ABSTRACT

A Hypnosis Intervention Reduces Anxiety Among Postmenopausal Women with Hot Flashes: Results from a Randomized Controlled Trial

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Anxiety is common, yet under-treated, among women in menopause and postmenopause. This study examined the effect of a hypnotic intervention designed to reduce hot flashes, on anxiety levels of postmenopausal women. Anxiety was assessed using the State-Trait Anxiety Inventory, the Hospital Anxiety and Depression Scale-Anxiety subscale, and a visual analogue scale. Additionally, trait anxiety and hypnotizability were tested as moderators of anxiety reductions. Significant reductions in anxiety were found from baseline to endpoint and follow-up and hypnosis was superior to the control condition. Additionally, ratings of Current Anxiety decreased from pre-session to post-session at each weekly visit and the pre-session scores reduced continuously. Trait anxiety and hypnotizability were found to significantly moderate anxiety reductions. These data provide initial support for the use of hypnosis to reduce symptoms of anxiety among postmenopausal women.

A Hypnosis Intervention Reduces Anxiety Among Postmenopausal Women with Hot Flashes: Results from a Randomized Controlled Trial

by

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# CHAPTER ONE

# Introduction

## *Anxiety*

Anxiety symptoms include both somatic and cognitive or affective aspects (Gelenberg, 2000; Koksal, Power, & Sharp, 1991). Somatic, or physical, factors can include sweating, shortness of breath, increased heart rate, and muscle tension (Ree, French, MacLeod, & Locke, 2008). Affective factors involve worry, apprehension, and a lack of concentration often accompanied by intrusive thoughts. Feelings of anxiety are adaptive to a certain level. In "normal" or mild ranges, anxiety motivates individuals to adapt, seek safety, and carry out necessary tasks by providing a sense of unease when the task is not complete (Thwaites & Freeston, 2005). However, anxiety is on a continuum, and as symptom levels increase, anxiety becomes problematic (Craske et al., 2011). Worry begins to occur often and persist in the absence of a clear and present threat. Activation of the sympathetic nervous system, or the "fight or flight" response, also occurs, which causes the somatic symptoms (Brosschot, Gerin, & Thayer, 2006).

Boundaries of symptom severity along the distribution vary depending on each individual's predispositions and the amount of hindrance that stressors place on their life. The presentation of specific symptoms are often heterogenous between individuals as well. It is important to consider what symptoms are primarily occurring, whether symptoms are physical or cognitive, which symptoms are considered the most problematic to the individual, and any comorbid problems (Gelenberg, 2000; Koksal,

Power, & Sharp, 1991). These considerations illustrate that anxiety issues are often difficult to diagnose and treat.

Symptomatic anxiety is a pervasive problem within the general population. Anxiety can manifest as disorders or specific phobias, such as social anxiety disorder, post-traumatic stress disorder (PTSD), general anxiety disorder (GAD), and panic disorders (Craske et al., 2011). A*nxiety* also can refer to the general feelings of worry, restlessness, dread, and physical symptoms like increased heart rate or rapid breathing, which may or may not be appropriate to categorize as an anxiety disorder. Group classification is helpful in clinical diagnoses, treatment decisions, and in research of specific symptom types. However, the use of cutoffs at which a symptom or its level of severity is considered a disorder can be arbitrary and imprecise (Olatunji et al., 2010). For instance, the point at which worry, a key feature of anxiety, becomes dysfunctional depends on the individual's perceptions of controllability, themes, and frequency of worry (Gladstone & Parker, 2003; Olatunji et al., 2010). Symptoms of anxiety, whether somatic or cognitive, are not easily dichotomized.

Diagnostic criteria for disorders related to anxiety found in the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) contain specifications that symptoms last consistently for a certain number of months, are not attributable to comorbid medical conditions, comprise a specific minimum number of components, and severely impact functioning (American Psychiatric Association, 2013). Often troublesome symptoms do not fit all criteria and are not classified as clinically significant. This "subthreshold" or "subclinical" general anxiety has a lifetime prevalence of approximately 20% (Haller et al., 2014).

*Effects of Anxiety*

Anxiety can affect daily life in the absence of clinical psychopathology. Symptoms that do not meet the full criteria for an anxiety disorder can be persistent and cause considerable impact on daily functioning, potentially damaging quality-of-life, ability to carry out daily tasks, and relationships. Besides being draining and debilitating on its own, anxiety increases risks for comorbidities and may worsen the outcomes of existing conditions (Haller et al., 2014, Okasha, 2009). Most notably, the presence of subclinical general anxiety is a major risk factor for development of GAD, which highlights the need for early interventions (Kertz et al., 2001, Rucci et al., 2003).

The presence of subclinical anxiety is also associated with structural and functional neurological changes that are similar to alterations seen in clinically diagnosed anxiety disorders. Reported presence of anxiety symptoms within a healthy, nonclinical population is associated with gray matter volume changes in brain areas (i.e., middle temporal gyrus, Rolandic operculum, precuneus, and middle cingulate cortex) which have a role in emotional regulation, interception, and social functioning (Besteher et al., 2017). Cognitive control can be adversely altered with subclinical levels of anxiety, leading to less adaptive thought processes (Ansari & Derakshan, 2011; Ng, Chan, & Schlaghecken, 2012). Decreased activity is seen within the dorsolateral prefrontal cortex during low attention demanding tasks, providing evidence for the concentration difficulties often seen with anxiety (Bishop, 2009). Data from studies of the epidemiological, neurological, and psychological effects of anxiety provide evidence that even when symptoms are not considered clinical, harmful effects are present.

## *Anxiety in Women, Aging, and Menopause*

### *Sex Differences in Anxiety*

Women, throughout life, have higher prevalence of cognitive anxiety and worry (McLean & Anderson, 2009; Robichaud, Dugas, & Conway, 2003). Across cultures and in non-clinical populations, women are more likely to experience negative affect (Lynn & Martin, 1997; Costa, Terracciano, & McCrae, 2001), are more fearful of experiencing symptoms of anxiety (Deacon, Abramowitz, Woods, & Tolin, 2003; Stewart, Taylor, & Baker, 1997), and display a more negative orientation to problem-solving (Robichaud, Dugas, & Conway, 2003). These responses are often nonadaptive and can contribute to worsening of symptoms. Biologically, women have stronger adrenocortical responses to stressful stimuli than men (Kajantie & Phillips, 2006). Neuroimaging evidence shows that women have greater activation in brain regions which mediate attention to potential threats (McClure, Monk, Nelson, Zarahn, & Leibenluft, 2004), suggesting that sex differences in processing of information impact the likelihood of viewing a situation as a threat and increasing vigilance.

There are many factors that may help explain sex and gender differences in anxiety. Vulnerability for anxiety issues is influenced by genetic heritability more for women than for men (Lake, Eaves, Maes, Heath, & Martin, 2000). Greater genetic vulnerability is more likely to be expressed in the presence of some environmental and sociocultural influences (Hettema, Prescott, Myers, Neale, & Kendler, 2005). For women, conformity to socialized gender roles is significantly associated with higher trait anxiety () and presence of anxiety symptoms (Bander & Betz, 1981; Biaggio & Nielsen, 1976). More negative affective tendencies in girls emerge around the same age at which

subtle gender role socialization manifests (Martin, Ruble, & Szkrybalo, 2002). The widespread evidences and contributions to increased anxiety prevalence in women, provide insight into the importance of studying anxiety and potential treatments within this population.

*Anxiety in Aging*

Even more common than in the general population, the presence of anxiety increases in the aging population (Beaudreau & O'hara, 2008). In older adults, higher anxiety state and level of trait anxiety are associated with trouble falling asleep, increased nighttime awakenings, and poor social and daily life functioning, even when anxiety levels are subclinical (Spira, Friedman, Aulakh, Lee, Sheikh, & Yesavage, 2008). For aging women, sources of anxiety include preconceived attitudes toward aging and menopause, deterioration of health and function, and perceived lack of support (Barrett & Robbins, 2008; Bauld, & Brown, 2009; Ramírez & Palacios-Espinosa, 2016). Additionally, issues with body image, which are often a source of anxiety throughout a woman's life, may become more pronounced through middle age (Barrett & Robbins, 2008; Saucier, 2004).

*Anxiety in Menopuase*

In addition to an increase in anxiety often seen during the normal aging process, women experiencing menopause or postmenopause are at an added risk (Bromberger et al., 2013). Though there have been mixed findings of increased occurrence of specific anxiety disorders in menopause, problematic symptoms of anxiety are prevalent (Hickey, Bryant, & Judd, 2012). Among women of menopausal age, approximately 51% report

experiencing anxiety symptoms of irritability and nervousness within two weeks (Avis et al., 2001), though it has been previously found that 23% report anxiety within the past two months (Porter et al., 1996). These symptoms occur frequently (i.e., at least six times within a two-week period) for 16 to 18% of women entering menopause (Bromberger et al., 2003).

*Menopause*

Menopause is the termination of the menstrual cycle due to changes in sex hormone levels, and it is retrospectively said to have occurred once menses have been absent for one year (Takahashi & Johnson, 2015). The term *menopause* is often used interchangeably with the term *perimenopause*, which describes the transition rather than a timepoint. Natural menopause begins when oocytes are no longer produced within the ovaries and the menstrual cycle becomes highly irregular. The average age of menopause is 51 years in the United States, but a range of 48 to 55 is common worldwide (Takahashi & Johnson, 2015). Surgical menopause occurs when cessation of menses is induced by damage to the ovaries. This is often due to bilateral oophorectomy, or removal of both ovaries, but can also include severe injury by cancer treatments (Acosta et al., 2009).

Over 85% of women experience problematic symptoms, often beginning many years before menopause, when the transition first begins. Neuroendocrine changes have been theorized as explanations of symptoms related to mood, sleep, cognition, and well-being in women. The decrease of estrogen, and to a lesser degree progesterone, seen during menopause highly affects the central nervous system (Arpels, 1996; Walf & Frye, 2006). The presence and severity of symptoms vary between individuals, but the most common include hot flashes, sleep disturbances, cognitive changes, and disordered mood

(Acosta et al., 2009; Sussman et al., 2015). Symptoms are often interrelated and can affect each other (Schnatz, Whitehurst & O'Sullivan, 2010).

Postmenopause is the stage following menopause. Estrogen remains low, and symptoms often continue, but can gradually begin to decline. Different symptoms may also emerge. Urogenital symptoms and issues with sexuality become more common during this stage. In general, menopause symptoms last five to seven years but can persist for 15 or more years, well into postmenopause (North American Menopause Society, 2014).

*Intersections of Anxiety and Other Menopausal Symptoms*

Women in postmenopause are significantly more likely to experience anxiety than women before menopause (Cagnacci et al., 1997). There is evidence that decreases of estrogen greatly affect the brain, most notably the hippocampus and amygdala, which are involved in emotion and anxiety regulation (Rodríguez-Landa et al., 2015; Walf & Frye, 2006). In animal models, administration of synthetic estrogen decreases anxiety behaviors (Walf & Frye, 2006).

Approximately 8% of women report anxiety as a symptom specific to menopause, separate from co-involvement of other symptoms (Sussman et al., 2015). The presence of anxiety is a factor that increases distress and impairs quality of life in menopause (Masood, Rashid, Masrrat, & Mazahir, 2016; Núñez-Pizarro et al., 2017), which can cause worsening of concomitant symptoms. Though anxiety can be an independent symptom of menopause, it may coincide with concurrent symptoms (Hickey, Bryant, & Judd, 2012). These other factors in menopause may affect the presence and level of

anxiety (Deeks, 2003; Schnatz, Whitehurst & O'Sullivan, 2010). Conversely, anxiety may affect the presence and level of other symptoms (Freeman et al., 2005).

One symptom that is highly related to anxiety are vasomotor symptoms, which include hot flashes and night sweats. Of menopausal symptoms, hot flashes are the most common, affecting over 80% of women in menopause. Hot flashes are the symptoms for which the majority of women seek treatment (Thurston & Joffe, 2011; Sussman et al., 2015). Anxiety level is significantly associated with both severity and frequency of hot flashes in perimenopause and postmenopause but not in premenopausal women (Juang, Wang, Lu, Lee, & Fuh, 2005). This association remains after statistically controlling for menopause stage, depressive symptoms, smoking, BMI, estradiol, race, & age (Freeman et al., 2005). Additionally, anxiety symptoms may predict the risk of hot flashes (Freeman & Sammel, 2016; Freeman et al., 2005). Both anxiety levels at the previous assessment period and change in anxiety from the previous assessment period significantly predict hot flashes. Compared with those in the normal anxiety range, women with moderate anxiety were three times more likely to report hot flashes and women with high anxiety were five times more likely to report hot flashes (Freeman et al., 2005).

Given the significant associations between anxiety and hot flashes, a distinction between the two is complex (Hanisch, Hantsoo, Freeman, Sullivan, & Coyne, 2008). Some physical symptoms of anxiety, such as muscle tension, shaking, and stomachache, are easily differentiated from hot flashes. Other somatic anxiety symptoms and those of hot flashes are analogous (i.e., sweating, increased heart rate), and differentiation between the two is difficult. In a non-clinically anxious postmenopausal population,

associations between anxiety and hot flashes could be related to the intersection of somatic anxiety and hot flash symptoms (Lermer et al., 2011). The affective and cognitive aspects of anxiety are easily differentiated from vasomotor symptoms. When only psychological factors are assessed, the association between hot flash score is not always significant (Lermer et al., 2011), though the clear majority of studies that do find significant correlations are using self-report questionnaires which primarily assess cognitive and affective factors. In some cases, it may be that anxiety and vasomotor symptoms present with equivalent features, and this should be considered in treating women in postmenopause.

Significant associations have been found between poor sleep quality and anxiety among women of menopause age (Cheng et al., 2008; Hollander et al., 2001). One of the best predictors of sleep disturbance in postmenopausal women is the presence of anxiety (Freedman & Roehrs, 2007). Anxiety in menopause is also associated with urogenital symptoms and sexual health. Decreased frequency of intercourse is influenced by anxiety more than desire, sexual satisfaction, and opinions about the importance of sexuality (Channon & Ballinger, 1986). Additionally, degree of sexual dysfunction is positively correlated with greater anxiety in some women (Schnatz, Whitehurst & O'Sullivan, 2010).

Though symptoms are often correlated and present together, it is not fully determined whether some symptoms have a causal effect on others. Anxiety may affect severity and impact of other symptoms beyond the effects of estrogen decline alone (Channon & Ballinger, 1986; Freedman & Roehrs, 2007; Freeman et al., 2005; Freeman

& Sammel, 2016; Hollander et al., 2001), though many studies show only correlations without directional causality between symptoms.

It is estimated that 47 million women reach menopause each year globally, with 1.1 billion women reaching postmenopause by 2025 (Hill, 1996). In the United States, it is estimated that 6000 women reach menopause daily (Takahashi & Johnson, 2015). With advances in medicine, the average human lifespan is increasing, but age of menopause onset is not. Therefore, the percentage of women's lives in which they are in a postmenopausal phase is likely to continue to increase from the current estimate of 30 percent. Given the substantial overlap in menopausal symptomology, anxiety associated with menopause is a considerable public health issue.

*Treatment Options*

For general menopause symptoms, pharmacological hormone replacement therapy (HRT) is often used (Takahasi & Johnson, 2015). Because menopausal symptoms are caused in large part by a decrease of estrogen, replacing this hormone synthetically can assuage some issues. Although, hormonal factors are often not the sole determinant of symptom presence or severity (Channon & Ballinger, 1986; Freedman & Roehrs, 2007; Freeman et al., 2005; Hollander et al., 2001). There is some evidence that HRT may be of benefit specifically for anxiety in menopause (Cagnacci et al., 1997). However, side effects of HRT include increased risk of cardiovascular disease, breast cancer, cognitive decline, and depression (Takahasi & Johnson, 2015). HRT is contraindicated for longterm use and if used, should be titrated to the lowest dose needed to improve symptoms (Takahasi & Johnson, 2015). Ultimately, HRT has a poor risk-to-benefit ratio which limits the utilization of HRT (Women's Health Initiative, 2002).

Anxiety can also be treated separately with anxiolytics like benzodiazepines or Buspirone or antidepressants like selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs). However, the use of anxiolytics or antidepressants is a general treatment for anxiety and does not account for other symptoms that are likely present surrounding menopause. Additionally, desired effects of these drugs often do not appear for weeks, and adverse effects include insomnia, drowsiness, decreased libido, among others (Ensrud et al., 2012). The presence of other symptoms and potential interactions with other medications is a large consideration when choosing a treatment option within this population (Gelenberg, 2000).

A key to treating a heterogenous group of symptoms, like those seen in menopause, is to take individual experiences into account (Deeks, 2003). This complicates treatment and may explain why pharmacology is successful for some patients but predominately adverse in others. Research of nonpharmacological treatments for anxiety in menopause or postmenopuase is extremely limited. There is evidence that cognitive behavioral therapy (CBT; Hunter, Coventry, Hamed, Fentiman, & Grunfeld, 2009) and CBT combined with physical exercise (Duijts et al., 2012) can help to reduce menopausal symptoms induced by breast cancer treatments. A CBT intervention for hot flashes may also reduce feelings of anxiety (Hunter & Liao, 1996).

Women are interested in nonpharmacological options for managing menopause symptoms (Hunter et al., 2004), but there is insufficient information available from healthcare providers and researchers (Ma, Drieling, Stafford, 2006). The best course of treatment would ideally involve educating women on symptom triggers and providing

strategies for coping with multiple stressors, while treating the underlying symptoms (Hickey, Bryant, & Judd, 2012).

### *Hypnosis for Anxiety in Menopause*

One promising treatment for anxiety related to other symptoms is hypnosis, which is defined as "A state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion" (Elkins, Barabasz, Council, & Spiegel, 2015). Clinical hypnosis is the induction of a hypnotic state followed by suggestions which target therapeutic goals. Hypnosis is versatile in that strong evidence exists for its effectiveness in many medical and psychological issues such as chronic pain, nausea, surgical recovery, bruxism, gastrointestinal disorders, and procedural anxiety (Adachi, Fujino, Nakae, Mashimo, & Sasaki, 2014; Elkins, 2016; Kekecs, Nagy, & Varga, 2014). Hypnosis can be delivered face-to-face by a licensed therapist in any number of session, but for many patients, hypnosis can also be of benefit through pre-recorded audio or self-hypnosis.

Hypnosis is generally a relaxing experience for patients and research participants alike which may partly explain its efficacy. In clinical practice, hypnosis is often used for relaxation and anxiety reduction, but empirical research is limited mostly to case studies. Much of the literature involves specific anxiety events (e.g., dentist visits, test taking, etc.), anxiety disorders, or phobias. Little empirical research has examined the effects of hypnosis on general or menopausal anxiety, and even fewer studies assess anxiety specific to a menopausal population.

Clinical hypnosis is effective at treating other symptoms of menopause. Hypnosis has been shown to ameliorate subjectively and objectively-measured hot flashes among

breast cancer survivors (Elkins et al., 2008, 2007) and postmenopausal women (Elkins et al., 2013). Anxiety was significantly reduced following a hypnotic intervention in a population of breast cancer survivors experiencing hot flashes (Johnson et al., 2016). This evidence suggests that hypnosis could be used to simultaneously treat concurrent symptoms seen in postmenopuase, rather than treating specific symptoms separately.

### *Study Rationale*

Given the relationship between hot flashes and anxiety, it is possible that a hypnosis intervention designed for hot flash relief could also significantly reduce anxiety. However, the effect of hypnotic induction for hot flashes on anxiety in menopause has not been specifically analyzed. Because the majority of women in menopause present with vasomotor symptoms, it is critical to examine whether an intervention that targets a primary symptom like hot flashes also ameliorates feelings of anxiety.

This study is a retrospective analysis of the anxiety measures from a five-year study funded by the National Center for Complementary and Integrative Health (NCCIH) titled "Hypnosis for Hot Flashes Among Postmenopausal Women: A Randomized Clinical Trial" (Elkins et al., 2013). The degree of change in anxiety was assessed on two validated measures over the 12-week course of the study, which included a five-week intervention and a follow-up visit seven weeks later. Additionally, changes in pre-treatment and post-treatment ratings of anxiety for those in the hypnosis group were assessed for the five study sessions. Hypnotizability, or a person's innate ability to respond readily to hypnotic suggestion, and anxiety as a trait variable are analyzed as moderator of the anxiety reduction response to hypnosis. Ultimately, this study will

answer whether a hypnosis intervention produced reciprocal benefit for hot flashes and symptoms of anxiety among women in postmenopause.

# CHAPTER TWO

## Methods and Materials

### *Study Design*

A detailed description of the study design, data collection methods, and group interventions have been previously published (Elkins, Fisher, & Johnson, 2010; Elkins et al., 2013). The study was designed and conducted as a single-blind, randomized, controlled clinical trial to evaluate the effectiveness of clinical hypnosis in reducing hot flashes. This research was approved by the institutional review board at Baylor University and all participants provided informed consent. Data collection was funded in part by grant U01AT004634-05 awarded to Dr. Gary Elkins from the National Center for Complementary and Alternative Medicine of the National Institutes of Health.

### *Participants*

A total of 187 postmenopausal women who were experiencing hot flashes entered into the study. Participants were randomly assigned to either a hypnosis intervention or structured-attention control.

#### *Eligibility Criteria*

Participants were eligible if they were in postmenopause as defined by: no menstrual period in the past 12 months or no menstrual period in the past 6 months and a medically documented history of follicle-stimulating hormone (FSH) level greater than 40 or have had a bilateral oophorectomy. Because this study investigated hot flashes,

participants were eligible if they had a minimum of 7 hot flashes per day or at least 50 hot flashes per week at baseline. In addition, participants were able to attend weekly sessions, were aged over 18 years and able to give consent for participation, and they had discontinued other therapies for hot flashes for at least one month prior to enrollment.

*Exclusion Criteria*

Participants were excluded from participation if they were receiving simultaneous treatment for hot flashes, including any complementary, alternative, or integrative treatments. Participants were also excluded if they have any medical or psychiatric condition that in the opinion of the investigator put the participant at potential risk during the study, were concurrently using hypnosis for any reason, or were not fluent in English.

*Randomization*

Screening for eligibility took place over the telephone. Those who met criteria for participation in the study completed baseline measures. After the baseline data were collected, the participants were randomized to either the hypnosis intervention or to a structured-attention control group. Random assignment was made sequentially from a computer-generated, confidential list of permuted blocks of unpredictable size. The list was generated to provide equal probabilities to the study arms.

*Data Collection*

After randomization, participants completed five weekly study visits which included data collection and sessions of either hypnosis or structured attention, depending on group allocation. At each study visit, participants were asked to report any adverse events from the past week and incidents were logged. A follow-up visit was completed at

week 12, seven weeks after completion of the fifth session. An overview of the chronology of the study is provided graphically in Figure 2.1.

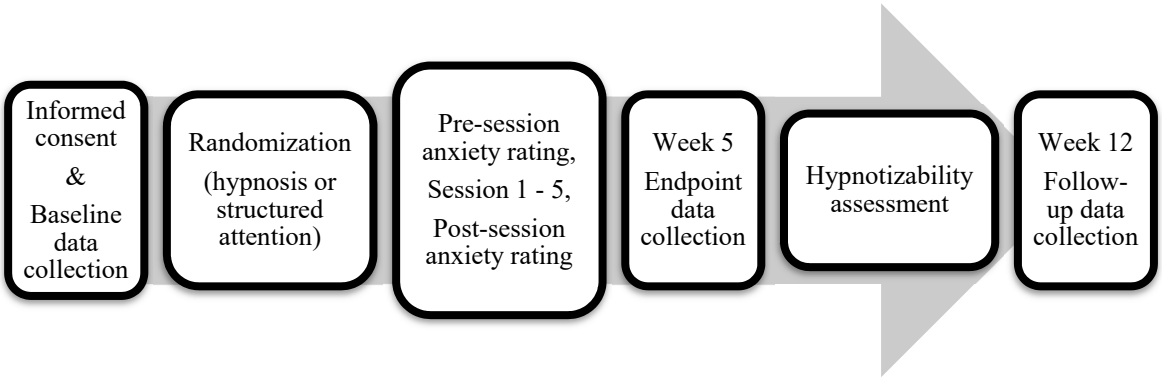


*Figure 2.1*. Study Design.

## *Intervention Groups*

### *Treatment Intervention*

Participants in the treatment group met with a therapist for 5 weekly sessions of clinical hypnosis. The intervention therapist adhered to a treatment manual to ensure equal treatment between participants. Clinical hypnosis was delivered by clinicians who were trained in the administration of clinical hypnosis, following established standards.

The weekly treatment intervention was approximately 45 minutes. The session involved a hypnotic induction followed by suggestions for coolness, relaxation, and mental imagery of a safe place. Instructions were given to help participants learn self-hypnosis in order to further practice. A recorded hypnotic induction was given to each participant, and they were asked to practice self-hypnosis daily, with or without the audio recordings. A checklist was used at the end of each session by the therapists and data collectors to ensure treatment and data compliance.

*Control Intervention*

The structured-attention intervention was developed to match the treatment intervention so that both groups equally received encouragement, symptom monitoring, interactive discussion with a therapist, and exposure to a therapeutic setting. A checklist was also used at the end of each structured attention session to ensure treatment and data collection compliance.

Participants in the control group also attended five weekly sessions in a therapeutic environment. Research therapists followed a treatment manual throughout each 45-minute session to ensure equal treatment. During each session the participants' symptoms were discussed, and therapists employed attentive listening, encouraging exchange, monitoring of symptoms, and avoidance of negativity. Information about hot flashes and their possible causes were given, but no hypnotic induction or suggestions for coolness were delivered. Participants were given an audio recording which included educational information on hot flashes and were asked to listen daily. This recording was approximately the same length as the recorded hypnotic induction but made no mention of hypnosis.

*Outcome Measures*

Outcomes are anxiety using the State-Trait Anxiety Inventory (STAI), Hospital Anxiety and Depression Scale (anxiety subscale; HADS-A), and pre-session and post-session ratings of Current Anxiety on a visual analog scale (VAS). Hypnotizability and trait anxiety were assessed as potential moderators of the level of anxiety reduction. The HADS-A and STAI were given at week 0 (baseline), week 5 (endpoint), and week 12 (follow-up). Current Anxiety VAS ratings were asked at the beginning and end of each

session from week one to week five. Hypnotizability as measured by with the Elkins hypnotizability scale (EHS) was assessed at the end of the last session. A representation of the data collection schedule is provided in Table 2.1.

Table 2.1. *Data Collection Schedule.*

| Measure | Baseline | Session 1 | Session 2 | Session 3 | Session 4 | Session 5 (Endpoint) | Week 12 (Follow-up) |
|---|---|---|---|---|---|---|---|
| HADS-A | X | | | | | X | X |
| STAI-S | X | | | | | X | X |
| Pre-session VAS | | X | X | X | X | X | |
| Post-session VAS | | X | X | X | X | X | |
| STAI-T | X | | | | | | |
| EHS | | | | | | X | |

*Hospital Anxiety and Depression Scale, Anxiety Subscale (HADS-A)*

HADS-A is a self-report scale consisting of seven items (Snaith & Zigmond, 1986). It measures general anxiety and fear symptoms within the past week. HADS-A demonstrates high internal reliability (α = .84; Bedford, de Pauw, & Grant, 1997; Lisspers, Nygren, & Söderman, 1997). It also shows appropriate concurrent validity with other measures of self-report anxiety: r = 61 to .83 with Beck's Depression Inventory (BDI), r = .50 to .68 with the General Health Questionnaire (GHQ), r = .69 to .75 with the Clinical Anxiety Scale (CAS), r = .64 to .81 with the STAI, and r = .49 to .73 with the Symptom Checklist 90 Scale (SCL-90; Bjelland, Dahl, Haug, & Neckelmann, 2002).

*State-Trait Anxiety Inventory (STAI), State Subscale (STAI-S), Trait Subscale (STAI-T)*

STAI is a self-report assessment device for the study of anxiety in adults (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The inventory includes two separate subscales, 20 questions each of both in-the-moment anxiety state (STAI-S) and

stable trait anxiety (STAI-T). Answers to statements are indicated on a 4-point scale ranging from 'not at all' to 'completely.' Total scores on each subscale can range from 20 to 80, with a higher score indicating higher anxiety. Test-retest reliability for the scale ranges from .62 to .86. Construct validity is supported by the STAI's association with other measures of trait-anxiety, such as the Taylor Manifest Anxiety Scale (.80) and the IPAT Anxiety Scale (.75).

*Current Anxiety Rating Self-report VAS*

At both the beginning and end of each weekly session, participants were asked "How anxious do you feel right now?" The VAS consisted of a single 10 cm line with the statement "Completely relaxed" at one end and "Completely anxious" at the opposite end. Participants marked where on the line they felt their current anxiety level lie. This VAS was scored by measuring in cm and taking that number as their rating (range = 0 to 10). This simple scale has shown validity and reliability in measuring anxiety (Davey, Barratt, Butow, & Deeks, 2007; Williams, Morlock, & Feltner, 2010).

*Elkins Hypnotizability Scale (EHS)*

Hypnotizability is defined as "An individual's ability to experience suggested alterations in physiology, sensations, emotions, thoughts, or behavior during hypnosis"(Elkins, Barabasz, Council, & Spiegel, 2015). The EHS consists of a brief hypnosis induction and 12 items designed to measure ability to respond to hypnotic suggestion in a time efficient manner (Elkins, 2014). Patients or research participants receive a score from 0 to 12, which can further be categorized as very low (0-1), low (2-3), middle (4-8), high (9-10), and very high (11-12) in hypnotizability. Internal

consistency (α = .78 to .85; Elkins, Johnson, Johnson, & Sliwinski, 2015; Kekecs, Bowers, Johnson, Kendrick, & Elkins, 2016) and test-retest reliability (.93) are satisfactory (Elkins, Fisher, & Johnson, 2012). Concurrent validity (ρ= .86) and convergent validity (r = .82 to .91) with the gold standard in hypnotizability assessment, the Stanford Hypnotic Susceptibility Scale, Form C, is high (Elkins, 2014; Elkins, Fisher, & Johnson, 2012; Kekecs, Bowers, Johnson, Kendrick, & Elkins, 2016). The EHS allows participants to demonstrate multiple factors of hypnotic responding for a more robust conceptualization (Elkins, Johnson, Johnson, & Sliwinski, 2015).

### *Statistical Analyses*

Statistical analyses were conducted using SPSS version 25.0 (IBM Corp, 2017). Analyses were separate for each of three study aims detailed below.

#### *Aim 1*

The purpose of aim 1 was to determine whether a five-week hypnosis intervention for hot flashes effectively reduces anxiety as compared to a health education control group, measured by the HADS-A and the STAI-S. To test effectiveness between groups on the HADS-A and the STAI-S, two separate mixed effects, repeated measures ANOVA were conducted at 3 timepoints. We hypothesized that anxiety as measured by the HADS-A and the STAI-S will significantly reduce from baseline to follow-up for the hypnosis group, and the hypnosis group will see significantly greater reductions than the control group.

*Aim 2*

The purpose of aim 2 was to determine whether Current Anxiety ratings changed consistently from pre-session to post-session within the hypnosis group. Additionally, we tested whether pre-session ratings reduced over the course of 5 sessions, which would indicate that participants were becoming less anxious even before using hypnosis. To test within group effectiveness, two separate repeated measures ANOVA were conducted at 5 timepoints using Current Anxiety ratings on the VAS. The first ANOVA assessed the within session changes, and the other assessed only pre-session ratings. A Bonferroni correction was applied to adjust the error rate for individual analyses. We hypothesized that Current Anxiety ratings would decrease from pre-session to post-session at each visit, and that Current Anxiety ratings would decrease overall from the first visit to the last.

*Aim 3*

The purpose of Aim 3 was to determine potential moderators of anxiety reduction within the hypnosis group. Hypnotizability as measured by the EHS and trait anxiety as measured by baseline scores on the STAI-T were analyzed as moderators. To test for moderation, a random effects, repeated measures ANOVA with covariate effects was conducted with reductions on the HADS-A at three timepoints as the outcome variable. We hypothesized that hypnotizability scores would not significantly moderate anxiety reductions within the hypnosis group. This would mean that hypnotizability as a trait is not a sole determinant of therapeutic response. However, it is believed that those who were higher in hypnotizability would see more reduction in anxiety, more quickly, while those with lower hypnotizability would see similar reduction in anxiety, but with changes

occurring less quickly over the course of the intervention. The majority of individuals are in the mid-range of hypnotizability (Elkins, 2014), and we hypothesized that those in the middle (scoring 4 to 8) will see significant anxiety reductions. Additionally, we hypothesized that trait anxiety would moderate anxiety reductions within the hypnosis group. It is believed that higher trait anxiety at baseline would cause less reduction in anxiety, while those with lower trait anxiety will see more reduction in anxiety over the course of the intervention.

# CHAPTER THREE

# Results

## *Participant Information and Demographics*

Of the 187 participants, 93 were randomized to the hypnosis treatment group and 94 to the control group. The mean age of the participants was 54.6 (*SD* = 6.8; range = 39-75) years. Reported races of the participants were White or Caucasian (73.8%, n = 138), Black or African-American (16.6%, n = 31), and Native American, Asian, or Hispanic (9.6%, n = 18). The majority of participants had attended college (63.7%, n = 119) and were married (65.2%, n = 122). Complete demographic information for the participants was previously reported in an article covering the primary results of the original study (Elkins et al., 2013). Participants were satisfied with the intervention and there were no adverse events or unintended effects related to the study intervention for either group (Elkins et al., 2013).

## *Aim 1 Results*

HADS-A and STAI-S scores at baseline, endpoint, and follow-up were assessed for between group differences. Table A.1 lists descriptive statistics and score differences from baseline to week 6 and week 12 for the HADS-A and STAI-S. Figure 3.1 shows group means for the HADS-A and Figure 3.2 shows group means for the STAI-S.

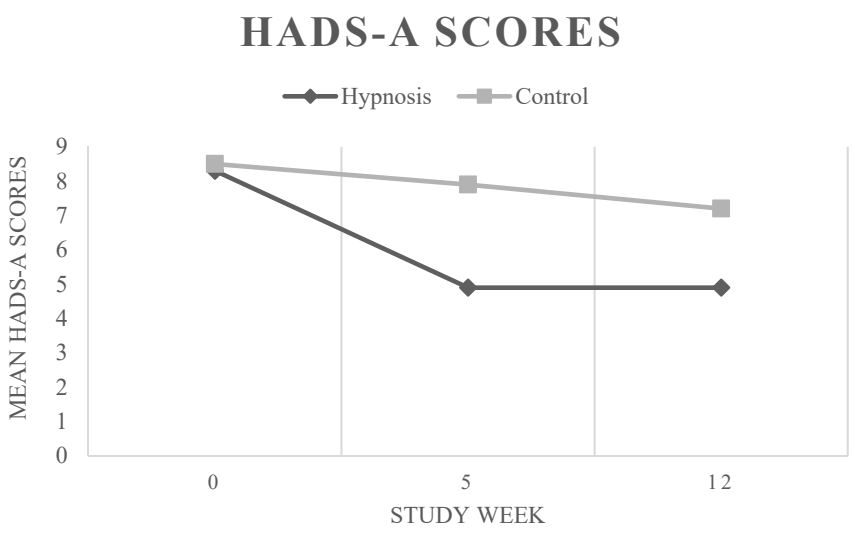


*Figure 3.1.* Mean Scores on the HADS-A at Three Timepoints for the Hypnosis Group (diamonds) and the Control Group (squares).

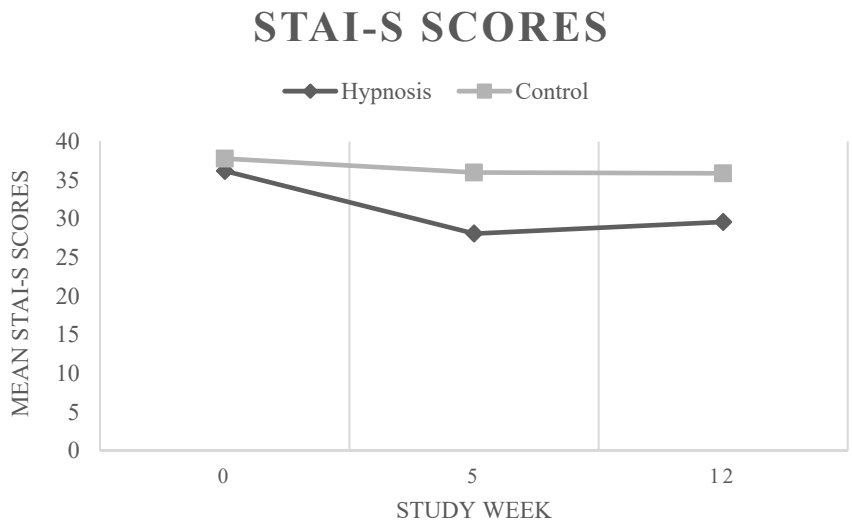


*Figure 3.2.* Mean Scores on the STAI-S at Three Timepoints for the Hypnosis Group (diamonds) and the Control Group (squares).

Repeated measures ANOVAs were conducted to compare the effect of intervention group on anxiety over the course of the study. There was a significant, medium effect of group allocation and time of assessment on HADS-A ($F_{(2,152)} = 18.585$,

$\eta_p 2 = .196$, $p < .001$). There was also a significant, medium effect of group allocation and time of assessment on STAI-S ($F_{(2,140)} = 10.537$, $\eta_p 2 = .131$, $p < .001$). Hypnosis was found to be superior to structured attention in reducing anxiety on both measures. Group allocation had a medium effect on changes in anxiety.

### *Aim 2 Results*

Table A.2 summarizes descriptive statistics of the weekly ratings and shows differences between pre-session and post-session ratings at each weekly visit. For the first study visit, the average pre-session Current Anxiety rating, as reported on a VAS, was 4.6 (*SD* = 2.4), with a mean anxiety reduction of 3.5 at the post-session rating. The largest pre-session to post-session change occurred during the first visit. During the other four sessions, the differences ranged from 2.0 to 2.6, so reductions in anxiety continued at each subsequent session. Figure 3.3 illustrates trends in weekly reductions in self-reported anxiety.

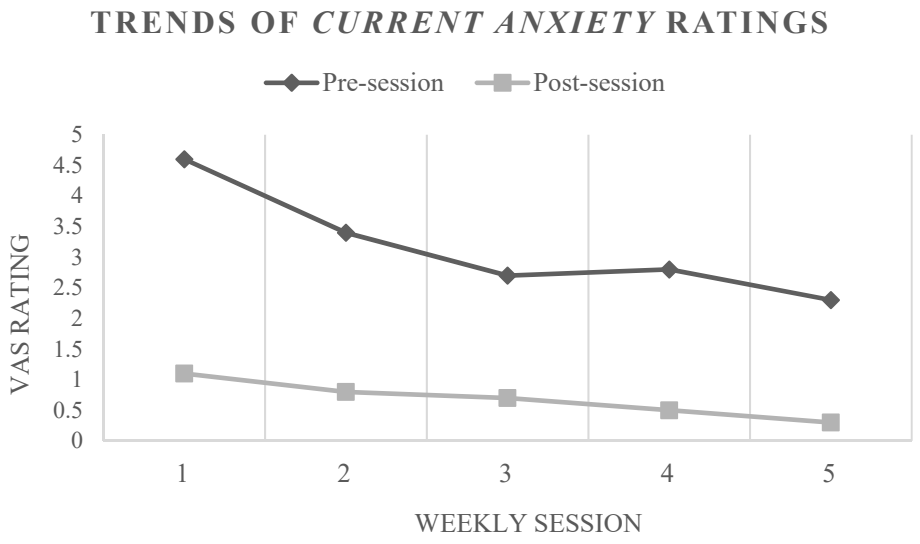


*Figure 3.3.* Trends in Pre-session (diamonds) and Post-session (squares) Current Anxiety Ratings per for Five Weekly Sessions of Hypnosis

Repeated measures ANOVAs were conducted to compare the effect of the hypnosis intervention on Current Anxiety ratings throughout the five study visits. There was a significant effect of hypnosis on changes in Current Anxiety ratings from pre-session to post-session at each study visit ($F_{(4, 80)} = 9.127$, $\eta_p 2 = .313$, $p < .001$ ). Paired-samples t tests of change in pre- to post-session ratings for Session 1 and Session 5 were statistically significant (Session 1: $t_{(86)} = 7.632$, d = 0.82, $p < .001$, Mean difference = 1.75, 95% CI [1.29, 2.20]; Session 5: $t_{(86)} = 5.62$, d = 0.60, $p < .001$, Mean difference = .76, 95% CI [.49, 1.03]). Figure 3.4 illustrates these reductions in Current Anxiety ratings for each hypnosis session.

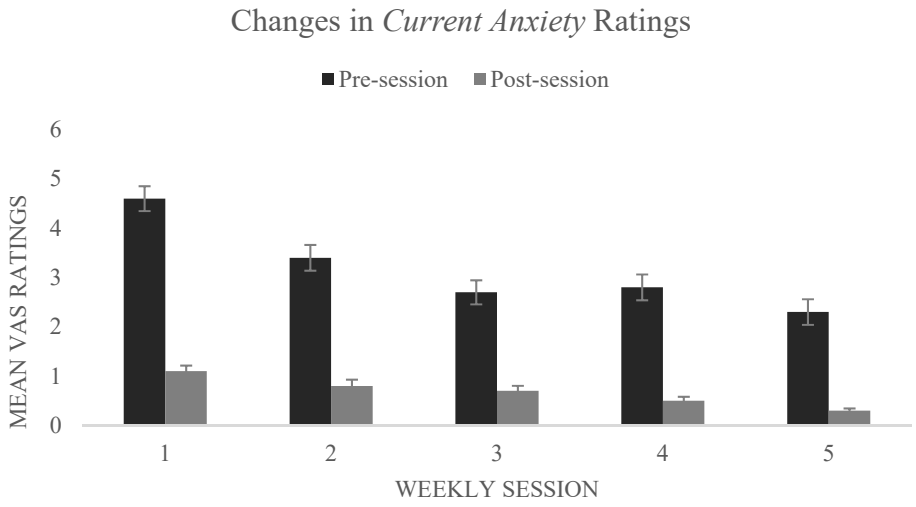


*Figure 3.4.* Reductions in Pre-session and Post-session Current Anxiety Ratings per for Five Weekly Sessions of Hypnosis

Additionally, significant differences were present in pre-session ratings from week one to week five ($F_{(4,80)} = 15.073$, $\eta_p 2 = .430$, $p < .001$), with effects of hypnosis on consistent reductions throughout the five-week intervention period. A paired-samples t test of pre-session ratings for week 1 (before first hypnosis session) and week 5

(endpoint) was statistically significant ($t_{(83)} = 7.208$, d = 0.79, $p < .001$, Mean difference = 2.33, 95% CI [1.69, 2.97]).

### *Aim 3 Results*

The mean hypnotizability score on the EHS for the hypnosis group was 7.7 (*SD* = 3.2). The EHS mean is consistent with previous studies showing a normal distribution in hypnotizability, with the majority of scores ranging from 4 to 8 and being classified in the middle range (Elkins, Johnson, Johnson, & Sliwinski, 2015; Kekecs et al., 2016). Hypnotizability assessments were missing for 11 participants, and these were therefore excluded from this analysis. The average baseline trait anxiety score (STAI-T) for the hypnosis group was 39.1 (*SD* = 11.0).

Repeated measures ANOVA was conducted to assess the moderation effects of hypnotizability and trait anxiety on anxiety reductions within the hypnosis group. Anxiety reductions were measured by HADS-A scores at the three timepoints (baseline, endpoint, and week 12 follow-up). There was a significant interaction with medium effect between anxiety reductions and hypnotizability scores ($F_{(2, 64)} = 3.390$, $\eta_p 2 = .096$, $p = .04$). Figure 3.5 illustrates changes in HADS-A scores separated by hypnotizability classifications.

The interaction between reductions anxiety reductions and baseline trait anxiety scores was also significant ($F_{(2, 64)} = 7.570$, $\eta_p 2 = .191$, $p = .001$ ). Figure 3.6 shows changes in HADS-A scores separated by trait anxiety quartile. This is for illustrative purposes only, as score quartiles for the STAI-T have no validated clinical interpretation.

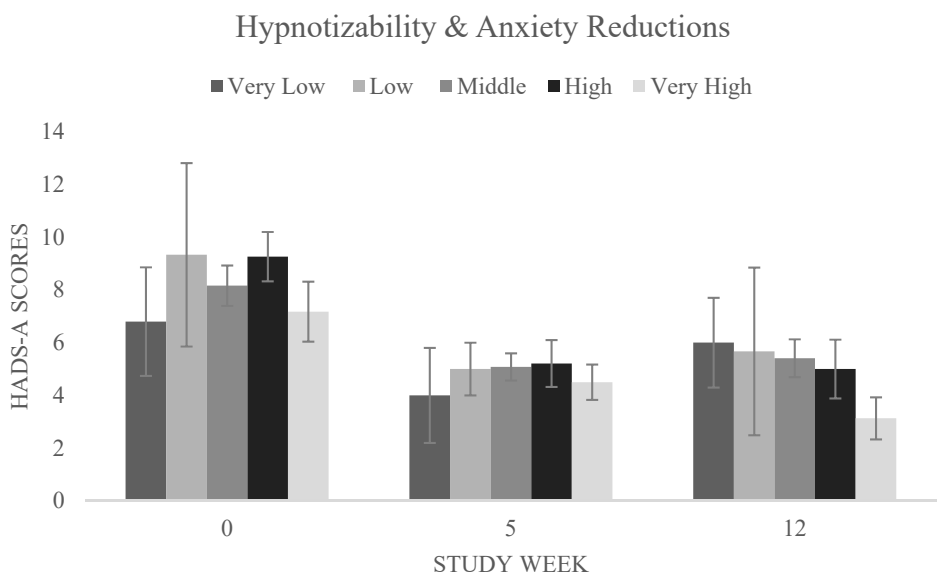


*Figure 3.5.* Hypnotizability Classification and HADS-A Scores at Three Timepoints.

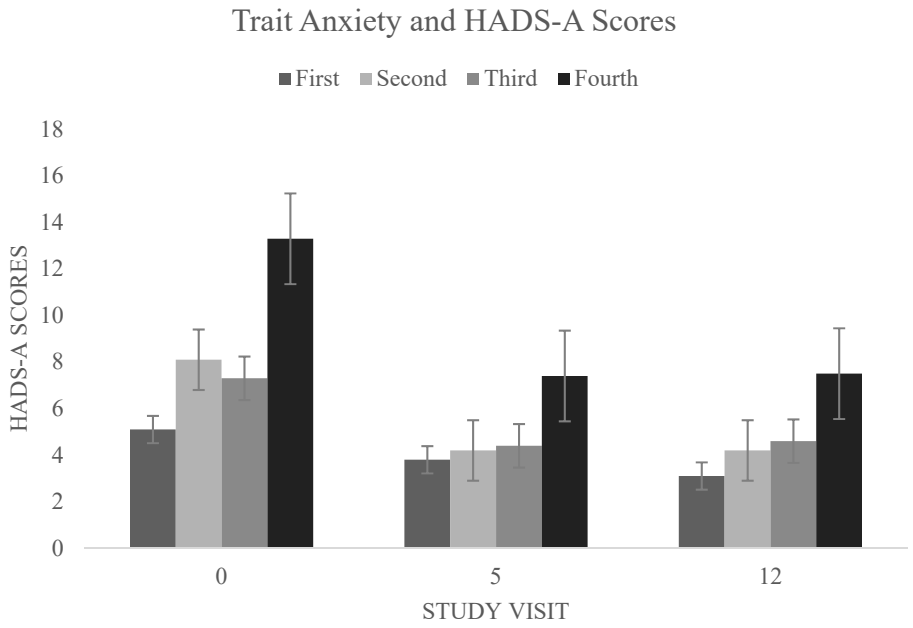


*Figure 3.6.* Trait Anxiety Quartile and Scores on the HADS-A at Three Timepoints

# CHAPTER FOUR

## Discussion and Conclusions

### *Discussion*

#### *Aim 1*

Reductions in scores on the HADS-A and the STAI-S were found to be significantly different based on participants' group allocation. Hypnosis was superior to structured attention in reducing anxiety on both of the measures. Participants in both groups received encouragement, symptom monitoring, attentive listening, and interactive exchange with a therapist weekly in a therapeutic environment. Both groups also received recordings to take home to listen to daily while relaxing. The only difference between groups was the treatment group experienced hypnosis during their weekly visits and listened to the hypnosis recording at home. Hypnosis was shown to reduce anxiety symptoms beyond relaxation and visits to a professional, encouraging setting.

#### *Aim 2*

Reductions in ratings of Current Anxiety were seen weekly for those in the hypnosis group. At each weekly session, participants reported feeling less anxious after hypnosis than they had felt at the beginning of the session before hypnosis. Examining only the anxiety pre-session ratings, demonstrated that as the study continued, participants were feeling less anxious even at the beginning of their sessions.

Pre-session to post-session differences were smaller in weeks two through five likely because anxiety ratings were starting out smaller at each session. The largest

change from pre-session to post-session Current Anxiety ratings occurred during the first study visit. However, there continued to be differences from pre-session to post during each remaining session, indicating that participants continued to see reductions in in-the-moment anxiety at each session regardless of having experienced hypnotic induction the previous weeks.

*Aim 3*

Both hypnotizability scores and anxiety as a trait variable were shown to moderate reductions in anxiety as measured by change in HADS-A scores over the course of the study.

Hypnotizability was found to be a moderator of anxiety reduction, contrary to the original hypothesis. This may partially be due to the finding that individuals with anxiety disorders are more likely to have higher hypnotizability (Bryant, 2012), and therefore an interaction could have occurred if some participants had anxiety disorders. We did not assess that in this study.

Often, research of hypnotizability involves only dichotomous "highs" and "lows" (those scoring near the highest end of the scale versus those near the lowest end). However, in research of therapeutic effects, it is vital to assess those who lie in the middle of the scale. Because the majority of individuals score in this mid-range, a hypnosis intervention that is beneficial to the majority of individuals scoring 4 to 8, will be beneficial in a large proportion of the population. In the current study, though the moderation analysis was significant, individuals at all hypnotizability levels saw symptom improvement. Hypnotizability was likely found as a moderator partially due to the lack of maintained anxiety reduction of the "lows" after the study sessions had ended.

In clinical practice, these patients would likely benefit from additional maintenance sessions.

As shown in Figure 3.5 above, participants who scored very low or low in hypnotizability had significant reductions in anxiety from baseline to week 5 endpoint. Their anxiety scores remained below baseline at the week 12 follow-up visit, but scores were higher than at endpoint. For those in the middle and high range, anxiety scores at follow-up remained very close to the reduced endpoint scores. Participants who were determined to be very high in hypnotizability continued to see improvements beyond the end of study sessions.

Previous studies have found that hypnotizability did not moderate anxiety reduction as measured by a numeric rating scale (Johnson et al., 2016). Research assessing the influence of hypnotizability on therapeutic response to other symptoms have yielded mixed findings. Further research is warranted to answer this question.

Trait anxiety was found to moderate anxiety reductions, as was originally hypothesized. Participants with higher trait anxiety did not report scores as low as those with less trait anxiety, though they did experience significant reductions from baseline. Participants who had mild to very low trait anxiety at baseline experienced some reduction in anxiety, but floor effects in scores were seen. However, those with little trait anxiety reported lower anxiety scores consistently at each assessment point. As shown in Figure 3.6, participants at each quartile of baseline trait anxiety scores experienced reductions during the study.

*Limitations*

Anxiety was not a symptom for which participants were screened, as the primary outcome of the original study was hot flashes. A sample of individuals with varying levels of anxiety would produce a more accurate basis for testing moderation variables of anxiety reductions during a hypnosis intervention. For instance, the range of possible scores on the STAI-T is 20 to 80, yet the range of scores in our sample was 20 to 66. While valid cut-offs for the interpretation of STAI-T scores are not available, it would appear that mild and moderate trait anxiety is well-represented in our sample, yet severe trait anxiety is not. Future studies should screen participants for the presence of moderate to severe baseline trait anxiety.

## *Conclusions*

In this study, hypnosis was more effective in relieving anxiety than a commonly used control group who received the same amount of sessions, encouragement, and monitoring. For those in the treatment group, ratings of in-the-moment anxiety at the beginning of session reduced each week, and rating further reduced after a hypnotic induction each week. Hypnotizability and trait anxiety were both shown to moderate the effects of a five-week hypnosis intervention on anxiety reductions. However, regardless of trait anxiety score and hypnotizability level, participants in this study experienced significant symptom improvement from their baseline scores.

Though this hypnosis intervention was designed primarily to ameliorate hot flashes, anxiety also significantly reduced weekly during sessions. For the majority of participants, anxiety remained reduced seven weeks after the end of the five study sessions. This finding is relevant to clinicians and researchers working with individuals in

the menopause transition because of the high rate of women who experience hot flashes and the substancial association between anxiety and vasomotor symptoms. The North American Menopause Society (NAMS) now recommends hypnosis as a treatment for vasomotor symptoms (Carpenter et al., 2015). Showing that a hypnosis intervention can reduce anxiety as well as hot flashes provides vital information into the utility of this easily integrated treatment.

Future studies should assess the effectiveness of hypnosis at relieving anxiety symptoms in general populations and in individuals presenting with varying levels of baseline anxiety. Additionally, research investigating the effectiveness of hypnosis in relieving physical anxiety in addition to perceived anxiety is crucial. Examining hypnotic suggestions which target physiological anxiety symptoms may additionally elucidate the mechanisms of how hypnosis creates changes in anxiety.

This research demonstrates that hypnosis is a versatile and valuable tool for those working with a population of women in postmenopause. Not only does a hypnotic intervention relieve acute anxiety, but only five sessions of hypnosis can create anxiety reductions that continue for weeks.

# APPENDIX

# APPENDIX A

## Supplemental Results

Table A.1. *Descriptive Statistics of Anxiety Questionnaires and Amount of Change in Scores from Baseline to Week 6 and Baseline to Week 12*

| | | | | | | Mean change from Baseline | |
|---|---|---|---|---|---|---|---|
| Measure | Week | Clinical hypnosis Mean(*SD*) | n | Structured attention control Mean(*SD*) | n | Clinical hypnosis | Structured attention control |
| HADS-A | BL | 8.3*(4.4)* | 92 | 8.5*(4.7)* | 94 | -- | -- |
| | 5 | 4.9*(3.1)* | 80 | 7.9*(4.7)* | 89 | -3.4 | -0.6 |
| | 12 | 4.9*(4.1)* | 75 | 7.2*(4.7)* | 85 | -3.4 | -1.3 |
| STAI-S | BL | 36.2*(11.2)* | 85 | 37.8*(12.5)* | 90 | -- | -- |
| | 5 | 28.1*(9.0)* | 84 | 36.0*(12.7)* | 86 | -8.1 | -1.8 |
| | 12 | 29.6*(10.9)* | 72 | 35.9*(13.0)* | 84 | -6.6 | -1.9 |

Note: HADS-A = Hospital anxiety and depression scale-anxiety subscale, STAI-S = State-trait anxiety inventory-state score, BL = baseline

Table A.2. *Descriptive Statistics of Current Anxiety VAS Ratings, Pre-session and Post-session at Visits One to Five and Amount of Change from Pre-session to Post-session Ratings for Those in the Hypnosis Group*

| | | | | Mean change from pre-session to post-session |
|---|---|---|---|---|
| Measure | Week | Clinical hypnosis Mean(*SD*) | n | Clinical hypnosis |
| Pre-session VAS | 1 | 4.6*(2.4)* | 91 | -- |
| | 2 | 3.4*(2.4)* | 88 | -- |
| | 3 | 2.7*(2.3)* | 87 | -- |
| | 4 | 2.8*(2.4)* | 85 | -- |
| | 5 | 2.3*(2.4)* | 84 | -- |
| Post-session VAS | 1 | 1.1*(1.1)* | 91 | -3.5 |
| | 2 | 0.8*(1.2)* | 88 | -2.6 |
| | 3 | 0.7*(1.0)* | 87 | -2.0 |
| | 4 | 0.5*(0.7)* | 85 | -2.3 |
| | 5 | 0.3*(0.4)* | 84 | -2.0 |

Note: VAS = visual analogue scale

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