were considered "completers" and those who did not were considered study "dropouts." Accordingly, total attrition was 19 (38%). MANOVA revealed that there was not a significant difference between the 31 completers and 19 dropouts at baseline in age, BMI, clinical characteristics (FTND, ASI, daily cigarette count), or cortisol levels (p's > 0.25). Fourteen participants (42%) dropped out from the YOGA condition, and 5 (29%) from WL. Chi-square analyses revealed that study attrition did not differ significantly between conditions ($\chi 2 = 1.20$, $p = .27$).

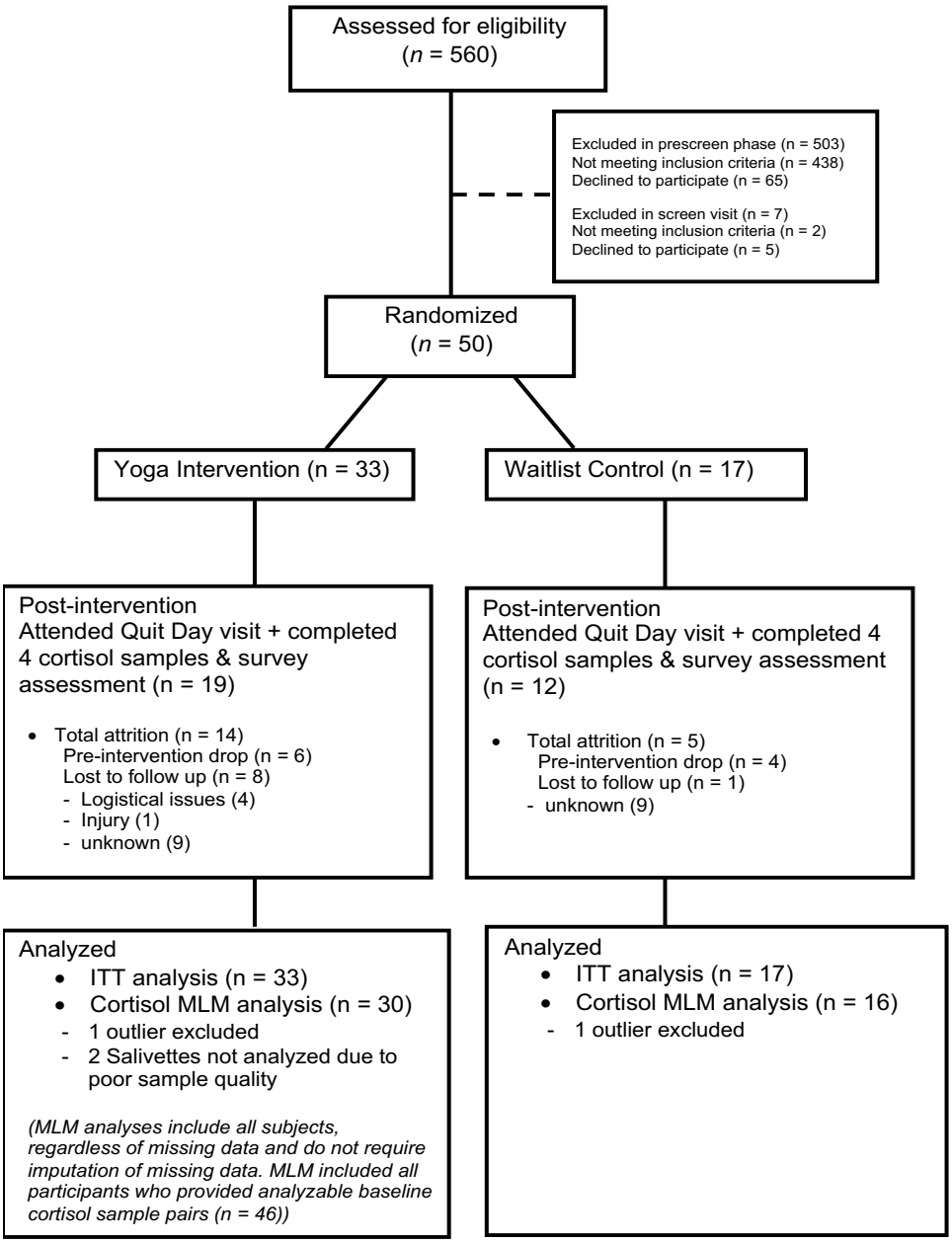


FIGURE 3.3. CONSORT DIAGRAM

Self-Guided Quit-Attempt

Verified by biological CO levels (ppm ≥ 8), 17 of 31 (55%) study completers who attended the Quit Day visit successfully attempted to quit smoking on Quit Day. In YOGA, 10

out of 19 (52.63%) participants achieved 12-hr abstinence; in WL, 7 out of 12 (58.33%) participants achieved 12-hr abstinence ($\chi 2 = 0.10$, $p = .76$).

Intervention Adherence

Twenty percent of the sample (see CONSORT diagram, **Figure 3.3**) dropped out during the first week (before yoga sessions began). Two participants dropped out (both in YOGA) during the early intervention phase (i.e., prior to completing 1 week or less of yoga), and the 7 remaining (1 in WL, 7 in YOGA) occurred between weeks 3-9. Among the 19 study completers assigned to YOGA, yoga class compliance was generally poor; on average, participants attended just over *half* of the assigned, 16-class yoga dose over 8 weeks ($M = 8.44$ classes; $SD = 4.20$).

Hypothesis Testing.

Effect of Yoga on Cortisol. Contrary to prediction, our 2-level MLM showed that the (D_{BL} x COND) effect on salivary cortisol was not significant ($b = .021$, $t(109) = .500$, $p = 0.618$), such that there was no significant difference between conditions in the change in average salivary cortisol levels between BL and post-treatment. The model also suggested that yoga did not influence during-withdrawal cortisol, as neither the 3-way (D_{QUIT} x COND x QUIT_ATTEMPT), nor the 4-way (D_{QUIT} x COND x QUIT_ATTEMPT x TIME_OF_DAY), interactions were significant. The non-significant (D_{QUIT} x COND x QUIT_ATTEMPT) interaction ($b = -.092$, $t(74) = -1.494$, $p = 0.139$) revealed that there was no significant difference between conditions in the change in average salivary cortisol levels between post-treatment Day 1 and Quit Day 2. The non-significant D_{QUIT} x COND x QUIT_ATTEMPT x TIME_OF_DAY interaction ($b = -.016$, $t(73) = -.131$, $p = 0.896$) revealed that there was no significant difference

between conditions in the change in salivary cortisol slope between post-treatment Day 1 and Quit Day 2.

When we re-ran the model, however, dropping the 4-way interaction term, the (D_{QUIT} x COND x QUIT_ATTEMPT) effect on salivary cortisol concentrations became marginally significant, b = -.097, t(87) = -1.936, p = 0.056. To further investigate this relationship, we interpreted the two-way (D_{quit} x QUIT_ATTEMPT) interaction effect within each group. Examining the relation in WL required first reverse-coding the COND variable (i.e., 0 = WL, 1 = YOGA) and then re-running the model. Results showed that the (D_{quit} x QUIT_ATTEMPT) relation was significant for YOGA, b = 0.080, t(97) = 2.218, p = .029, but not for WL, b = -0.017, t(106) = -0.404, p = .687. This illustrated that the change in average diurnal cortisol from pre-quit Day 1 to Quit Day 2 for YOGA depended on abstinence status. Specifically, average diurnal cortisol concentrations in YOGA significantly reduced from pre-quit to quit day for attempters, while in lapsers, concentrations increased (see **Figure 3.4**). For WL, quit-status did not moderate the difference in cortisol observed from Day 1 to Day 2, as cortisol reduced for both attempters and lapsers (though slighter drops were observed in lapsers, as would be expected).

Figure 3.5 and **Figure 3.6** display morning and evening cortisol changes, respectively. Indicated by a non-significant (COND*D_{quit}) interaction within quit attempters (QUIT_ATTEMPT coded "0" = attempters, "1 = lapsers"), condition did not moderate the difference in morning (b = 0.026, t(53) = -.313, p = .755) or evening (b = -0.003, t(63) = -.068, p = .946) cortisol concentration differences between pre-quit Day 1 and Quit Day 2. Important to note, we observed morning drops in cortisol between pre-quit and quit day (i.e., in the expected

direction given nicotine deprivation) for attempters in both conditions (**Figure 3.5**). However, in the evening YOGA attempters demonstrated no change, and WL attempters peculiarly increased their cortisol on average (**Figure 3.6**).

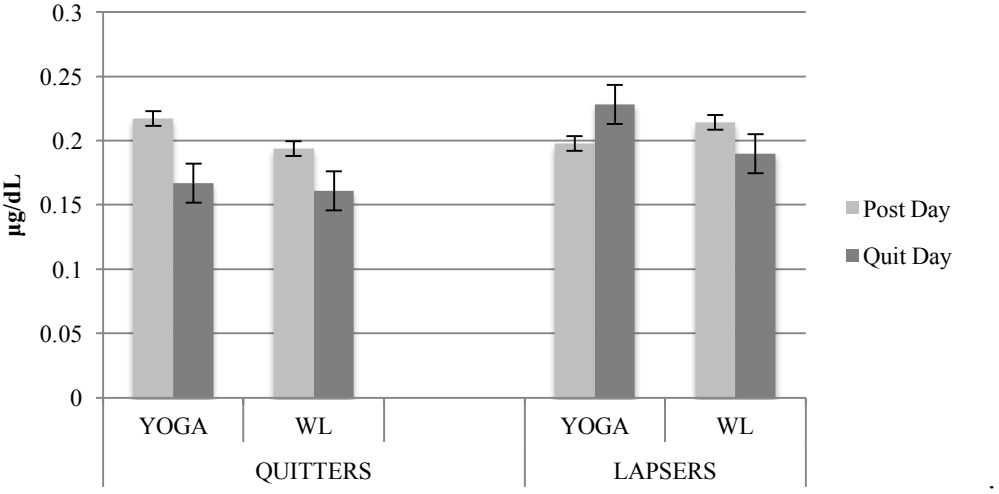


FIGURE 3.4. CHANGE IN AVERAGE DIURNAL SALIVARY CORTISOL FROM POST-TREATMENT (PRE-QUIT DAY) TO QUIT DAY AS A FUNCTION OF CONDITION AND QUIT STATUS

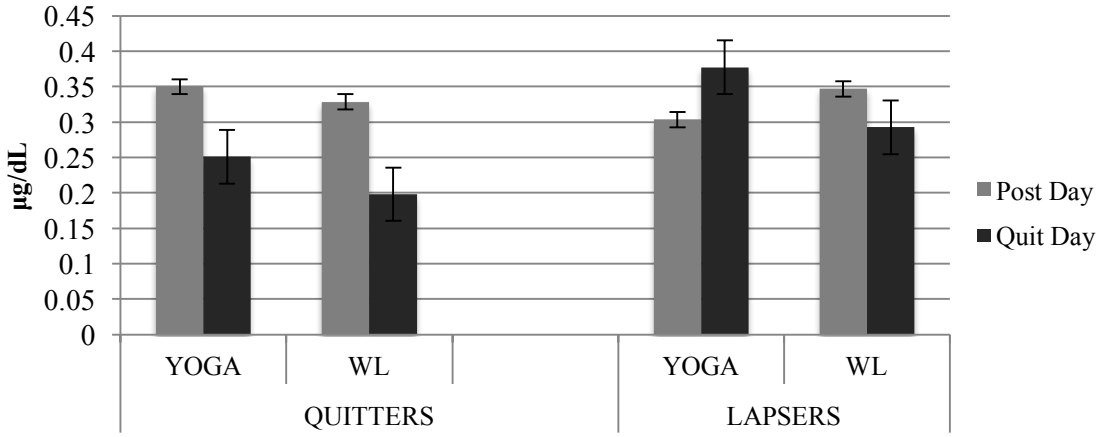


FIGURE 3.5. CHANGE IN MORNING SALIVARY CORTISOL FROM POST TREATMENT (PRE-QUIT DAY) TO QUIT DAY AS A FUNCTION OF CONDITION AND QUIT STATUS.

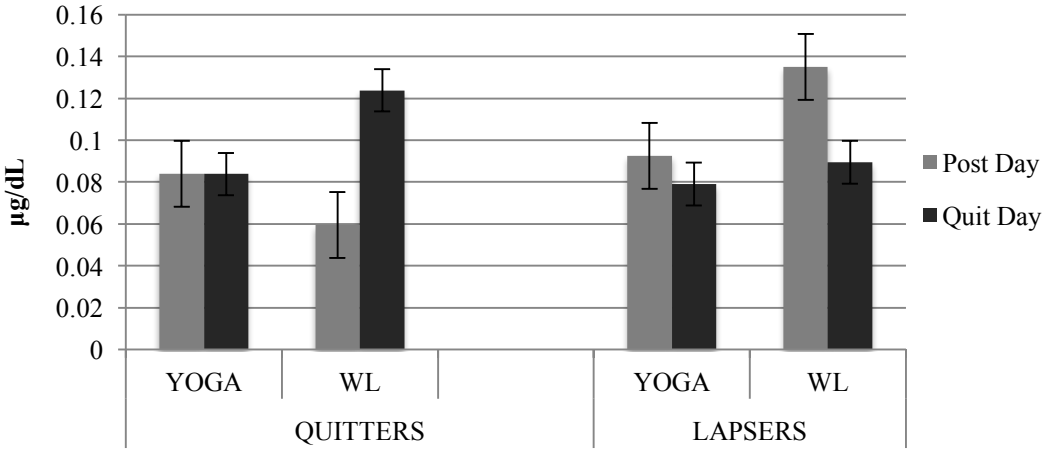


FIGURE 3.6. CHANGE IN EVENING SALIVARY CORTISOL FROM POST-TREATMENT (PRE-QUIT DAY) TO QUIT DAY AS A FUNCTION OF CONDITION AND QUIT STATUS.

To better understand the role of nicotine deprivation status as a determinant of diurnal cortisol alterations, we examined QUIT_ATTEMPT as a moderator of cortisol concentration changes across conditions by re-running our model with COND coded YOGA = "-0.5", WL = "0.5." Consistent with the extant nicotine withdrawal literature, we found that the D_{quit} x TIME_OF_DAY interaction was significant for attempters, $b = 0.144$, $t(75) = 3.146$, $p = .002$), but not for lapsers, $b = -.039$, $t(76) = -.787$, $p = .694$. As depicted in **Figures 3.7** and **Figure 3.8**, the relation was such that morning cortisol reduced for successful attempters between Day 1 and Day 2, yielding a flatter diurnal cortisol slope on Quit Day.

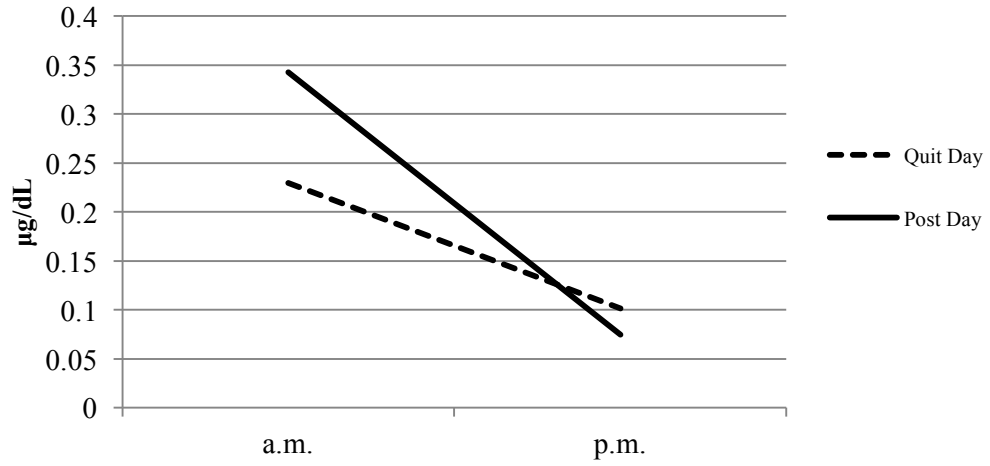


FIGURE 3.7. CHANGE IN DIURNAL SALIVARY CORTISOL FROM POST-TREATMENT (PRE-QUIT DAY) TO QUIT DAY FOR SUCCESSFUL ATTEMPTERS.

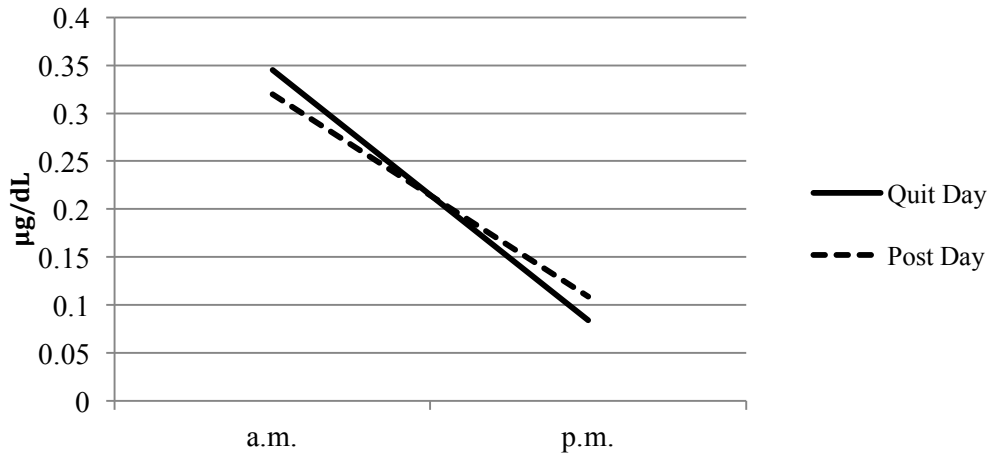


FIGURE 3.8. CHANGE IN DIURNAL SALIVARY CORTISOL BETWEEN POST-TREATMENT (PRE-QUIT DAY 1) AND QUIT DAY 2 FOR LAPSERS.

Specific Aim 2. Mean MNWS-R (15-item) for the 31 individuals who completed the measure the evening of Quit Day was 23.66 (*SD* = 11.22). Results of ANCOVA showed that the COND x QUIT_ATTEMPT interaction effect on MNWS-R was not significant (i.e., $F(1,28) = 0.269$, $p > .05$), revealing no mean difference between YOGA and WL in withdrawal severity based on quit-attempt status. Estimated mean for YOGA was 24.90, (*SD* = 10.18) and for WL was 22.66 (*SD* = 13.30). Contrary to what is shown in the smoking literature (Weinberger et al., 2007; Toll et al., 2007), neither QUIT_ATTEMPT (main effect) nor the covariates included in the model (Baseline FTND, ASI) predicted MNWS-R (p's > 0.053). However, the non-significant baseline ASI effect on MNWS-R was large but not significant ($F(1,28) = 4.156$, $p = .053$, $\eta 2 = 0.141$).

Specific Aim 3. Results of our Poisson regression using an ITT approach ($N = 50$) revealed that neither FTND ($b = 0.006$, $\chi 2(1) = 0.009$, $p = .923$) nor COND ($b = 0.123$, $\chi 2(1) =$

0.037, p = .663) were significant predictors of days abstinent, with the model predicting a mean of 1.25 days abstinent for YOGA (SE = .198) and 1.11 days abstinent for WL (SE = .260). Baseline ASI significantly predicted days abstinent (b = 0.031, $\chi 2(1) = 5.793$, p = .016), showing that higher pre-treatment ASI was associated with lengthier abstinence duration. The completer analysis (n = 31) showed similar results, as there was no effect of COND (b = 0.395, $\chi 2(1) =$ 0.632, p = .427) or baseline FTND (b = 0.038, $\chi 2(1) = 0.140$, p = 0.708). The model estimated mean abstinence duration of 2.237 days for YOGA and 1.506 for WL. In contrast to the ITT analysis, however, baseline ASI did not predict days abstinent for completers (b = 0.033, $\chi 2(1) =$ 1.889, p = 0.169).

Exploratory Analysis of the Effect the Yoga Intervention on Smoking Behavior.

Tapering. Though participants were not instructed to change their cigarette consumption before Quit Day, it is possible that engagement in yoga (i.e., a regular health behavior) influenced participants to alter their smoking habits. Since significantly reducing one's nicotine dependence via tapering pre-quit could impact the experience of withdrawal on Quit Day, a separate MLM analysis evaluating the longitudinal change in weekly TLFB point-prevalence revealed a significant main effect of Time (b = -1.721, $t(93) = -6.633$, p = 0.000) and a significant COND*Time effect (b = 0.917, $t(92) = 2.167$, p = 0.033), indicating YOGA reduced self-reported smoking over time.

Discussion

The present study represents a novel effort to translate basic research findings to an RCT designed to target withdrawal-related relapse through yoga. We evaluated the efficacy of an 8-week hatha yoga intervention to (1) reduce cortisol levels prior to a self-guided tobacco quit

attempt; (2) attenuate cortisol drops and subjective nicotine withdrawal symptoms during the initial 12-hrs post-quit; and (3) achieve superior smoking cessation outcomes to a waitlist control group, evidenced by longer sustained abstinence during 1-week follow-up.

Results were generally inconsistent with our hypotheses. Specifically, we failed to find pre-to-post intervention differences between the yoga condition (YOGA) and waitlist (WL) in ad-libitum diurnal salivary cortisol concentrations. Analyses also failed to show that yoga was able to target withdrawal parameters during a post-intervention quit-attempt (week 9). Specifically, there were no group differences on quit-day in subjective withdrawal symptoms or in the change in diurnal cortisol from pre-quit day. Consistent with this pattern, post-quit abstinence duration was equivalent between conditions, disproving our hypothesis that YOGA would by superior to WL for achieving early smoking cessation. Promising from a harm-reduction perspective, however, a final exploratory analysis showed the yoga intervention influenced participants to taper down their weekly cigarette usage prior to quit.

Despite null findings across major aims, our trial represents an innovative application of yoga. This study is one of the first behavioral intervention attempts to reduce hypercortisolism in smokers, positioning it as a stepping point for further investigation of ways to address tobacco related HPA-axis dysregulation. One other trial to our knowledge has applied programmed yoga for smoking cessation and nicotine withdrawal symptoms (Bock et al., 2012). However, ours is the first to our knowledge to explore cortisol as a potential mechanism of yoga's influence on withdrawal and withdrawal-related relapse in distress-vulnerable smokers.

Our study also adds to the growing number of intervention studies finding capacity to detect changes in cortisol secretion patterns across time through repeated saliva sampling.

Speaking to the reliability of our methodology, we found that for each day that samples were taken (i.e., baseline, post-intervention, quit day), 12-hr patterns observed were in accordance with the normal trajectory of decline from morning to evening (Edwards, Clow, Evans, & Hucklebridge, 2001). Furthermore, participants who successfully attempted to quit smoking illustrated the hypothesized during-withdrawal cortisol drops (Cohen, al'Absi, & Collins, 2004; Frederick et al., 1998; Ussher et al., 2006). We were also able to detect changes related to nicotine deprivation. Across study conditions, successful quit attempters reduced their diurnal average and slope in salivary cortisol between pre-quit day and quit day. Subjective withdrawal ratings on quit day were consistent with experience of withdrawal. The sample mean for the MNWS-R was 23.66 (*SD* = 11.22), which is comparable to other studies examining the effects of attempted nicotine deprivation (Hughes & Hatsukami; Toll et al., 2007). Together, these results encourage future attempts to compare salivary cortisol levels before and after a tobacco quit attempt in an intervention context.

Potential explanations for our lack of significant between-group differences are small sample size and intervention non-adherence. First, high attrition lowered our sample size and thus statistical power for detecting effects. The study was originally powered for our target *N* of 50 participants (assuming approximately group equal sizes) to be able to detect medium to large effects. Our randomization procedure yielded unequal groups (YOGA = 33; WL = 17). In addition, 38% (*n* = 19) of our sample dropped out following enrollment reducing our final sample size to 31. This is within the typical range of attrition rate among other behavioral smoking cessation interventions (Bryant et al., 2011; Stead & Lancaster, 2012; Stead, Carroll, & Lancaster, 2000). Nevertheless, it is possible that attrition prevented our ability to detect between

group differences on some outcomes, particularly instances when there may have been smaller effect sizes. Small group cells can be particularly problematic for detecting statistical differences between study conditions in cortisol biomarker due to wide sample heterogeneity (Kirschbaum & Hellhammer, 2007).

The nature of the relation found between covariates and one of our outcomes supports the likelihood that power influenced detection of effects. Results of our test of between-group differences in subjective nicotine withdrawal symptoms did not support the prediction that YOGA would display less severe withdrawal (MNWS-R scores) than WL; this was not necessarily surprising given that we were unable to find yoga efficacious for targeting cortisol (i.e., the mechanism considered as giving rise to withdrawal distress). Interestingly, however, covariates, baseline nicotine dependence (FTND) and AS (ASI), did not predict withdrawal either, which is inconsistent with the evidence in the smoking literature supporting the convergent validity of the MNWS-R (Weinberger et al., 2007; Toll et al., 2007). The relation between ASI and MNWS-R approached marginal significance with a large effect size, highlighting the likelihood that attrition may have played a role in reducing statistical power to detect effects.

We employed MLM to examine cortisol aims because it is able to address some of the challenges posed by having large amounts of missing data. Though MLM cannot correct for biomarker heterogeneity per se, it is a preferred ITT approach for evaluating nested, longitudinal data given its advantage of being able to include subjects regardless of missing data and adjust model parameters for observation frequency and study duration (i.e., characteristics that optimize power in smaller samples; Fritz & MacKinnon, 2007). However, attrition may have significantly

impacted MLM findings as well. Because all attrition occurred prior to or during the intervention phase, no post-intervention cortisol samples were gathered for dropouts. Accordingly, MLM analysis (n = 46) estimated post-intervention levels for dropout participants in the model equation based off of baseline levels. It is possible that data projections from baseline introduced significant error variance reducing the sensitivity of our test.

In addition to high rates of dropout, we observed poor intervention adherence. Participants assigned to YOGA attended on average just over *half* of the assigned, 16-class yoga dose over 8 weeks, ultimately preventing our ability to evaluate the yoga prescription we suspected would be beneficial for targeting nicotine withdrawal and early relapse. Worth nothing, the proportion of total of yoga classes attended in our study was slightly greater than that which was observed a recent aerobic exercise intervention trial conducted in high AS smokers, which found that participants attended 44% (20 out of 45) of the 30-minute sessions assigned (Smits et al., 2016). On the contrary, other yoga intervention trials conducted in female smokers (who were not screened for AS; Bock et al., 2013) and in other low DT samples (i.e., women with stress-induced eating tendencies; Hopkins et al., 2016) have achieved superior adherence to ours. Bock and colleagues (2012) achieved low attrition and 76% yoga class adherence in an RCT that evaluated a yoga intervention of comparable style, duration, and dose-intensity in 55 female smokers. (Bock et al., 2012). Overall, these discrepancies underscore the difficulties engaging tobacco users with elevated AS in health behavior change strategies.

Potentially related to attrition and adherence differences, our findings related to withdrawal and cessation were inconsistent with those by Bock et al. (2012). Results from this trial showed that 8-week *Vinyasa* yoga + standard smoking cessation CBT was superior to CBT

+ a wellness contact control for reducing withdrawal symptom severity and achieving short-term (12-hr and 7-day) abstinence (Bock et al., 2012). The discrepancy between our findings and theirs suggests that providing access to a yoga intervention is insufficient for its effective implementation, particularly for populations characterized by behavioral avoidance (i.e., tobacco smokers with elevated AS). Findings by Bock and colleagues (2012) also suggest that yoga may be most clinical effective for treating smoking when used to augment the effects of other behavioral intervention strategies. This may especially be the case for more severe clinical groups of smokers, such as those with elevated AS, who may benefit from more intensive methods to enhance treatment adherence and boost therapeutic efficacy of standard treatments. Our exploratory analysis, showing yoga that, relative to WL, YOGA participants effectively reduced their cigarette intake from Baseline to Week 9, promotes programmed yoga as a potentially effective preparatory aid for quitting smoking. As such, its effects may also be optimized when applied in combination with strategies that can acutely mitigate early-lapse processes.

Given that we failed to meet aims pertaining to cortisol, answers to questions of whether (1) yoga can down-regulate cortisol in smokers prior to a quit attempt, and (2) this effect can engender resistance to post-quit cortisol drops during deprivation, remain unknown. We focused on cortisol as a putative mechanism of nicotine withdrawal severity and early relapse (Cohen, al ‘Abasi, & Collins, 2004; Frederick, 1998; Pomerleau, Garcia, Pomerleau, & Cameron, 1992; Ussher et al., 2006). Yoga was chosen as our strategy for targeting cortisol in smokers given outcomes from previous exercise/yoga intervention trials, finding 6-12 week yoga beneficial for altering cortisol within conditions marked by HPA-axis dysregulation (Banasik et al., 2011;

Riley & Park, 2015; Ross & Thomas, 2010; Woolery et al., 2004). Though no behavioral intervention studies to our knowledge have made attempts at addressing chronic hypercortisolism in nicotine users, studies support 8-week moderate-to-vigorous intensity yoga as capable for lowering diurnal cortisol in other groups. Banasik and colleagues (2011), for example, compared 8-week, twice-weekly Iyengar-style yoga (i.e., comparable yoga "dose" to our study) to a waitlist control for lowering salivary diurnal cortisol levels in 18 breast cancer survivors, finding reduced a.m. and p.m. concentrations by post-treatment. Though the discussed findings by Bock et al. (2012) encourage the possibility that an 8-week dose is sufficient for augmenting smoking cessation CBT outcomes, their effects have not been replicated and do not speak to whether cortisol was mechanism of outcome. Our findings call for further research examining efficacy of yoga for mitigating biological withdrawal processes in smokers. Under this aim, studies should investigate dose-response relations by manipulating dose.

In addition to attrition and adherence, another potential limitation relates to timing of measurement. By assessing cortisol only at baseline and post-yoga, it is possible that we failed to capture meaningful during-intervention changes that occurred, particularly during weeks wherein greater study participation and yoga class attendance was observed. Furthermore, participants collected cortisol samples at home, therefore, we cannot verify that instructions were followed. Measurement of peak diurnal cortisol (i.e., 30 minutes after waking) is particularly contingent on successful timing of measurement given that levels vary greatly over the CAR trajectory. Even slight deviation from the collection protocol could have introduced significant error variance into our between-day comparisons.

Encouraging of the feasibility/acceptability of yoga as a clinical treatment, we did not face difficulties recruiting interest for participation the Austin, Texas community. As a qualitative observation, most of our enrolled participants stated eagerness to initiate yoga during the program orientation during the baseline visit. Behavioral performance, however, was clearly inconsistent with stated interests. As an attempt to bolster engagement and collect smoking data, the study PI and laboratory research assistants called each participant weekly to briefly check-in regarding their participation. However, this strategy failed to foster adequate motivation and accountability to reinforce adherence. Guided by the impressive adherence results from Bock et al. (2012), it is advisable that future yoga intervention trials include components to bolster clinical and social support, as well as to teach sills for successful behavior change and stress-coping. Strategies used by Bock and colleagues (2012) included evidence-based counseling and a cohort enrollment procedure. The advantages of using of group social support and combining behavioral support with other behavioral and pharmacological interventions to optimize exercise adherence and effectiveness is also supported by outcomes from standard care smoking cessation interventions (Stead & Lancaster, 2012).

We also considered clinical explanations relevant to AS smokers for non-adherence. A secondary analysis from the aforementioned RCT on hot yoga for affective eating by Hopkins and colleagues published in 2015 found that BMI and low DT were time-varying predictors of weekly adherence rates. This suggests that the very characteristic we aimed to address with yoga may have prevented participants from reaping benefit. Though identification of adherence barriers is beyond the scope of the present study, follow-up analysis examining adherence predictors is warranted. Overall, the summarized information suggests that successful yoga

programs in the future will have adequate resources and individually tailored clinical supports in place to promote engagement and commitment, while addressing concerns that could negatively impact behavior.

In light of our findings and their limitations, we make several final recommendations for further research. To further understand the clinical utility and mechanisms underlying the effects of yoga on withdrawal and smoking cessation, additional intervention trials with multiple intervention arms will be needed. This will allow for determining the comparative advantage of yoga-augmented treatment over stand-alone yoga for smoking and its underlying mediators. In order to establish evidence of dose-efficacy and specificity for the potential benefits of yoga in tobacco users, these experimental trials should also compare various yoga styles, intensities, and intervention durations. We suggest that future efforts to examine cortisol as a driving mediator of the effects of hatha *Vinyasa* effects pay particular attention to the practical and methodological limitations noted from the present study. Finally, given that our results only extend to women, future studies are warranted to examine yoga's effect on cortisol and nicotine withdrawal in men, especially men with elevated AS.

The overarching objective of this study was to evaluate biobehavioral effects of a yoga intervention designed for targeting nicotine withdrawal and risk-of-relapse in smokers with low DT (i.e., elevated AS). Results indicated 8-week hatha *Vinyasa* yoga was not effective for targeting cortisol, ameliorating withdrawal, or achieving abstinence in smokers. Two major factors we suspect undermined potential intervention efficacy with yoga were attrition and intervention non-adherence. Though our aims were not supported, this study adds to the growing body of literature evaluating the mental and physical health effects of yoga. Furthermore, results

add to the emerging body of work investigating exercise as a strategy to address the maladaptive role of affective vulnerabilities on additive behaviors. In conclusion, this RCT represents a novel attempt to translate experimental paradigms to clinical treatment. Limitations and findings hold recommendations for future efforts to explore the role of yoga in the withdrawal-relapse relation.

General Discussion

This research was guided by the need for improved treatments for addictive behaviors. A common aim of the three RCTs presented in this dissertation was to evaluate the benefits of varied exercise modalities in populations with factors that put them at risk for maladaptive behavioral coping tendencies (e.g., binge-eating, treatment dropout, smoking). With a particular focus on ways to modify DT and its consequences, the specific objective of this line of work is to identify potential moderators and explanatory mechanisms of the effects of aerobic exercise and yoga in samples with low distress tolerance. Support for the aims across studies was mixed.

Summary of Findings

Studies 1 and 2 aimed to target distress intolerance directly. Study 1 represents a secondary analysis from a previous trial conducted by our research group, which found efficacy of a brief, 2-week vigorous-intensity exercise intervention for reducing AS. Our objective was to examine gender as an individual difference predictor of AS response to aerobic exercise. Results showed that AS reduced less-readily for women as compared to men in response to brief, two-week exposure to vigorous aerobic activity. This finding pointed to the possibility that clinical responses to exercise vary by gender, perhaps due to differences between sexes in biological responding to exercise. Clinical implications include the potential benefit of gender-tailored strategies to reduce distress vulnerability.

Appropriately, Study 2 evaluated hot hatha yoga as a tailored intervention strategy for women with problems characterized by elevated stress coupled with poor affect regulation (i.e., resulting in stress-induced eating tendencies). Study 2 extended initial work on the efficacy of exercise for AS by targeting a novel application of yoga for enhancing low emotional DT. We

also found that reduced DT was an explanatory mechanism of psychopathology symptom reductions observed with yoga (Study 2). Specifically, this study showed an 8-week yoga intervention effectively increased DT and reduced emotional eating tendencies. Moreover, mediation analyses confirmed enhanced-DT as a driving mechanism of emotional eating changes. This finding builds off of the body of evidence supporting exercise for enhancing DT (Broman-Fulks et al., 2004; Broman-Fulks & Storey, 2008; Smits et al., 2008), while extending the evidence to the modality of yoga.

In light of their findings and the call to consider multiple avenues by which yogic exercise can address the contribution of DT substance relapse, the aim of Study 3 was to examine biobehavioral pathways of yoga's potential for reducing risk of early relapse in women with low DT (high-AS). We aimed to do so by targeting cortisol levels with 8-week, twice weekly *Vinyasa* yoga (a dynamic, moderate-to-vigorous intensity yoga style). We hypothesized yoga would regulate cortisol secretion patterns in the HPA-axis from pre-to-post intervention so that prior to a quit-attempt, so that during a quit-attempt typical drops in cortisol during withdrawal would be attenuated. We predicted that reduced subjective nicotine withdrawal-symptoms and smoking cessation success (i.e., lengthier abstinence duration) would accompany these effects. By investigating mediators of the effects of hatha yoga, the broader goal of Study 3 was to translate important basic experimental research findings to early-stage intervention development efforts. Ultimately, results indicated 8-week hatha *Vinyasa* yoga was not effective for targeting cortisol, ameliorating withdrawal, or achieving abstinence in smokers. Two likely confounds limiting the efficacy of our intervention were attrition and poor intervention adherence.

Novel Contributions to the Literature. Despite null findings on major aims for Study 3, our results showed that diurnal cortisol patterns for each assessment day (baseline, post-intervention, quit day) were in accordance with the normal trajectory of decline that occurs from morning to evening (Edwards, Clow, Evans, & Hucklebridge, 2001). Furthermore, results regarding the difference between pre-and post-quit cortisol levels in successful abstainers replicated previous research findings showing an acute cortisol decline results from nicotine deprivation (Cohen, al 'Abasi, & Collins, 2004; Frederick et al., 1998; Ussher et al., 2006). These findings add to the literature demonstrating reliability for examining diurnal cortisol patterns over repeated measurement points.

Our exploratory finding also adds to smoking cessation literature. Participants were not explicitly instructed to alter their smoking habits leading up to quit day, however, we considered this a possibility given their involvement in a health behavior change intervention (Prochaska, Spring, & Nigg, 2008). Interestingly, we found that yoga facilitated during-intervention reductions over time in cigarette smoking (i.e., tapering). This suggests yoga may be a useful preparatory aid for quitting smoking. Alternatively, this argues for yoga as a harm reduction intervention for smokers not motivated for complete cessation.

Implications for Exercise Intervention Implementation

Population-specific adherence barriers should be identified and addressed. Research suggests that some of the characteristics specific to our samples may make it challenging for them to initiate and adhere to behavioral interventions. In fact, the nature of characteristics specific to those with AS (i.e., fear of autonomic arousal and its consequences) can lead to anxious avoidance of exercise specifically (Broocks et al., 1997). In Study 2, a secondary

publication from the parent trial showed that BMI and low DT significantly predicted of weekly adherence (Baird et al., 2015). This highlights a paradoxical challenge that a major characteristic we aim to target with exercise has potential to prevent many from having the chance to benefit. Study 3 findings prompts for further examination of moderator characteristics, including BMI and DT, as determinants of adherence to *Vinyasa* yoga.

It is suggested in the literature that BMI may be a particularly important aspect to consider in the context of programmed exercise for women low in DT. Previous findings indicate that individuals with higher BMI tend to enjoy exercise less than normal-eight individuals. Specifically, as exercise intensity increases, overweight and obese individuals experience more aversive somatic sensations and greater during-exercise negative affect (Ekkekakis & Lind, 2006). Importantly, tendency to associate the experience of exercise with negative consequences can deter future exercise performance. Moreover, high BMI individuals with AS have shown to experience greater levels of fear during exercise (Smits et a., 2010). This work suggests that BMI may be a particular in the exercise adherence of patients with predisposed vulnerability to aversive somatic and/or affective states.

Second, women are more likely than men to present with body image concerns and disordered eating patterns related to self-objectification (Cash, Theriault, & Annis, 2004) and fear of negative evaluation (DeBoer & Smits, 2013; DeBoer et al., 2013) that could impede their engagement in community-based exercise. Exercising in a group setting has potential to trigger such concerns. Though popular and appealing for many, the stereotypes associated with yoga in particular (e.g., thin, flexible body ideal), could feasibly exacerbate exercise avoidance.

Though BMI was in the healthy range in our sample, fear of weight gain is a significant reason many smokers, particularly women, are reticent to quit smoking (Pomerleau, Zucker, & Stewart, 2001). This further highlights the salience of addressing body image and weight control in low DT smokers. The CBT intervention in the trial conducted by Bock et al. (2012) specifically included a module for addressing weight concern. We suspect that weight concern may be an important variable impacting the effects of yoga on smoking cessation outcomes.

To address acute negative affect during exercise and fear of exercise, adding components of mindfulness and exposure-based interventions may help to target such behavioral barriers, while also potentially augmenting the exercise-DT relation. As a pre-intervention strategy, these techniques may help to modify anxious apprehension and experiential avoidance, thereby helping participants ease into and better-tolerate an exercise program.

Acceptance and Commitment Therapy (ACT; Hayes, 2003) is one mindfulness-based approach that may be particularly effective when combined with exercise. By integrating mindfulness awareness practices with committed action to personal values, ACT may serve as a motivational tool to behaviorally persist in the face of distress. Initial support for the utility of ACT in smokers comes from Brown and colleagues, who conducted a pilot trial evaluating mindful acceptance-based augmentation to standard CBT to target DT in smokers with a history of repeated relapse (Brown et al., 2013). Among those who completed the trial, 81% were able to remain abstinent for longer than 72 hours, and 43% maintained abstinence for over one month (Brown et al., 2013).

Finally, there is reason to investigate not only negative, but also positive clinical predictors of adherence. For example, we suspect that some of the non-specific factors that

enhance adherence in clinical therapy (e.g., rapport and therapeutic alliance; Martin, Garske, & Davis, 2000) may also help participants engage in exercise. It is possible that the low attrition observed in Study 1 was in part related to face-to-face attention and contact (i.e., participants reported to familiar clinical laboratory staff for their sessions). Though providing yoga in a similar context may have helped lower attrition, it is important to continue developing and delivering interventions in naturalistic settings to enhance generalizability of findings. Strategies to important to consider ways to help participants to feel generally accepted and supported at their place of exercise to effectively perform yoga in the community. Other positive predictors of yoga/exercise adherence worth investigation that stem from the positive psychology literature include self-compassion, mindfulness, and resilience (Gard et al., 2012; di Manincor et al., 2016).

Adherence, and therefore, efficacy may depend on aspects of study design and measurement. Our three RCTs varied based on intervention length (2, 8 week), exercise modality (yoga, aerobic running), session dose (60 vs. 90 minutes) and distress intolerant population of interest (men/women with AS; women with stress-eating tendencies; female tobacco smokers with AS). We suspect that the differential attrition and adherence observed across studies could be related to their procedural variations.

In studies conducted in AS samples, contrasting attrition rates were observed (21% and 38% for Study 1 and Study 3, respectively). One possibility is that a 2-week intervention is more feasible for populations with AS than lengthier exercise interventions. Furthermore, exercise sessions in Study 1 were conducted onsite and facilitated/supervised by laboratory clinicians, guiding participants through exercise-based somatic “exposure” sessions. In addition,

participants were oriented to the distress exposure by providing incremental distress ratings during their exercise sessions. It is possible that having clinician support/contact while participants attended to uncomfortable sensations bolstered during-exercise effort and confidence in being able to remain in the session and intervention.

Regarding session dose, we chose to employ 60-minute sessions in Study 3 (i.e., as opposed to 90-minute sessions employed in Study 2) to balance potential for efficacy with feasibility. However, still, we did not have positive outcomes related to intervention adherence efficacy. Comparatively, Study 2 showed efficacy for targeting emotional DT using 90-minute sessions. Moreover, the parent study for Study 2 showed that this yoga dose was able to target cortisol (Hopkins et al., 2016). It is possible that longer yoga sessions may be required to alter HPA-axis functioning dysregulations associated with habitual nicotine use. Alternatively, it is possible that the 8-week delay in re-assessing cortisol after baseline prevented us from capturing meaningful changes that occurred during the intervention, particularly during weeks when great yoga class attendance was observed. Employing a briefer yoga intervention or assessing cortisol more frequently and in close proximity following yoga performance (as was the case in Study 1) may improve the likelihood of detecting effects. Ultimately, the lack of analogous trials for comparison in the area of yoga for cortisol in smokers suggests future research will benefit from testing a variety of designs and procedures.

Health behavior change research may guide integrative approaches for achieving adherence to an exercise intervention. Some evidence in the health behavior literature suggests physical activity interventions can be efficacious for achieving multiple health behavior change (Prochaska, Spring, & Nigg, 2008). However, it may be overly ambitious to expect to tackle one

difficult-to-change health behavior (i.e., quitting smoking) with another (i.e., exercise adoption). Together, the literature in healthy populations, as well as in those with affective vulnerabilities, reinforce the effectiveness of implementing exercise from a multifaceted approach. Results from the trial by Bock et al., (2012) suggests that in addition to standard evidence based counseling (i.e., CBT), integrating mechanisms for social support and accountability into the program structure can be useful. Other empirically sound approaches for exercise implementation incorporate proven strategies for achieving successful behavior change. Self-efficacy, beliefs about treatments, and motivational readiness are three major targets of such techniques (Riekert, Ockene, & Pbert, 2013).

Future Directions

In light of the findings and the limitations of each of the studies, discussed in turn, we offer several next-step recommendations for future studies. Non-significant findings in Study 3 highlight the difficulty in studying biobehavioral mechanisms of intervention outcome. Indeed, there are a complex and dynamic interplay of factors involved in HPA-axis functioning with implications for impacting cortisol levels. We advise future studies to incorporate large sample sizes to reduce sample heterogeneity. In addition, future attempts to specifically examine during-withdrawal cortisol may consider measuring and controlling for other, potentially competing influences on HPA activity. Given that quitting smoking is stressful, one potentially important factor to consider in future research studies examining withdrawal is acute stress. There is evidence that nicotine and acute stress can interact to potentiate HPA-axis release of cortisol (Pomerleau & Pomerleau, 1990). The link between perceived stress and nicotine deprivation in predicting cortisol levels is not clear. However, future studies should investigate this. At the

least, future treatment studies should aim to differential the effects of their intervention on withdrawal-related cortisol levels from those of stress.

To determine the comparative efficacy of yoga in DT-related conditions, intervention trials are needed comparing yoga and exercise to active control conditions. In addition, trials will be needed to test dose-response effects for yoga. This will require manipulating adherence to predict differential efficacy based on yoga performance. Dose efficacy studies should be conducted in predicting a range of possible biobehavioral outcomes (e.g., DT, AS, HPA-axis functioning) and in a range of populations with behavioral addictions and other conditions that may benefit. Furthermore, large-scale studies will be needed to determine the cost-effectiveness of yoga. These trials will also help to pinpoint for whom practicing yoga over traditional exercise (or vice versa) is preferred. Finally, given that our results on yoga only extend to women, future studies are warranted to examine effect of yoga on cortisol and nicotine withdrawal in low DT men.

Conclusion

Previous research calls for improving the effectiveness, feasibility, and tolerability of treatments for substance and non-substance-related addictive disorders. Novel interventions are particularly warranted that can address the contribution of low DT to addiction maintenance, relapse, and treatment attrition. Treatments for enhancing DT in psychopathology to date have involved mindful acceptance and behavioral exposure; and so far, these techniques appear effective in low DT substance users with tobacco addiction. Exercise (especially of the aerobic type) emerges as another efficacious behavioral candidate for addressing low DT. In addition,

exercise holds practical and health-promoting potential for addressing public health burden of SUDs.

Guided by this background of literature, we conducted three RCTs that aimed to target biobehavioral factors implicated in the role of affective vulnerability in addiction maintenance and relapse. These trials represent important steps to extend the application of exercise and yoga to treat distress vulnerable groups, namely those at-risk for anxiety disorders and addictive behaviors (eating, tobacco use).

Because prescribed exercise and yoga will be most effective in its clinical application when reserved for patients who are prone to benefit, future efforts should continue to focus on identifying moderators and mechanisms of response with adjunct and stand-alone exercise, and to compare their effects. We encourage these pursuits particularly within affect-vulnerable populations prone to addictive disorders who warrant improved intervention strategies. Exercise-ready candidates will also be those sufficiently motivated for behavioral change and who can functionally tolerate vigorous physical exertion. Pinpointing these groups and addressing each of their individually tailored needs and preferences through the appropriate exercise dose, modality (e.g., running, yoga), and therapeutic mechanism will require continued empirical efforts.

References

Abrantes, A. M., Strong, D. R., Lejuez, C. W., Kahler, C. W., Carpenter, L. L., Price, L. H., . . . Brown, R. A. (2008). The role of negative affect in risk for early lapse among low distress tolerance smokers. *Addictive Behaviors, 33,* 1394-1401.

Adam, T. C. & Epel, E. S. (2007). Stress, eating, and the reward system. *Physiology & Behavior, 91*, 449-458.

Adinoff, B., Junghanns, K., Kiefer, F., & Krishnan-Sarin, S. (2005). Suppression of the HPA axis stress-response: Implications for relapse. *Alcoholism: Clinical and Experimental Research, 29*(7), 1351-1355.

al'Absi, M., Hatsukami, D., Davis, G. L., & Wittmers, L. E. (2004). Prospective examination of effects of smoking abstinence on cortisol and withdrawal symptoms as predictors of early smoking relapse. *Drug and Alcohol Dependence, 73,* 267-278.

al'Absi, M., Hatsukami, D., Davis, G. L., & Wittmers, L. E. (2004). Prospective examination of effects of smoking abstinence on cortisol and withdrawal symptoms as predictors of early smoking relapse. *Drug and Alcohol Dependence, 73,* 267-278.

Allen, S. S., Bade, T., Hatsukami, D., & Center, B. (2008). Craving, withdrawal, and smoking urges on days immediately prior to smoking relapse. *Nicotine & Tobacco Research*, *10*(1), 35-45.

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Arlington, VA: American Psychiatric Publishing.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Anestis, M. D., Selby, E. A., Fink, E. L., & Joiner, T. E. (2007). The multifaceted role of distress tolerance in dysregulated eating behaviors. *International Journal of Eating Disorders*, *40*(8), 718–726.

Arora, S., & Bhattacharjee, J. (2008). Modulation of immune response in stress by yoga. *International Journal of Yoga, 1,* 45-55.

Asmundson, G. J., Fetzner, M. G., DeBoer, L. B., Powers, M. B., Otto, M. W., & Smits, J. A. J. (2013). Let's get physical: A contemporary review of the anxiolytic effects of exercise for anxiety and its disorders. *Depression and Anxiety*, *30*, 362-373.

Bailey, S. L., & Heitkemper, M. M. (1991). Morningness-eveningness and early-morning salivary cortisol levels. *Biological Psychology, 32,* 181-192.

Baker, T. B., Piper, M. E., McCarthy, D. E., Majeskie, M. R., & Fiore, M. C. (2004). Addiction motivation reformulated: An affective processing model of negative reinforcement. *Psychological Review, 111*, 33-51.

Banasik, J., Williams, H., Haberman, M., Blank, S. E., & Bendel, R. (2011). Effect of Iyengar yoga practice on fatigue and diurnal salivary cortisol concentration in breast cancer survivors. *Journal of the American Association of Nurse Practitioners, 23*, 135-142.

Barlow, D. H., Allen, L. B., & Choate, M. L. (2004). Toward a unified treatment for emotional disorders. *Behavior Therapy*, *35*, 205-230.

Barlow, D. H., Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Allen, L. B., & May, J. T. E. (2010). *Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide*. Oxford University Press.

Baer, R. A. (2009). Self-focused attention and mechanisms of change in mindfulness-based treatment. *Cognitive Behaviour Therapy*, *38*(sup1), 15–20.

Baird, S. O., Hopkins, L. B., Medina, J. L., Rosenfield, D., Powers, M. B., & Smits, J. A. (2016). Distress tolerance as a predictor of adherence to a yoga intervention: moderating roles of BMI and body image. *Behavior modification*, *40*, 199-217.

Barnes, P. M., Bloom, B., & Nahin, R. L. (2008). Complementary and alternative medicine use among adults and children: United States, 2007. *National Health Statistics Report, 12*, 1-23.

Beck, A. T., Epstein, N., Brown, G., & Steer, R. A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology, 56,* 893-897.

Beck, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4,* 561-571.

Berger, B. G., & Owen, D. R. (1988). Stress reduction and mood enhancement in four exercise modes: Swimming, body conditioning, hatha yoga, and fencing. *Research Quarterly for Exercise and Sport*, *59*(2), 148–159.

Bernstein, A., Zvolensky, M. J., Vujanovic, A. A., & Moos, R. (2009). Integrating anxiety sensitivity, distress tolerance, and discomfort intolerance: A hierarchical model of affect sensitivity and tolerance. *Behavior Therapy*, *40*(3), 291–301.

Bhui, K., & Fletcher, A. (2000). Common mood and anxiety states: Gender differences in the protective effect of physical activity. *Social Psychiatry and Psychiatric Epidemiology*, *35*, 28-35.

Blackwell, E., de Leon, C. F. M., & Miller, G. E. (2006). Applying mixed regression models to the analysis of repeated-measures data in psychosomatic medicine. *Psychosomatic Medicine*, *68*, 870-878.

Bock, B. C., Marcus, B. H., King, T. C., Borelli, B., & Roberts, M. R. (1999). Exercise effects on withdrawal and mood among women attempting smoking cessation. *Addictive Behaviors, 24,* 399-410.

Bock, B. C., Morrow, K. M., Becker, B. M., Williams, D. M., Tremont, G., Gaskins, R. B., ... & Marcus, B. H. (2010). Yoga as a complementary treatment for smoking cessation: Rationale, study design, and participant characteristics of the Quitting-in-Balance study. *BMC Complementary and Alternative Medicine, 10*, 14-21.

Brewer, J. A., Mallik, S., Babuscio, T. A., Nich, C., Johnson, H. E., Deleone, C. M., ... & Rounsaville, B. J. (2011). Mindfulness training for smoking cessation: Results from a randomized controlled trial. *Drug and Alcohol Dependence, 119*, 72-80.

Brisbon, N. M., & Lowery, G. A. (2011). Mindfulness and levels of stress: A comparison of beginner and advanced hatha yoga practitioners. *Journal of Religion and Health*, *50*, 931–941.

Broman-Fulks, J. J., & Storey, K. M. (2008). Evaluation of a brief aerobic exercise intervention for high anxiety sensitivity. *Anxiety, Stress & Coping: An International Journal*, *21*(2), 117–128.

Broman-Fulks, J. J., Berman, M. E., Rabian, B. A., & Webster, M. J. (2004). Effects of aerobic exercise on anxiety sensitivity. *Behaviour Research and Therapy*, *42*, 125-136.

Broman-Fulks, J. J., Kelso, K., & Zawilinski, L. (2015). Effects of a single bout of aerobic exercise versus resistance training on cognitive vulnerabilities for anxiety disorders. *Cognitive behaviour therapy*, *44*(4), 240-251.

Broocks, A., Meyer, T. F., Bandelow, B., George, A., Bartmann, U., Rüther, E., & Hillmer-Vogel, U. (1997). Exercise avoidance and impaired endurance capacity in patients with panic disorder. *Neuropsychobiology*, *36*(4), 182-187.

Brown, R. A., Kahler, C. W., Zvolensky, M. J., Lejuez, C. W., & Ramsey, S. E. (2001). Anxiety sensitivity: Relationship to negative affect smoking and smoking cessation in smokers with past major depressive disorder. *Addictive Behaviors, 26*, 887-899.

Brown, R. A., Lejuez, C. W., Kahler, C. W., & Strong, D. R. (2002). Distress tolerance and duration of past smoking cessation attempts. *Journal of Abnormal Psychology, 111*, 180-185.

Brown, R. A., Lejuez, C. W., Kahler, C. W., Strong, D. R., & Zvolensky, M. J. (2005). Distress tolerance and early smoking lapse. *Clinical Psychology Review, 25*, 713-733.

Brown, R. A., Lejuez, C. W., Strong, D. R., Kahler, C. W., Zvolensky, M. J., Carpenter, L. L., ... & Price, L. H. (2009). A prospective examination of distress tolerance and early smoking lapse in adult self-quitters. *Nicotine and Tobacco Research, 11*, 493-502.

Brown, R. A., Palm, K. M., Strong, D. R., Lejuez, C. J., Kahler, C. W., Zvolensky, M. J., . . . Gifford, E. V. (2008). Distress tolerance treatment for early-lapse smokers: Rationale, program description, and preliminary findings. *Behavior Modification, 32,* 302-332.

Brown, R. A., Reed, K. M. P., Bloom, E. L., Minami, H., Strong, D. R., Lejuez, C. W., … Hayes, S. C. (2013). Development and preliminary randomized controlled trial of a

distress tolerance treatment for smokers with a history of early lapse. *Nicotine and Tobacco Research*, *15*.

Bryant, J., Bonevski, B., Paul, C., McElduff, P., & Attia, J. (2011). A systematic review and meta-analysis of the effectiveness of behavioural smoking cessation interventions in selected disadvantaged groups. *Addiction, 106*, 1568-1585.

Buckner, J. D., Keough, M. E., & Schmidt, N. B. (2007). Problematic alcohol and cannabis use among young adults: The roles of depression and discomfort and distress tolerance. *Addictive Behaviors*, *32*, 1957–1963.

Bujarski, S. J., Norberg, M. M., & Copeland, J. (2012). The association between distress tolerance and cannabis use-related problems: The mediating and moderating roles of coping motives and gender. *Addictive Behaviors*, *37*(10), 1181–1184.

Cappelleri, J. C., Bushmakin, A. G., Baker, C. L., Merikle, E., Olufade, A. O., & Gilbert, D. G. (2005). Revealing the multidimensional framework of the Minnesota nicotine withdrawal scale. *Current Medical Research and Opinion, 21*, 749-760.

Carei, T. R., Fyfe-Johnson, A. L., Breuner, C. C., & Brown, M. A. (2010). Randomized controlled clinical trial of yoga in the treatment of eating disorders. *Journal of Adolescent Health*, *46*(4), 346–351.

Center for Disease Control. (1999). Centers for disease control and prevent, final data for 1999. *National Vital Statistics Reports, 49*, 6-95.

Center for Disease Control. (2008). Smoking-attributable mortality, years of potential life lost, and productivity losses: United States, 2000-2004. *Morbidity and Mortality Weekly Report, 57,* 1226-1228.

Centers for Disease Control and Prevention (2012). Current cigarette smoking among adults-United States, 2011. *Morbidity and Mortality Weekly Report*, *61*, 889-894.

Chaouloff, F., Berton, O., & Mormède, P. (1999). Serotonin and stress. *Neuropsychopharmacology*, *21*, 28S-32S.

Chapman S., & MacKenzie, R. (2010). The global research neglect of unassisted smoking cessation: Causes and consequences. *PLoS Medicine, 7,* 1-6.

Cohen, L. M., al'Absi, M., & Collins, F. L. (2004). Salivary cortisol concentrations are associated with acute nicotine withdrawal. *Addictive Behaviors, 29*, 1673-1678.

Cooper, M. L., Frone, M. R., Russell, M., & Mudar, P. (1995). Drinking to regulate positive and negative emotions: A motivational model of alcohol use. *Journal of Personality and Social Psychology, 69*, 990–1005.

Copeland, A. L., Martin, P. D., Geiselman, P. J., Rash, C. J., & Kendzor, D. E. (2006). Smoking cessation for weight-concerned women: Group vs. individually tailored, dietary, and weight-control follow-up sessions. *Addictive Behaviors, 31,* 115-127.

Corey, S., Epel, E., Schembri, M., Pawlowsky, S., Cole, R., Araneta, M. R., ... & Kanaya, A. (2014). Effect of restorative yoga vs. stretching on salivary cortisol and psychosocial outcomes in individuals with the metabolic syndrome: The PRYSMS randomized controlled trial. *The Journal of Alternative and Complementary Medicine*, *20*, A22-A22.

Curtis, K. J. B., Osadchuk, A., & Katz, J. (2011). An eight-week yoga intervention is associated with improvements in pain, psychological functioning, and mindfulness and changes in cortisol levels in women with fibromyalgia. *Journal of Pain Research, 4,* 189-201.

Danaei, G., Ding, E. L., Mozaffarian, D., Taylor, B., Rehm, J., Murray, C. J. L., & Ezzati, M. (2009). The preventable causes of death in the United States: Comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Medicine, 6,* 1-23.

Daughters, S. B., Lejuez, C. W., Bornovalova, M. A., Kahler, C. W., Strong, D. R., & Brown, R. A. (2005). Distress tolerance as a predictor of early treatment dropout in a residential substance abuse treatment facility. *Journal of Abnormal Psychology*, *114*, 729.

DeBoer, L. B., Powers, M. B., Utschig, A. C., Otto, M., & Smits, J. A. J. (2012). Exploring exercise as an avenue for the treatment of anxiety disorders. *Expert Review of Neurotherapeutics, 12*, 1011-1022.

DeBoer, L. B., Tart, C. D., Presnell, K. E., Powers, M. B., Baldwin, A. S., & Smits, J. A. J. (2012). Physical activity as a moderator of the association between anxiety sensitivity and binge eating. *Eating Behaviors*, *13*(3), 194–201.

Degenhardt, L., & Hall, W. (2012). Extent of illicit drug use and dependence, and their contribution to the global burden of disease. *The Lancet*, *379*(9810), 55-70.

Dey, S., Singh, R. H. & Dey, P. K. (1992). Exercise training: Significance of regional alterations in serotonin metabolism of rat brain in relation to antidepressant effect of exercise. *Physiology and Behavior*, *52*, 1095-1099.

de Manincor, M., Bensoussan, A., Smith, C. A., Barr, K., Schweickle, M., Donoghoe, L. L., ... Fahey, P. (2016). Individualized yoga for reducing depression and anxiety, and improving well-being: A randomized controlled trial. *Depression and Anxiety*, *33*(9), 816-828

Dimeff, L. A., & Linehan, M. M. (2008). Dialectical behavior therapy for substance abusers. *Addiction Science and Clinical Practice*, *4*(2), 39–47.

Dimidjian, S., Hollon, S. D., Dobson, K. S., Schmaling, K. B., Kohlenberg, R. J., Addis, M. E., ... & Jacobson, N. S. (2006). Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. *Journal of Consulting and Clinical Psychology*, *74*, 658.

Dishman, R. K., Dunn, A. L., Youngstedt, S. D., Davis, J. M., Burgess, M. L., Wilson, S. P., & Wilso, M. A. (1996). Increased open field locomotion and decreased striatal $GABA_A$ binding after activity wheel running. *Physiology and Behavior, 60*(3), 699-705.

Dozois, D. J., Seeds, P. M., & Collins, K. A. (2009). Transdiagnostic approaches to the prevention of depression and anxiety. *Journal of Cognitive Psychotherapy*, *23*(1), 44-59.

Dugas, M. J., Buhr, K., & Ladouceur, R. (2004). The Role of Intolerance of Uncertainty in Etiology and Maintenance. In R. G. Heimberg, C. L. Turk, & D. S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice* (pp. 143–163). New York, NY, US: Guilford Press.

Dunn, A. L., Reigle, T. G., Youngstedt, S. D., Dishman, R. K., & Armstrong, R. B. (1996). Brain norepinephrine and metabolites after treadmill training and wheel running in rats. *Medicine and Science in Sports and Exercise,* 28, 204-209.

Dunn, A. L., Trivedi, M. H., Kampert, J. B., Clark, C. G., & Chambliss, H. O. (2005). Exercise treatment for depression: Efficacy and dose response. *American Journal of Preventive Medicine*, *28*(1), 1-8.

Dunn, A. L., Trivedi, M. H., Kampert, J. B., Clark, C. G., & Chambliss, H. O. (2005). Exercise treatment for depression: Efficacy and dose response. *American Journal of Preventive Medicine, 28*(1), 1-8.

Edwards, S., Clow, A., Evans, P., & Hucklebridge, F. (2001). Exploration of the awakening cortisol response in relation to diurnal cortisol secretory activity. *Life Sciences*, *68*, 2093-2103.

Ekkekakis, P., & Lind, E. (2006). Exercise does not feel the same when you are overweight: the impact of self-selected and imposed intensity on affect and exertion. *International Journal of Obesity*, *30*, 652.

Elibero, A., Janse Van Rensburg, K., & Drobes, D. (2011). Acute effects of aerobic exercise and hatha yoga on craving to smoke. *Nicotine and Tobacco Research, 13,* 1140-8.

Elliot, C. A., Kennedy, C., Morgan, G., Anderson, S. K., & Morris, D. (2012). Undergraduate physical activity and depressive symptoms: A national study. *American Journal of Health Behavior, 36*(2), 230-241.

Erickson, K. I., Voss, M. W., Prakash, R. S., Basak, C., Szabo, A., Chaddock, L., ... & Kramer, A. F. (2011). Exercise training increases size of hippocampus and improves memory. *Proceedings of the National Academy of Sciences, 108*(7), 3017-3022.

Fekedulegn, D. B., Andrew, M. E., Burchfiel, C. M., Violanti, J. M., Hartley, T. A., Charles, L. E., & Miller, D. B. (2007). Area under the curve and other summary indicators of repeated waking cortisol measurements. *Psychosomatic Medicine, 69*, 651-659.

Fiore, M. C., Novotny, T. E., Pierce, J. P., (1990). Methods used to quit smoking in the United States: Do cessation programs help? *The Journal of the American Medical Association, 263,* 2760-2765.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. W. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition (SCID-I/NP).* New York, NY: Biometrics Research, New York State Psychiatric Institute.

Frederick, S. L., Reus, V. I., Ginsberg, D., Hall, S. M., Munoz, R. F., & Ellman, G. (1998). Cortisol and response to dexamethasone as predictors of withdrawal distress and abstinence success in smokers. *Biological Psychiatry, 43,* 525–530.

Friedman, J., Ravnikar, V. A., & Barbieri, R. L. (1987). Serum steroid hormone profiles in postmenopausal smokers and nonsmokers. *Fertility and Sterility, 47,* 398.

Fritz, M. S., & MacKinnon, D. P. (2007). Required sample size to detect the mediated effect. *Psychological Science*, *18*, 233-239.

Gard, T., Brach, N., Hölzel, B. K., Noggle, J. J., Conboy, L. A., & Lazar, S. W. (2012). Effects of a yoga-based intervention for young adults on quality of life and perceived stress: The potential mediating roles of mindfulness and self-compassion. *The Journal of Positive Psychology*, *7*(3), 165–175.

Gardenswartz, C. A., & Craske, M. G. (2001). Prevention of panic disorder. *Behavior Therapy, 32*(4), 725-737.

Garland, E. L., Gaylord, S. A., Boettiger, C. A., & Howard, M. O. (2010). Mindfulness training modifies cognitive, affective, and physiological mechanisms implicated in alcohol

dependence: Results of a randomized controlled pilot trial. *Journal of Psychoactive Drugs*, *42*(2), 177–192.

Gavin, J., McBrearty, M., & Sēguin, D. (2006). The psychology of exercise. *IDEA Health & Fitness Source, 3*(2). Retrieved from http://www.ideafit.com/fitness-library/psychology-exercise-1.

Gearhardt, A. N., Grilo, C. M., DiLeone, R. J., Brownell, K. D., & Potenza, M. N. (2011). Can food be addictive? Public health and policy implications. *Addiction*, *106*(7), 1208-1212.

Geraghty, A. W. A., Torres, L. D., Leykin, Y., Perez-Stable, E. J., & Munoz, R. F. (2012). Understanding attrition from international internet health interventions: A step towards global eHealth. *Health Promotion International, 28*(3), 442-452.

Goeders, N. E. (2003). The impact of stress on addiction. *European Neuropsychopharmacology, 13*, 435-441.

Goeders, N. E. (2003). The impact of stress on addiction. *European Neuropsychopharmacology, 13*(6), 435-441.

Granath, J., Ingvarsson, S., von Thiele, U., & Lundberg, U. (2006). Stress management: A randomized study of cognitive behavioural therapy and yoga. *Cognitive Behaviour Therapy*, *35*(1), 3–10.

Hamer, M., Taylor, A., & Steptoe, A. (2006). The effect of acute aerobic exercise on stress related blood pressure responses: A systematic review and meta-analysis. *Biological Psychology, 71*, 183-190.

Hamer, R., & Simpson, P. (2009). Last observation carried forward versus mixed models in the analysis of psychiatric clinical trials. *American Journal of Psychiatry, 166*(6), 639-641.

Harms, C. A. (2006). Does gender affect pulmonary function and exercise capacity? *Respiratory Physiology and Neurobiology, 151*(2), 124-131.

Harms, C. A., Wetter, T. J., McClaran, S. R., Pegelow, D. F., Nickele, G. A., Nelson, W. B., ... & Dempsey, J. A. (1998). Effects of respiratory muscle work on cardiac output and its distribution during maximal exercise. *Journal of Applied Physiology, 85*(2), 609-618.

Heatherton, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström test for nicotine dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction*, *86*, 1119-1127.

Hedeker, D., & Gibbons, R. D. (2006). *Longitudinal Data Analysis*. Hoboken, NJ: John Wiley & Sons, Inc.

Hewitt, J. (1990). *Complete Yoga Book* (Reissue edition). New York, NY: Schocken.

Hofmann, S. G., Andreoli, G., Carpenter, J. K., & Curtiss, J. (2016). Effect of hatha yoga on anxiety: A meta-analysis. *Journal of Evidence-Based Medicine*, *9*, 116-124.

Hogle, J. M., & Curtin, J. J. (2006). Sex differences in negative affective response during nicotine withdrawal. *Psychophysiology*, *43*, 344-356.

Holaway, R. M., Heimberg, R. G., & Coles, M. E. (2006). A comparison of intolerance of uncertainty in analogue obsessive-compulsive disorder and generalized anxiety disorder. *Journal of Anxiety Disorders*, *20*(2), 158–174.

Hopkins, L. B., Medina, J. L., Baird, S. O., Rosenfield, D., Powers, M. B., & Smits, J. A. J. (2016). Heated hatha yoga to target cortisol reactivity to stress and affective eating in women at risk for obesity-related illnesses: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 84*, 558-564.

Huang, F. J., Chien, D. K., & Chung, U. L. (2013). Effects of hatha yoga on stress in middle-aged women: *Journal of Nursing Research*, *21*(1), 59–66.

Hughes, J. R., & Brandon, T. H. (2003). A softer view of hardening. *Nicotine and Tobacco Research, 5*(6), 961.

Hughes, J. R., & Hatsukami, D. (1986). Signs and symptoms of tobacco withdrawal. *Archives of General Psychiatry*, *43*, 289.

Hughes, J. R., Higgins, S. T., & Bickel, W. K. (1994). Nicotine withdrawal versus other drug withdrawal syndromes: Similarities and dissimilarities. *Addiction*, *89*, 1461-1470.

Hughes, J. R., Higgins, S. T., & Hatsukami, D. (1990). Effects of abstinence from tobacco: A critical review. *Research Advances in Alcohol and Drug Problems, 10*, 317-398.

Hunt-Shanks, T., Blanchard, C., & Reid, R. D. (2009). Gender differences in cardiac patients: A longitudinal investigation of exercise, autonomic anxiety, negative affect, and depression. *Psychology, Health, and Medicine, 14*(3), 375-385.

Iyengar, B. K. S., & Menuhin, Y. (1995). *Light on Yoga: Yoga Dipika* (Revised edition). New York, NY: Schocken.

Jarvis, M. J., Tunstall-Pedoe, H., Feyerabend, C., Vesey, C., & Saloojee, Y. (1987). Comparison of tests used to distinguish smokers from nonsmokers. *American Journal of Public Health, 77*, 1435-1438.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*, 593-602.

Kirschbaum, C., Wüst, S., & Hellhammer, D. (1992). Consistent sex differences in cortisol responses to psychological stress. *Psychosomatic Medicine, 54*(6), 648-657.

Kirkwood, G., Rampes, H., Tuffrey, V., Richardson, J., & Pilkington, K. (2005). Yoga for anxiety: A systematic review of the research evidence. *British Journal of Sports Medicine*, *39*(12), 884–891.

Kotz, D., Brown, J., & West, R. (2014). 'Real-world' effectiveness of smoking cessation treatments: a population study. *Addiction, 109*(3), 491-499.

Kraemer, H. C., Stice, E., Kazdin, A., Offord, D., & Kupfer, D. (2001). How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *American Journal of Psychiatry*, *158*(6), 848–856.

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry*, *59*(10), 877–883.

Kudielka, B. M., Gierens, A., Hellhammer, D. H., Wüst, S., & Schlotz, W. (2012). Salivary cortisol in ambulatory assessment—some dos, some don'ts, and some open questions. *Psychosomatic Medicine, 74*(4), 418-431.

Leeman, R. F., Quiles, Z. N., Molinelli, L. A., Terwal, D. M., Nordstrom, B. L., Garvey, A. J., & Kinnunen, T. (2006). Attritition in a multi-component smoking cessation study for females. *Tobacco Induced Diseases, 3*, 59-71.

Leventhal, A. M., & Zvolensky, M. J. (2015). Anxiety, depression, and cigarette smoking: A transdiagnostic vulnerability framework to understanding emotion–smoking comorbidity. *Psychological Bulletin, 141*, 176.

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A. (1993). Development of the perceived stress questionnaire: A new tool for psychosomatic research. *Journal of Psychosomatic Research*, *37*(1), 19–32.

Leyro, T. M., Bernstein, A., Vujanovic, A. A., McLeish, A. C., & Zvolensky, M. J. (2011). Distress tolerance scale: A confirmatory factor analysis among daily cigarette smokers. *Journal of Psychopathology and Behavioral Assessment*, *33*(1), 47–57.

Leyro, T. M., Zvolensky, M. J., & Bernstein, A. (2010). Distress tolerance and psychopathological symptoms and disorders: A review of the empirical literature among adults. *Psychological Bulletin*, *136*(4), 576–600.

Linehan, M. (1993). *Cognitive-behavioral Treatment of Borderline Personality Disorder*. New York, NY: The Guilford Press.

Linehan, M. (1987). Dialectical behavioral therapy: A cognitive behavioral approach to parasuicide. *Journal of Personality Disorders*, *1*(4), 328–333.

Linke, S. E., & Ussher, M. (2015). Exercise-based treatments for substance use disorders: evidence, theory, and practicality. *The American journal of drug and alcohol abuse*, *41*, 7-15.

MacKinnon, D. P. (2008). Multilevel Mediation Models. In *Introduction to Statistical Mediation Analysis* (pp. 237–274). New York, NY: Taylor & Francis Group, LLC.

MacKinnon, D. P., Fairchild, A. J., & Fritz, M. S. (2007). Mediation analysis. *Annual Review of Psychology*, *58*, 593.

MacKinnon, D. P., Fritz, M. S., Williams, J., & Lockwood, C. M. (2007). Distribution of the product confidence limits for the indirect effect: Program PRODCLIN. *Behavior Research Methods, 39*, 384-389.

MacKinnon, D. P., Lockwood, C. M., Hoffman, J. M., West, S. G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods*, *7*(1), 83–104.

MacPherson, L., Stipelman, B. A., Duplinsky, M., Brown, R. A., & Lejuez, C. W. (2008). Distress tolerance and pre-smoking treatment attrition: Examination of moderating relationships. *Addictive Behaviors, 33,* 1385-1393.

Maller, R., & Reiss, S. (1992). Anxiety sensitivity in 1984 and panic attacks in 1987. *Journal of Anxiety Disorders*, *6*, 241 – 247.

Mansell, W., Harvey, A., Watkins, E., & Shafran, R. (2009). Conceptual foundations of the transdiagnostic approach to CBT. *Journal of Cognitive Psychotherapy*, *23*(1), 6-19.

Marlatt, G. A., & Chawla, N. (2007). Meditation and alcohol use. *Southern Medical Journal, 100*, 451-454.

Mastorakos, G., Pavlatou, M., Diamanti-Kandarakis, E., & Chrousos, G. P. (2005). Exercise and the stress system. *Hormones (Athens)*, *4*, 73-89.

McCarthy, D. O. (2012). Biological Measurement in Intervention Research. In: B. M. Melnyk & D. Morrison-Beedy (Eds.), *Designing, Conducting, Analyzing, and Funding Intervention Research* (135-148). New York, NY: Springer Publishing Company.

McHugh, R. K., & Otto, M. W. (2012). Refining the measurement of distress intolerance. *Behavior Therapy*, *43*(3), 641–651.

McHugh, R. K., Reynolds, E. K., Leyro, T. M., & Otto, M. W. (2013). An examination of the association of distress intolerance and emotion regulation with avoidance. *Cognitive Therapy and Research*, *37*(2), 363–367.

McIver, S., O'Halloran, P., & McGartland, M. (2009). Yoga as a treatment for binge eating disorder: A preliminary study. *Complementary Therapies in Medicine*, *17*(4), 196–202.

McLeish, A. C., Zvolensky, M. J., & Bucossi, M. M. (2007). Interaction between smoking rate and anxiety sensitivity: Relation to anticipatory anxiety and panic-relevant avoidance among daily smokers. *Journal of Anxiety Disorders*, *21*, 849-859.

McNally, R. J. (2002). Anxiety sensitivity and panic disorder. *Biological Psychiatry, 52*(10), 938-946.

McNally, R. J., & Lorenz, M. (1987). Anxiety sensitivity in agoraphobics. *Journal of Behavior Therapy and Experimental Psychiatry, 18*(1), 3-11.

Meeker, W. Q., Cornwell, L. W., Aroian, L. A. (1980). Selected Tables in Mathematical Statistics Vol VII. Providence, RI: American Mathematical Society.

Meeusen, R., & De Meirleir, K. (1995). Exercise and brain neurotransmission. *Sports Medicine, 20*(3), 160-188.

Meyer, J. S., & Novak, M. A. (2012). Minireview: Hair cortisol: A novel biomarker of hypothalamic-pituitary-adrenocortical activity. *Endocrinology,153*(9), 4120-4127.

Michalsen, A., Grossman, P., Acil, A., Langhorst, J., Ludtke, R., Esch, T.,…Dobos, G. J. (2005). Rapid stress reduction and anxiolysis among distressed women as a consequence of a three-month intensive yoga program. *Medical Science Monitor, 11, 555–561.*

Morissette, S. B., Tull, M. T., Gulliver, S. B., Kamholz, B. W., & Zimering, R. T. (2007). Anxiety, anxiety disorders, tobacco use, and nicotine: a critical review of interrelationships. *Psychological bulletin*, *133*, 245.

Murray, H. W., McHugh, R. K., Rowley, T. C., Sirota, A. D., & Otto, M. W. (2010). Development and validation of the smoking cue appeal survey. *Substance Use and Misuse*, *45*, 2152-2161.

Neacsiu, A. D., Rizvi, S. L., & Linehan, M. M. (2010). Dialectical behavior therapy skills use as a mediator and outcome of treatment for borderline personality disorder. *Behaviour Research and Therapy*, *48*(9), 832–839.

Neeper, S. A., Gómez-Pinilla, F., Choi, J., & Cotman, C. W. (1996). Physical activity increases mRNA for brain-derived neurotrophic factor and nerve growth factor in rat brain. *Brain Research, 726*(1-2), 49-56.

Nelson, C. R. (2013). *The effect of exercise on anxiety sensitivity in sedentary adults with an alcohol use disorder* (Doctoral dissertation, Saint Louis University).

NIDA. (2012, December 18). National Institute on Drug Abuse to Announce Results of 2012 Monitoring the Future Survey. Retrieved from https://www.drugabuse.gov/news-events/news-releases/2012/12/national-institute-drug-abuse-to-announce-results-2012-monitoring-future-survey on 2017, July 19.

Nides, M., Rakos, R.F., Gonzales, D., Murray, R.P., Tashkin, D.P, Bjornson-Benson, W.M., … Connett, J.E. (1995). Predictors of initial smoking cessation and relapse through the first 2 years of the lung health study. *Journal of Consulting and Clinical Psychology, 63*, 60-69.

O'Connor, P. J., Raglin, J. S., & Martinsen, E. W. (2000). Physical activity, anxiety, and anxiety disorders. *International Journal of Sport Psychology, 31*(2), 136-155.

Olatunji, B. O., & Wolitzky-Taylor, K. B. (2009). Anxiety sensitivity and the anxiety disorders: A meta-analytic review and synthesis. *Psychological Bulletin, 135*(6), 974.

Ouwens, M. A., van Strien, T., & van der Staak, C. P. F. (2003). Tendency toward overeating and restraint as predictors of food consumption. *Appetite*, *40*(3), 291–298.

Pagliari, R., & Peyrin, L. (1995). Norepinephrine release in the rat frontal cortex under treadmill exercise: A study with microdialysis. *Journal of Applied Physiology, 78*(6), 2121-2130.

Palmer J., Vacc N., & Epstein J. (1988). Adult inpatient alcoholics: Physical exercise as a treatment intervention. *Journal of Studies on Alcohol and Drugs*, *49*, 418-421.

Pascoe, M. C., & Bauer, I. E. (2015). A systematic review of randomised control trials on the effects of yoga on stress measures and mood. *Journal of Psychiatric Research, 68*, 270-282.

Perkins, K. A. (2014). Improving efficiency of initial tests for efficacy in smoking cessation drug discovery. *Expert Opinion on Drug Discovery*, *9*, 1259–1264

Peterson R. A., & Reiss, S (1992). *Anxiety Sensitivity Index Manual 2*. Worthington, OH: International Diagnostic Systems.

Peterson, R. A., & Plehn, K. (1999). Measuring anxiety sensitivity. In S. Taylor (Ed.), *Anxiety sensitivity: Theory, research, and treatment of the fear of anxiety* (pp. 61-81). Hillsdale, NJ: Erlbaum.

Petruzzello, S. J., Landers, D. M., Hatfield, B. D., Kubitz, K. A., & Salazar, W. (1991). A meta-analysis on the anxiety-reducing effects of acute and chronic exercise. *Sports Medicine, 11*(3), 143-182.

Piasecki, T. M., Jorenby, D. E., Smith, S. S., Fiore, M. C., & Baker, T. B. (2003). Smoking withdrawal dynamics: II. Improved tests of withdrawal-relapse relations. *Journal of Abnormal Psychology*, *112*, 14.

Piper, M. E, Piasecki, T. M., Federman, E. B., Bolt, D. M., Smith, S. S., Fiore, M. C., & Baker, T. B. (2004). A multiple motives approach to tobacco dependence: The Wisconsin inventory of smoking dependence motives. *Journal of Consulting and Clinical Psychology, 72,* 139-154.

Pomerleau, C. S., Garcia, A. W., & Powerleau, O. G. C. (1992). The effects of menstrual phases and nicotine abstinence on nicotine intake and on the biochemical and subjective measures in women smokers: A preliminary report. *Psychoneroendocrinolgy, 17*, 627-638.

Pomerleau, C. S., Majchrezak, M. I., & Pomerleau, O. F. (1989). Nicotine dependence and the Fagerström Tolerance Questionnaire: a brief review. *Journal of Substance Abuse, 1*, 471-477.

Pomerleau, O. F., & Pomerleau, C. S. (1990). Cortisol response to a psychological stressor and/or nicotine. *Pharmacology Biochemistry and Behavior*, *36*, 211-213.

Potenza, M. N. (2014). Non-substance addictive behaviors in the context of DSM-5. *Addictive Behaviors*, *39*(1).

Prakash, R., Dubey, I., Abhishek, P., Gupta, S. K., Rastogi, P., & Siddiqui, S. V. (2010). Long-term vihangam yoga meditation and scores on tests of attention. *Perceptual and Motor Skills*, *110*(3C), 1139–1148.

Prochaska, J. J., Spring, B., & Nigg, C. R. (2008). Multiple health behavior change research: An introduction and overview. *Preventive Medicine, 46*(3), 181-188.

Raghavendra, R. M., Vadiraja, H. S., Nagarathna, R., Nagendra, H. R., Rekha, M., Vanitha, N., ... Kumar, V. (2009). Effects of a yoga program on cortisol rhythm and mood states in early breast cancer patients undergoing adjuvant radiotherapy: A randomized controlled trial. *Integrative Cancer Therapies, 8*, 37-46.

Raudenbush, S., Bryk, A., Cheong, Y. F., & Congdon, R. (2004). HLM 6: Hierarchical and nonlinear modeling [Computer software]. *Lincolnwood, IL: Scientific Software International*.

Raudenbush, S. W., & Xiao-Feng, L. (2001). Effects of study duration, frequency of observation, and sample size on power in studies of group differences in polynomial change. *Psychological Methods, 6*(4), 387.

Reiss, S., & McNally, R. (1985). Expectancy model of fear. In S. Reiss & R. R. Bootzin (Eds.), *Theoretical Issues in Behavior Therapy* (pp. 107-121). San Diego, CA: Academic Press.

Reiss, S., Peterson, R. A., Gursky, D. M., & McNally, R. J. (1986). Anxiety sensitivity, anxiety frequency, and the prediction of fearfulness. *Behaviour Research and Therapy, 24*(1), 1-8

Reiss, S., Peterson, R., Gursky, D., & McNally, R. (1986). Anxiety sensitivity, anxiety frequency, and the prediction of fearfulness. *Behaviour Research and Therapy, 24,* 1-8.

Riekert, K. A., Ockene, J. K., & Pbert, L. (Eds.). (2013). *The handbook of health behavior*

change. Springer Publishing Company.

Rigotti, N. (2001). Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation. *Annals of Internal Medicine, 135,* 423-433.

Riley, K. E., & Park, C. L. (2015). How does yoga reduce stress? A systematic review of mechanisms of change and guide to future inquiry. *Health Psychology Review*, *9*, 379-396.

Ross, A., & Thomas, S. (2010). The health benefits of yoga and exercise: a review of comparison studies. *The Journal of Alternative and Complementary Medicine*, *16*, 3-12.

Sauer-Zavala, S., Boswell, J. F., Gallagher, M. W., Bentley, K. H., Ametaj, A., & Barlow, D. H. (2012). The role of negative affectivity and negative reactivity to emotions in predicting outcomes in the unified protocol for the transdiagnostic treatment of emotional disorders. *Behaviour Research and Therapy*, *50*, 551-557.

Saunders, J. B., Aasland, O. G., Babor, T. F., Fuente, J. R., & Grant, M. (1993). Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption. *Addiction*, 88, 791-804.

Sauvé, B., Koren, G., Walsh, G., Tokmakejian, S., & Van Uum, S. H. (2007). Measurement of cortisol in human hair as a biomarker of systemic exposure. *Clinical and Investigative Medicine, 30*(5), E183-E191.

Scerbo, F., Faulkner, G., Taylor, A., & Thomas, S. (2010). Effects of exercise on cravings to smoke: The role of exercise intensity and cortisol. *Journal of Sports Sciences*, *28*(1), 11-19.

Schell, F. J., Allolio, B., & Schoneke, O. W. (1993). Physiological and psychological effects of Hatha-Yoga exercise in healthy women. *International Journal of Psychosomatics: Official Publication of the International Psychosomatics Institute*, *41*, 46–52.

Schmidt, N. B., Richey, J. A., & Fitzpatrick, K. K. (2006). Discomfort intolerance: Development of a construct and measure relevant to panic disorder. *Journal of Anxiety Disorders*, *20*(3), 263–280.

Shapiro, D., Cook, I. A., Davydov, D. M., Ottaviani, C., Leuchter, A. F., & Abrams, M. (2007). Yoga as a complementary treatment of depression: Effects of traits and moods on treatment outcome. *Evidence-Based Complementary and Alternative Medicine*, *4*(4), 493–502.

Shiffman, S., & Waters, A. J. (2004). Negative affect and smoking lapses: A prospective analysis. *Journal of Consulting and Clinical Psychology*, *72*, 192.

Shiffman, S., West, R. J., & Gilbert, D. G. (2004). Recommendation for the assessment of tobacco craving and withdrawal in smoking cessation trials. *Nicotine and Tobacco Research, 6*, 599-614.

Shrout, P. E., & Bolger, N. (2002). Mediation in experimental and nonexperimental studies: New procedures and recommendations. *Psychological Methods*, *7*(4), 422–445.

Simons, J. S., & Gaher, R. M. (2005). The Distress Tolerance Scale: Development and validation of a self-report measure. *Motivation and Emotion*, *29*(2), 83–102.

Singer, J. D., & Willett, J. B. (2003). *Applied longitudinal data analysis: Modeling change and event occurrence*. New York, NY: Oxford University Press, Inc.

Singh, N. A., Stavrinos, T. M., Scarbek, Y., Galambos, G., Liber, C., & Singh, M. A. F. (2005). A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 60*(6), 768-776.

Smith, C., Hancock, H., Blake-Mortimer, J., & Eckert, K. (2007). A randomised comparative trial of yoga and relaxation to reduce stress and anxiety. *Complementary Therapies in Medicine*, *15*(2), 77–83.

Smits, J. A. J., Berry, A. C., Tart, C. D., & Powers, M. B. (2008). The efficacy of cognitive-behavioral interventions for reducing anxiety sensitivity: A meta-analytic review. *Behaviour Research and Therapy, 46*, 1047-1054.

Smits, J. A., Berry, A. C., Rosenfield, D., Powers, M. B., Behar, E., & Otto, M. W. (2008). Reducing anxiety sensitivity with exercise. *Depression and Anxiety, 25*(8), 689-699.

Smits, J. A. J., Julian, K., Rosenfield, D., & Powers, M. B. (2012). Threat reappraisal as a mediator of symptom change in cognitive-behavioral treatment of anxiety disorders: A systematic review. *Journal of Consulting and Clinical Psychology, 80,* 624-635.

Smits, J. A., Powers, M. B., Berry, A. C., & Otto, M. W. (2007). Translating empirically supported strategies into accessible interventions: The potential utility of exercise for the treatment of panic disorder. *Cognitive and Behavioral Practice, 14*(4), 364-374.

Smits, J. A., Powers, M. B., Cho, Y., & Telch, M. J. (2004). Mechanism of change in cognitive-behavioral treatment of panic disorder: Evidence for the fear of fear mediational hypothesis. *Journal of Consulting and Clinical Psychology, 72*(4), 646-651.

Smits, J. A. J., Zvolensky, M. J., Rosenfield, D., Marcus, B. H., Church, T. S., Frierson, G., Powers, M. B., Otto, M. W., Davis, M. L., DeBoer, L. B., & Briceno, N. F. (2012). The efficacy of vigorous-intensity exercise as an aid to smoking cessation in adults with elevated anxiety sensitivity: Study protocol for a randomized controlled trial. *Trials, 13*, 207.

Smits, J. A., Zvolensky, M. J., Davis, M. L., Rosenfield, D., Marcus, B. H., Church, T. S., ... & Brown, R. A. (2016). The efficacy of vigorous-intensity exercise as an aid to smoking cessation in adults with high anxiety sensitivity: A randomized controlled trial. *Psychosomatic Medicine, 78*, 354-364.

Snell Jr., W. E. (1999). The multidimensional emotional awareness questionnaire. *Unpublished Data*.

Spina, R. J., Ogawa, T., Kohrt, W. M., Martin, W., Holloszy, J. O., & Ehsani, A. A. (1993). Differences in cardiovascular adaptations to endurance exercise training between older men and women. *Journal of Applied Physiology, 75*(2), 849-855.

Stathopoulou, G., Powers, M. B., Berry, A. C., Smits, J. A., & Otto, M. W. (2006). Exercise interventions for mental health: A quantitative and qualitative review. *Clinical Psychology: Science and Practice, 13*(2), 179-193.

Stead, L. F., & Lancaster, T. (2012). Combined pharmacotherapy and behavioural interventions for smoking cessation. *Cochrane Database Systematic Review, 10*. Retrieved from http://onlinelibrary.wiley.com/store/10.1002/14651858.CD008286.pub2/asset/CD008286.pdf?v=1&t=j5ah9ie8&s=d326a3db132f9c9b032bcf3a7081a6dbd4a67cf0.

Stead, L. F., Carroll, A. J., & Lancaster, T. (2000). Group behaviour therapy programmes for smoking cessation. *The Cochrane Library, 2*. Retrieved from http://www.ncsct.co.uk/usr/pub/group-behaviour-therapy-programmes.pdf

Stephens, M. A. C., & Wand, G. (2012). Stress and the HPA axis: Role of glucocorticoids in alcohol dependence. *Alcohol Research: Current Reviews, 34*, 468.

Stephens, M. A. C., & Wand, G. (2012). Stress and the HPA axis: Role of glucocorticoids in alcohol dependence. *Alcohol Research: Current Reviews, 34*(4), 468.

Steptoe, A., & Ussher, M. (2006). Smoking, cortisol and nicotine. *International Journal of Psychophysiology*, *59*, 228-235.

Stoller, C. C., Greuel, J. H., Cimini, L. S., Fowler, M. S., & Koomar, J. A. (2012). Effects of Sensory-enhanced yoga on symptoms of combat stress in deployed military personnel. *American Journal of Occupational Therapy*, *66*(1), 59–68.

Stone, A. A., Schwartz, J. E., Smyth, J., Kirschbaum, C., Cohen, S., Hellhammer, D., & Grossman, S. (2001). Individual differences in the diurnal cycle of salivary free cortisol: A replication of flattened cycles for some individuals. *Psychoneuroendocrinology, 26*, 295-306.

Stranahan, A. M., & Mattson, M. P. (2012). Recruiting adaptive cellular stress responses for successful brain aging. *Nature Reviews. Neuroscience*, *13*, 209.

Subramaniam, M., Wang, P., Soh, P., Vaingankar, J. A., Chong, S. A., Browning, C. J., & Thomas, S. A. (2015). Prevalence and determinants of gambling disorder among older adults: A systematic review. *Addictive Behaviors*, *41*, 199-209.

Tarnopolsky, L. J., MacDougall, J. D., Atkinson, S. A., Tarnopolsky, M. A., & Sutton, J. R. (1990). Gender differences in substrate for endurance exercise. *Journal of Applied Physiology, 68*(1), 302-308.

Taylor, S. E. (1999). Anxiety sensitivity: Theory, research, and treatment of the fear of anxiety. Mahwah, NJ: Lawrence Erlbaum Associates, Inc.

Taylor, S., Koch, W. J., & McNally, R. J. (1992). How does anxiety sensitivity vary across the anxiety disorders? *Journal of Anxiety Disorders, 6*(3), 249-259.

Telch, M. J., Shermis, M. D., & Lucas, J. A. (1989). Anxiety sensitivity: Unitary personality trait or domain-specific appraisals? *Journal of Anxiety Disorders, 3*(1), 25-32.

Telch, C. F., Stewart, W., & Linehan, M. M. (2001). Dialectical behavior therapy for binge eating disorder. *Journal of Consulting and Clinical Psychology*, *69*(6), 1061–1065.

Tofighi, D., & MacKinnon, D. P. (2011). RMediation: An R package for mediation analysis confidence intervals. *Behavior Research Methods, 43*(3), 692-700.

Tolin, D. F., Abramowitz, J. S., Brigidi, B. D., & Foa, E. B. (2003). Intolerance of uncertainty in obsessive-compulsive disorder. *Journal of Anxiety Disorders*, *17*(2), 233–242.

Toll, B. A., O'malley, S. S., McKee, S. A., Salovey, P., & Krishnan-Sarin, S. (2007). Confirmatory factor analysis of the Minnesota nicotine withdrawal scale. *Psychology of Addictive Behaviors, 21*(2), 216.

Trivedi, M. H., Greer, T. L., Grannemann, B. D., Chambliss, H. O., & Jordan, A. N. (2006). Exercise as an augmentation strategy for treatment of major depression. *Journal of Psychiatric Practice, 12,* 205-211.

Truax, P. A., Addis, M. E., Koerner, K., Gollan, J. K., Gortner, E., & Prince, S. E. (1996). A component analysis of cognitive-behavioral treatment for depression. *Journal of Consulting and Clinical Psychology, 64*(2), 295-304.

Uebelacker, L. A., Epstein-Lubow, G., Gaudiano, B. A., Tremont, G., Battle, C. L., & Miller, I. W. (2010). Hatha Yoga for depression: Critical review of the evidence for efficacy, plausible mechanisms of action, and directions for future research. *Journal of Psychiatric Practice*, *16*(1), 22–33.

U.S. Census Bureau (2013). *Texas Cities Lead Nation in Population Growth, Census Bureau Reports.* Retrieved from http://www.census.gov/newsroom/releases/archives/population/cb13-94.html.

U.S. Department of Health and Human Services. (2003). Those who continue to smoke: Is achieving abstinence harder and do we need to change our interventions? *U.S. Department of Health and Human Services, National Institutes of Health, National Cancer Institute.*

U.S. Department of Health and Human Services (2004). The health consequences of smoking: A report of the surgeon general. *U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office of Smoking and Health.*

U.S. Department of Health and Human Services (2014). The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention,

National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

Ussher, M., Nunziata, P., Cropley, M., & West, R. (2001). Effect of short bout of exercise on tobacco withdrawal symptoms and desire to smoke. *Psychopharmacology, 158,* 66-72.

Ussher, M., Taylor, A., & Faulkner, G. (2008). Exercise interventions for smoking cessation. *Cochrane Database of Systematic Reviews, 4.* Retrieved from https://www.researchgate.net/profile/Michael_Ussher/publication/8056849_Exercise_interventions_in_smoking_cessation/links/00463520114761be2b000000/Exercise-interventions-in-smoking-cessation.pdf.

Ussher, M., West, R., Evans, P., Steptoe, A., McEwen, A., Clow, A., & Hucklebride, F. (2006). Reduction in cortisol after smoking cessation among users of nicotine patches. *Psychosomatic Medicine, 68,* 299-306.

Van Strien, T., Frijters, J. E. R., Bergers, G. P. A., & Defares, P. B. (1986). The Dutch Eating Behavior Questionnaire (DEBQ) for assessment of restrained, emotional, and external eating behavior. *International Journal of Eating Disorders*, *5*(2), 295–315.

Van Strien, T., Frijters, J. E. R., van Staveren, W. A., Defares, P. B., & Deurenberg, P. (1986). The predictive validity of the Dutch Restrained Eating Scale. *International Journal of Eating Disorders*, *5*(4), 747–755.

Van Strien, T., & Ouwens, M. A. (2003). Counterregulation in female obese emotional eaters: Schachter, Goldman, and Gordon's (1968) test of psychosomatic theory revisited. *Eating Behaviors*, *3*(4), 329–340.

Veale, D. M. W. C., Le Fevre, K., Pantelis, C., De Souza, V., Mann, A., & Sargeant, A. (1992). Aerobic exercise in the adjunctive treatment of depression: A randomized controlled trial. *Journal of the Royal Society of Medicine, 85*(9), 541.

Warner, K. E., Hodgson, T. A., & Carroll, C. E. (1999). Medical costs of smoking in the United States: estimates, their validity, and their implications. *Tobacco Control*, *8*, 290-300.

Watson, D., Clark, L. A., Weber, K., Assenheimer, J. S., Strauss, M. E., & McCormick, R. A. (1995). Testing a triparitite model: II. Exploring the symptom structure of anxiety and depression in student, adult, and patient samples. *Journal of Abnormal Psychology, 104,* 15-25.

Weinberger, A. H., Desai, R. A., & McKee, S. A. (2010). Nicotine withdrawal in US smokers with current mood, anxiety, alcohol use, and substance use disorders. *Drug and Alcohol Dependence, 108*, 7-12.

Weinberger, A. H., Reutenauer, E. L., Allen, T. M., Termine, A., Vessicchio, J. C., Sacco, K. A., ... George, T. P. (2007). Reliability of the Fagerström test for nicotine dependence, Minnesota Nicotine Withdrawal Scale, and Tiffany Questionnaire for Smoking Urges in smokers with and without schizophrenia. *Drug and Alcohol Dependence, 86*, 278-282.

Weitzman, E. D., Fukushima, D., Nogeire, C., Roffwarg, H., Gallagher, T. F., & Hellman, L. (1971). Twenty-four hour pattern of the episodic secretion of cortisol in normal subjects. *Journal of Clinical Endocrinology and Metabolism*, *33,* 14-22.

West, J., Otte, C., Geher, K., Johnson, J., & Mohr, D.C. (2004). Effects of hatha yoga and African dance on perceived stress, affect, and salivary cortisol. *Annals of Behavioral Medicine, 28*, 114-118.

West, R. J., Hajek, P., & Belcher, M. (1989). Severity of withdrawal symptoms as a predictor of outcome of an attempt to quit smoking. *Psychological Medicine, 19, 981–985.*

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., ... & Burstein, R. (2013). Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010. *The Lancet*, *382*(9904), 1575-1586.

Willett, J. B., Singer, J. D., & Martin, N. C. (1998). The design and analysis of longitudinal studies of development and psychopathology in context: Statistical models and methodological recommendations. *Development and Psychopathology, 10*(02), 395-426.

Wipfli, B. M., Rethorst, C. D., & Landers, D. M. (2008). The anxiolytic effects of exercise: A meta-analysis of randomized trials and dose-response analysis. *Journal of Sport and Exercise Psychology, 30*(4), 392.

Woolery, A., Myers, H., Sternleib, B. & Zeltzer, L. (2004). A yoga intervention for young adults with elevated symptoms of depression. *Alternative Therapies, 10*, 60-63.

Yau, M. Y. H., & Potenza, M. N. (2015). Gambling disorder and other behavioral addictions: recognition and treatment. *Harvard review of psychiatry*, *23*, 134.

Yoga Journal (2012). New study finds more than 20 million yogis in the US. *Yoga Journal Blogs/YogaBuzz*. Retrieved from http://blogs.yogajournal.com/yogabuzz/2012/12/new-study-find-more-than-20-million-yogis-in-u-s.html

Zhang, Z., Zyphur, M. J., & Preacher, K. J. (2009). Testing multilevel mediation using hierarchical linear models: Problems and solutions. *Organizational Research Methods*, *12*(4), 695–719.

Zschucke, E., Heinz, A., & Ströhle, A. (2012). Exercise and physical activity in the therapy of substance use disorders. *The Scientific World Journal*, *2012*.

Zvolensky, M. J., Bernstein, A., & Vujanovic, A. A. (Eds.). (2011). Distress tolerance: Theory, research, and clinical applications. New York, NY: Guilford Press.

Zvolensky, M. J., Feldner, M. T., Eifert, G. H., & Brown, R. A. (2001). Affective style among smokers: Understanding anxiety sensitivity, emotional reactivity, and distress tolerance using biological challenge. *Addictive behaviors*, *26*, 901-915.

Zvolensky, M. J., Gibson, L. E., Vujanovic, A. A., Gregor, K., Bernstein, A., Kahler, C., ... Feldner, M. T. (2008). Impact of posttraumatic stress disorder on early smoking lapse and relapse during a self-guided quit attempt among community-recruited daily smokers. *Nicotine and Tobacco Research, 10*(8), 1415-1427.

Zvolensky, M. J., Stewart, S. H., Vujanovic, A. A., Gavric, D., & Steeves, D. (2009). Anxiety sensitivity and anxiety and depressive symptoms in the prediction of early smoking lapse and relapse during smoking cessation treatment. *Nicotine and Tobacco Research, 11*, 323-331.

Zvolensky, M., Bonn-Miller, M., Bernstein, A., & Marshall, E. (2006). Anxiety sensitivity and abstinence duration to smoking. *Journal of Mental Health*, *15*, 659-670.