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AUTONOMIC IMBALANCE AND FEMALE SEXUAL AROUSAL DISORDER: THE IDENTIFICATION OF HEART RATE VARIABILITY LEVEL AS A MARKER AND TREATMENT TARGET

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Dedication

I dedicate this hefty document to Fabián Pineda. My pursuit of this degree brought him to the United States (to Texas, no less), and this particular project has disrupted weekend plans, vacations, and other non-academic activities. Nonetheless, he continues to stick around, embraces our animal family, and challenges me to disengage when appropriate (which is more often than I care to admit). Thank you for everything.

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Abstract

Autonomic imbalance and female sexual arousal disorder: The identification of heart rate variability level as a marker and treatment target

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Heart rate variability (HRV) is widely considered to be a noninvasive marker of autonomic nervous system (ANS) function. Defined as the degree of variability in the interval lengths between consecutive heartbeats, HRV reflects the relative balance of the two branches of the ANS, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Impaired autonomic function, indexed by HRV, has been associated with a number of pathophysiological conditions, including diabetes (Liao et al., 1995), atherosclerosis (Hayano et al., 1991), and hypertension (Chakko, Kessler, & Myerburg, 1993) as well as with a general risk of negative cardiac events (Yoo, Lee, Yi, Kim, & Kim, 2011). More recently, low resting HRV has also been associated with mental health conditions that are likely related to an imbalance in autonomic activity, including depression (Kemp et al., 2010), anxiety (Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012), and alcohol dependence (Quintana, Guastella, McGregor, Hickie, & Kemp, 2013). A large body of evidence indicates that autonomic balance plays a significant role in female sexual function. Moderate SNS dominance (relative to PNS

activity) has been shown to facilitate women's genital arousal in the laboratory (Lorenz, Harte, Hamilton, & Meston, 2012; Meston & Gorzalka, 1995, 1996a, 1996b). Based both on this established relationship between the SNS and female sexual function as well as a growing clinical literature indicating that impaired HRV is associated with negative health outcomes, my dissertation studies will investigate the relationship between HRV and female sexual arousal dysfunction. This line of research will help evaluate HRV as a marker of sexual arousal problems, advance our understanding of the mechanisms underlying the association between HRV and sexual arousal, and explore novel treatment strategies that focus specifically on HRV manipulation.

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1. INTRODUCTION

1.1. Definition and prevalence of female sexual arousal disorder

1.1.1. Definition of female sexual arousal and female sexual arousal disorder

Sexual arousal in women has been defined in various ways. Although some researchers consider the term to be synonymous with genital arousal, a broader understanding of the concept incorporates both physical and mental readiness for sexual activity. Janssen and colleagues have proposed that arousal can be broken down into two key components: (1) conscious and unconscious mental processing leading to an automatic genital response and (2) a cognitive process appraising the sexual content of the stimulus (Janssen, Everaerd, Spiering, & Janssen, 2000; Spiering, Everaerd, & Janssen, 2003). The physiological genital response involves changes that occur in the body to prepare for a sexual interaction (vaginal swelling, genital warmth, and lubrication). The cognitive appraisal of the sexual stimulus is often referred to as mental or subjective sexual arousal, and it reflects the psychological state of feeling "turned on." A woman may not feel "turned on" due to problems with recognizing, processing, or appraising genital response or to a lack of subjective excitement. The absence of either genital or subjective arousal may cause significant personal distress and interpersonal difficulty.

In the *DSM-IV-TR*, female sexual arousal disorder (FSAD) is defined as a persistent or recurrent inability to attain or maintain an adequate lubrication-swelling response until completion of the sexual activity. This disturbance must cause significant distress, and it must not be better explained or accounted for by another disorder or by the effects of a substance or a medical condition. The *DSM-5* Sexual Dysfunction Subworkgroup combined FSAD and another female sexual dysfunction diagnosis from *DSM-IV-TR*, hypoactive sexual desire disorder (HSDD) to create female sexual interest/arousal disorder (FSIAD). The new, combined disorder

is defined as a lack of, or significant reduction in, sexual interest or arousal. The Subworkgroup supported the establishment of the new disorder by referencing various forms of evidence to suggest that that desire and arousal cannot be reliably distinguished in women. Specifically, the Subworkgroup noted that psychophysiological data (such as vaginal pulse amplitude) does not differentiate sexually healthy women from women who report difficulties becoming genitally aroused (e.g., Laan, Van Driel, & Van Lunsen, 2008). It was also suggested that FSAD as a distinct disorder was problematic in that it focused exclusively on the impairment of genital response and did not incorporate women's subjective perceptions of arousal (Graham, 2010). Indeed, some experts believe that women's subjective arousal may be minimally influenced by genital congestion, especially at low or moderate levels of arousal (Cohen & Goldstein, 2016).

The merging of HSDD and FSAD into one diagnosis has led to substantial controversy in the field. Balon and Clayton (2014) reviewed the evidence against the establishment of the new disorder, namely the lack of field trials testing the validity of the FSIAD diagnosis and the lack of attention paid to problems with lubrication and other genital sensations that have long been associated with absent or impaired genital sexual arousal. Additionally, recent findings suggest that there is significant genetic sharing between arousal, lubrication, and orgasm, which is independent of desire (Burri, Greven, Leupin, Spector, & Rahman, 2012). In light of this controversy, some organizations, such as the International Society for the Study of Women's Sexual Health (ISSWSH) and the US Food and Drug Administration (FDA), have chosen to follow the DSM-IV-TR diagnostic criteria for HSDD and FSAD and have therefore maintained the conceptualization of desire and arousal as distinct constructs.

This dissertation will focus exclusively on female sexual arousal independent of sexual desire; therefore, the present studies will not adhere to *DSM-5* diagnostic criteria for FSIAD.

Rather, based on the observations of Janssen and colleagues (Janssen et al., 2000) and those of other experts (Basson et al., 2003; Giraldi, 2016) regarding the two key elements of female sexual arousal (genital arousal and subjective arousal), the present studies will follow an expanded version of *DSM-IV-TR* diagnostic criteria for FSAD. These expanded criteria will include a diminished genital response and/or lack of appraisal of the response in the genitals as well as an absent or diminished subjective arousal to sexual stimuli. For women, genital sexual arousal responses do not always coincide with the subjective experience of feeling aroused and "turned on." That is, women's arousal may be based more on the interpretation of the situation than on the genital response itself. It is possible that some women may have organic genital impairments that are limiting their genital response, whereas others may have normal genital responses but have trouble recognizing them or attending to them, as they are more focused on the lack of subjective arousal (Giraldi, 2016). Therefore, it is important to consider both physiological and subjective arousal concerns when conceptualizing FSAD.

1.1.2. Prevalence of sexual arousal problems in women

Sexual arousal dysfunction is relatively common among women, but prevalence rates are inconsistent across the literature. Prevalence studies of sexual arousal problems in women have focused primarily on self-reported lack of vaginal lubrication. These studies have found that 8-15% of all women and 21-31% of sexually active women report experiencing such difficulties (for review, see Lewis et al., 2004). Similarly, Bancroft and colleagues (2003) found that 31.2% of heterosexual women in the U.S. reported lubrication problems over the past month. Within the United Kingdom, the prevalence of persistent lubrication problems, lasting three months or more, ranged from 2.6% (Mercer et al., 2003) to 28% (Dunn, Croft, & Hackett, 1999). The incidence of lubrication problems is higher among women of peri- or postmenopausal years, with

one study reporting that 44% of postmenopausal women experience persistent or recurrent lubrication problems (Rosen, Taylor, Leiblum, & Bachmann, 1993). These studies have not always included all the information necessary to diagnose FSAD, as many did not inquire about distress or level of stimulation. However, research that does reference distress has found that lubrication problems do not lead to significant distress in many women (e.g., Bancroft et al., 2003; Shifren, Monz, Russo, & Segreti, 2008).

More recent epidemiological studies have examined the prevalence of arousal problems by evaluating women's scores on the arousal domain of the Female Sexual Function Index (FSFI; Rosen et al., 2000), a validated and widely-used self-report index that assess six domains of female sexual function (arousal, lubrication, desire, pain, orgasm, and satisfaction). A population-based study of women in the United Kingdom found that 11.4% of women reported recent arousal problems (Burri & Spector, 2011). In another population-based study across 20 provinces in Turkey, the prevalence of arousal problems was 44.9% (Çayan et al., 2016). A similarly high percentage of Iranian women (37.5%) report arousal problems (Safarinejad, 2006).

1.2. Etiology of female sexual arousal

1.2.1. Genital arousal

Vaginal lubrication is the first observable sign of genital arousal in women (Masters & Johnson, 1966). As arousal increases, vasocongestion in the tissues and increased capillary pressure force more fluid into the tissues, which increases the volume of fluid to the surface of the vaginal epithelium (Levin, 2003). Estrogen receptors throughout the vaginal epithelium and in the smooth muscle fibers of the muscularis play an important role in the production and maintenance of vaginal lubrication. These receptors are responsible for ensuring adequate lubrication and thickness of the vaginal wall. Androgens, including dehydroepiandrosterone

(DHEA), may also facilitate increased lubrication through aromatization to estrogens (Bancroft, 2002), which influence nerve transmission as well as maintain the health and integrity of vaginal tissue. Indeed, treating ovariectomized rats with topical DHEA resulted in the reversal of vaginal tissue atrophy and stimulated vaginal lubrication (Sourla, Flamand, Bélanger, & Labrie, 1998). DHEA and its sulfate account for 75% to 100% of estrogens in women, before and after menopause (Labrie, Bélanger, Cusan, & Candas, 1997; Labrie, Belanger, Simard, Luu-the, & Labrie, 1995). It is well known that, when circulating estrogen decreases after menopause, vaginal lubrication also decreases. Decreases in serum estrogen levels over time result in the thinning of the vaginal epithelium and the atrophy of smooth muscle in the vaginal wall, ultimately decreasing vasodilation, lubrication, and genital sensations (Berman, 2005). Fluctuations in the sodium-potassium balance of the vaginal tissue also mediate the production of vaginal lubrication (Wagner & Levin, 1978).

After about 20 seconds of sexual stimulation, the appearance of vaginal lubrication is followed by an increase in vaginal vasocongestion to the internal and external genitals. The vascular system of the vagina is a complex network. The vaginal artery, which is composed of numerous arteries on each side of the pelvis, is connected to both the anterior and posterior vaginal surfaces. During the initial phase of arousal, precapillary arterial dilation gradually shifts to arterialized blood flow and increased venus output (Wagner & Otteson, 1980). Blood flow into the vaginal and genital region leads to engorgement and swelling of tissue in the vestibule and venus plexus, which surround the lower portion of the vagina. As blood pools in these areas, the vaginal walls become dark purple. Vasocongestion results from increased heart stroke volume and from the dilation of smooth muscle cells in the arteries that supply genital tissue(Levin, 1980). Muscle relaxation allows for the lengthening and dilation of the vagina, the

protrusion of the clitoris, and the engorgement of the vestibular bulbs (Berman, 2005). The clitoris retracts under the clitoral hood, and uterine elevation also occurs, likely due to the contraction of parametiral muscle fibers that surround the vagina and uterus (Rosen & Beck, 1988). When the orgasmic platform, or the issues of the outer third of the vagina, is formed, complete vaginal vasocongestion has occurred (Masters & Johnson, 1966). Throughout this process, well-oxygenated blood is supplied to the skin and breasts (Levin, 2002), contributing to extra-genital sensations in the breasts, the nipples, and the inner thighs.

1.2.1.1. Sympathetic and parasympathetic contributions to genital arousal

Increased blood volume can be elicited by sensory stimulation or central nervous system activation; it is also facilitated by both the sympathetic and the parasympathetic branches of the autonomic nervous system. Diffuse sympathetic nervous system (SNS) discharge occurs during the later stages of sexual arousal (Jovanovic, 1971), which precedes the increases in heart rate and blood pressure that occur during orgasm (Fox & Fox, 1969). Specifically, increases in plasma norepinephrine, a marker of SNS activity, have been associated with increases in genital arousal during sexual activity (Wiedeking, Ziegler, & Lake, 1979). Research on the sexual function of women who have suffered spinal cord injuries also provides strong support for the involvement of both the SNS and the parasympathetic nervous system (PNS). Women with spinal cord injuries between areas T11 and L2 show a lack of lubrication when presented with an erotic stimulus (Sipski, Rosen, Alexander, & Gomez-Marin, 2004); this is the area of the spinal cord where the hypogastric, sympathetic nerves project to the genital region. The union of hypogastric nerves and splanchnic fibers, which align with the parasympathetic nervous system between areas S2 and S4 (Nappi, Ferdeghini, & Polatti, 2006), form the inferior hypogastric plexus. This plexus innervates the cervix, upper vagina, urethra, vestibular bulbs, and clitoris. At

the cervix, sympathetic and parasympathetic nerves join to form the paracervical ganglia (Nappi et al., 2006). Stimulation by friction and pressure activates the paracervical ganglia and other specialized nerve endings (Krantz, 1958), generating impulses to the spinal cord and likely to the vagus nerve (Komisaruk, Gerdes, & Whipple, 1997), which facilitates parasympathetic control of the heart and other organs.

Laboratory studies have used exercise paradigms to investigate the relationship between the SNS and genital arousal. In the first of these studies, Meston and Gorzalka examined the effects of acute exercise on genital arousal (Meston & Gorzalka, 1995). Participants were asked to complete 20 minutes of intense exercise prior to viewing a neutral film followed by an erotic film. The experimenters compared the participants' genital arousal post-exercise to their genital arousal during a session that did not involve exercise. Genital arousal was significantly higher during the post-exercise erotic film than during the erotic film in the no-exercise session. Importantly, there were no differences in genital responses between sessions during the neutral film, indicating that exercise did not simply increase blood flow to the genitals; rather, it prepared the vagina for sexual arousal so that her body could respond more efficiently when in a sexual context. In addition to testing the effects of SNS activation on genital arousal via exercise and ephedrine (Meston & Heiman, 1998), Meston and colleagues have also demonstrated that suppressing SNS activity via clonidine inhibits genital arousal in women (Meston, Gorzalka, & Wright, 1997). A more recent study identified an optimal level of SNS activation to facilitate genital sexual arousal in women (Lorenz et al., 2012). Lorenz et al. found that moderate increases in SNS activity were associated with the highest levels of genital arousal, whereas very low and very high SNS innervation resulted in lower levels of genital arousal.

Though Meston et al.'s work has consistently shown that increasing SNS activation facilitates genital sexual arousal in sexually functional women, facilitating increased PNS activity or restoring the balance of the SNS and the PNS may be more appropriate for women with sexual arousal problems. When the SNS is functioning adaptively, it engages the body's "fight or flight" system in response to eminent danger (De Kloet, Joels, & Holsboer, 2005); the body releases adrenaline and glucose, while increasing heart rate and blood pressure to meet the demands of the threatening situation. To contain the stress response and restore the body to homeostasis, the PNS activates the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of cortisol that helps inhibit the SNS. Sexual stimuli also activate both the SNS, increasing oxygen uptake and blood flow from the heart, and the PNS, generating impulses to the spinal cord.

Because genital arousal requires an optimal level of SNS activation (Lorenz et al., 2012; Meston & Gorzalka, 1996a), any activation that is above or below that threshold can result in impaired sexual arousal. For this reason, increasing SNS activity does not appear to enhance genital arousal for women who already have heightened sympathetic activity at baseline. In one study, when women with high baseline SNS activity, specifically women with PTSD and a history of childhood maltreatment (Yehuda, 2003), completed an exercise protocol intended to activate the SNS, they did not experience significant increases in genital arousal compared to controls (Rellini & Meston, 2006). Depending on the etiology of the individual arousal concern, women with sexual arousal problems may have high baseline SNS activity. Indeed, decreased sexual arousal has been associated with conditions that are characterized by an overactive SNS, like PTSD (for a review, see Yehuda, Lehrner, & Rosenbaum, 2015) and childhood sexual abuse (Westerlund, 1992). For these women, treatments that target PNS activation or aim to stabilize

the balance of the SNS and PNS, such as heart rate variability biofeedback, may more effectively facilitate genital arousal than treatments that increase SNS activity.

1.2.2. Subjective arousal

Subjective arousal requires attention to erotic cues. When a woman is exposed to a sexual stimulus, her genital response is largely automatic; her subjective response, however, depends on her level of attention to the erotic stimulus and to other arousing cues, such as her partner's excitement and her own genital sensations (Janssen et al., 2000). Experimental studies have provided evidence for a strong effect of attention on subjective arousal by demonstrating that distraction inhibits the sexual arousal response (Adams, Haynes, & Brayer, 1985; Cranston-Cuebas & Barlow, 1990; Dove & Wiederman, 2000; Salemink & van Lankveld, 2005). According to Barlow's model of sexual dysfunction (Barlow, 1986), a continued focus on sexual cues increases subjective arousal and positive affect, whereas an attentional shift to internal cues or to critical, self-evaluative thoughts leads to negative affect and decreases sexual arousal.

The degree to which women are able to mentally engage in sexual activity and experience subjective arousal is influenced by a number of psychosocial variables which may distract women from erotic cues. These include variables specific to the relationship and/or the partner, beliefs and attitudes about sexuality, and a history of sexual abuse and/or other negative sexual experiences.

Women who are generally satisfied with the quality of their intimate relationships and women who report high levels of emotional intimacy with their partners are less likely to experience decreased arousal (Jiann, Su, Yu, Wu, & Huang, 2009; Pascoal, Narciso, & Pereira, 2013). Relationship factors can affect sexual arousal function if the woman is unable to communicate her sexual preferences to her partner. Specific sexual acts may not be mentally

stimulating or pleasurable to the woman, or her partner may have limited sexual knowledge or skills. When partners communicate their sexual preferences and are responsive to sexual requests, they may help mitigate arousal and other types of sexual dysfunction (MacNeil & Byers, 1997, 2009).

Sexual problems in the male partner, particularly erectile dysfunction and premature ejaculation, can negatively affect a woman's sexual arousal. Successful treatment of erectile problems results in increased sexual arousal in the female partner, as well as improvements in other domains of sexual function. Indeed, one study found that pharmacotherapy for erectile dysfunction was associated with improved sexual arousal, desire, and satisfaction among female partners (Goldstein et al., 2005).

Women who internalize negative attitudes toward sexuality or toward themselves may be at greater risk of experiencing low subjective arousal. Internalized guilt and shame related to certain sexual activities or to sexual expression in general have particularly potent effects on subjective arousal. Guilt associated with sexual experiences or sexual feelings has deleterious effects on sexual desire and arousal, even after accounting for religiosity (Woo, Brotto, & Gorzalka, 2011, 2012). Similarly, negative views about the sexual self and negative expectations about sexual encounters have been associated with decreased subjective arousal in the laboratory (Middleton, Kuffel, & Heiman, 2008).

A history of sexual abuse or negative sexual experiences affects the beliefs and attitudes that women have toward sexual activity, and these beliefs may drive persistently low subjective sexual arousal (McCarthy & Farr, 2011). Many, but not all, women with a history of childhood sexual abuse avoid intimate sexual interactions and are less receptive to/turned on by sexual approaches from their partners (Rellini, 2008). Sexual abuse at any developmental stage, but

particularly if it occurs post-menarche but prior to one's first consensual sexual experience, increases sexual embarrassment and conservatism (Kilimnik & Meston, 2017), and therefore may affect a woman's ability to form sexually satisfying partnerships.

Sexual self-schemas, defined as cognitive generalizations about sexual aspects of the self that guide sexual behavior and influence the processing of sexually relevant information (Andersen & Cyranowski, 1994), differ between women with and without a history of childhood sexual abuse (Meston, Rellini, & Heiman, 2006; Stanton, Boyd, Pulverman, & Meston, 2015). It is likely that women with negative sexual self-schemas or women who have persistently negative associations with sexual activity are less mentally engaged during sex.

Negative affect can have wide-ranging effects on female sexual function, and depressed mood can adversely affect subjective arousal. Among patients with major depressive disorder, 40-50% of women reported decreased sexual arousal (Kennedy, Dickens, Eisfeld, & Bagby, 1999). These women were not taking antidepressant medications, which are well-known to inhibit sexual arousal (Baldwin & Mayers, 2003; Clayton, El Haddad, Iluonakhamhe, Ponce Martinez, & Schuck, 2014). The cognitive model of depression (Beck, 1974) suggests that women experiencing depressive symptoms are more likely to engage in negative self-talk, which is associated with lower arousal in both sexes (Nobre & Pinto-Gouveia, 2008).

Anxiety that is related to sexual function or that occurs during sexual activity negatively impacts subjective sexual arousal. Women with sexual problems have higher rates of anxiety than sexually healthy women (Brotto, Bitzer, Laan, Leiblum, & Luria, 2010), and women with anxiety disorders are more likely to have sexual arousal dysfunction (Kalmbach, Ciesla, Janata, & Kingsberg, 2012; van den Hout & Barlow, 2000). Among sexually functional women, acute

stress has been associated with decreased subjective sexual arousal (ter Kuile, Vigeveno, & Laan, 2007).

Concern over one's sexual performance, known as performance anxiety, can direct attention from sexual to non-sexual cues, ultimately leading to decreases in subjective sexual arousal. Performance concerns in women are often directed at body image and/or perceived sexual attractiveness. Negative thoughts about one's physical appearance (Satinsky, Reece, Dennis, Sanders, & Bardzell, 2012) or perceptions that a partner disapproves of one's body (Pascoal et al., 2013) can fuel anxiety and cognitive distraction during a sexual situation, as can fears of pregnancy and/or sexually transmitted infections.

1.3. Risk factors and markers associated with female sexual arousal dysfunction

There are several psychosocial and physiologic risk factors that are known to be associated with female sexual dysfunction. These risk factors include race, age, marital status, education level, depression, smoking, and a variety of chronic illnesses, including diabetes (Laumann, Paik, Rosen, & Page, 1999; Rosen, 2002; Abdo, Oliveira Jr., Moreira Jr., & Fittipaldi, 2004; Sidi, Puteh, Abdullah, & Midin, 2007; Salonia et al., 2004). Though these risk factors are associated with increased likelihood of the heterogeneous group of female sexual dysfunctions, they are not all relevant to sexual arousal dysfunction.

The strongest risk factor that has been associated with sexual arousal problems in women is age, which is likely due to the hormonal changes that are associated with menopause. In one study, 20% of women aged 20-40 reported sexual arousal problems; this percentage increased substantially with age, with more than 70% of women aged 60-69 reporting sexual arousal concerns (Ponholzer, Roehlich, Racz, Temml, & Madersbacher, 2005). Other risk factors that have been associated with sexual arousal problems include a history of sexual abuse, marital

difficulties, anxiety, depression, being single, and urinary incontinence (Dunn, Croft, & Hackett, 1998a; Fugl-Meyer & Sjogren, 1999; Lewis et al., 2010). It is important to note that these studies, like most epidemiological studies that assess the prevalence of sexual arousal concerns and risk factors for sexual arousal problems, did not differentiate between physiological and psychological sexual arousal. Therefore, it is unclear whether these risk factors are associated with genital arousal problems (i.e. lack of or reduced genital sensations) or with subjective sexual arousal problems (i.e. not feeling mentally "turned on").

1.4. Current treatments for sexual arousal problems in women

1.4.1. Hormonal treatments

Hormonal treatments for sexual arousal concerns are sometimes effective, but they are not appropriate for all women. A few studies have examined the effects of estradiol on sexual arousal (Dennerstein, Burrows, Wood, & Hyman, 1980; Everaerd, Laan, Both, & van der Velde, 2000; Sherwin, 1991). In general, the data suggest that topical or systemic estrogen supplementation my improve lubrication, reduce dryness, and decrease irritation. Testosterone-based treatments, have also showed some promise for women who are experiencing low sexual arousal as a result of biologically compromised natural levels of androgens (Woodis, McLendon, & Muzyk, 2012). Though there are currently no FDA-approved testosterone products for the treatment of low sexual arousal in women, due in part to lack of long-term safety studies, many clinicians prescribe "off label" testosterone, in the form of intramuscular injections or subcutaneous pellets. A precursor to the biosynthesis of estrogens, androgens are important for the vitality of vaginal tissues and necessary for reproductive function (Cohen & Goldstein, 2016). Women may have low androgen levels for a variety of different reasons, some of which include age (menopause), a history of oophorectomy, and the use of hormonal contraceptives

(Cohen & Goldstein, 2016). Tibolone, a 19-nor testosterone derivative and a selective tissue estrogenic activity regulator (Brotto & Luria, 2014), may also be effective in increasing arousal. Available in 90 countries (but not in the United States), Tibolone is typically used for the treatment of endometriosis and as hormone therapy for post-menopausal women. It has also been shown to increase both lubrication and desire and has been associated with an overall improvement in sexual function (Nijland et al., 2008). There are some concerns, however, that Tibolone may increase the risk of breast cancer recurrence (Kenemans et al., 2009) and stroke (Cummings et al., 2008) in older women.

The mechanism driving the effects of these hormone-based treatments is likely increased blood flow to the genitals. Estrogen and androgen supplementation improve the health and integrity of vaginal tissues, which in turn enables increased vasocongestion and engorgement of the vaginal walls. However, the side effects of hormonal treatments may dissuade some women from pursuing them. For these women, psychosocial treatments that have similar effects on genital arousal may be more appealing.

1.4.2. Nonhormonal treatments

Certain central nervous system neurotransmitters facilitate increases in sexual arousal. The neurotransmitter dopamine plays a key role in sexual motivation and reward; changes in levels of dopamine and in the activity of dopamine receptors have been shown to activate both sexual arousal and desire. Buproprion, a norepinephrine-dopamine reuptake inhibitor (NDRI) that has been approved by the FDA as an antidepressant (Wellbutrin) and as a smoking cessation aid (branded as Zyban), may have beneficial effects for women with sexual arousal disorder. When used to treat hypoactive sexual desire among non-depressed premenopausal women, buproprion (Wellbutrin) led to a modest improvement in both sexual arousal and sexual desire

(Segraves, Clayton, Croft, Wolf, & Warnock, 2004). Other dopamine agonists that have been used for this purpose include cabergoline and ropinirole (Afonso, Mueller, Stewart, & Pfaus, 2009). In addition, non-hormonal neuropeptides, specifically oxytocin and prolactin, have been used clinically to target increases in arousal and desire (for review, see Bancroft, 2005).

Vasoactive agents, specifically phosphodiesterase inhibitors (PDEis), have been investigated in several studies for the treatment of FSAD. In a small proportion of studies, women with FSAD reported increased physiological arousal after taking a phosphodiesterase type 5 inhibitor (PDE-5; e.g., sildenafil (Viagra)), but in general, these vasoactive drugs had no effect when compared with placebo (for a review, see Chivers & Rosen, 2010). It is important to note that, in the studies that did demonstrated a significant relationship between PDE-5s and increased genital arousal, the drugs did not increase participants' subjective arousal. This suggests that, for women, psychological factors such as relationship satisfaction, mood state, and context may play a more important role in facilitating increased sexual arousal than do physiological genital cues. If this is the case, drugs that target increasing vasocongestion are likely to be most effective in women whose primary complaint is decreased genital responding, experienced as decreases in lubrication and/or feelings of vaginal fullness or engorgement. For women who do not have a primary complaint of decreased genital sensations, a drug that increases vaginal engorgement will only be effective to the extent that the engorgement is detected and labeled as *sexual feelings*, thus contributing to increased subjective arousal.

Though there are no FDA-approved pharmacological treatments for sexual arousal problems in women, the EROS clitoral therapy device (Urometrics, St. Paul, Minnesota) has been approved to address arousal concerns. This small handheld device increases vasocongestion in the clitoral and labial region via a suction mechanism and has been reported to increase

vaginal lubrication and sensations (Billups et al., 2001). Recently, researchers have suggested that pharmacological treatment for sexual arousal concerns in women may need to combine a PDE-5 inhibitor with another agent, such as testosterone, that increases sensitivity to sexual cues (Poels et al., 2013).

1.4.3. Psychological treatments

Psychological treatments for low arousal include couples therapy that emphasizes adequate stimulation, the use of topical lubricants, and mindfulness training. Couples therapy may include psychoeducation surrounding the factors that affect arousal, as well as relationship-building exercises (e.g., scheduling times for physical and emotional intimacy), communication training (e.g., opening up about sexual needs and concerns), and sexual fantasy training (e.g., training people to develop and explore mental imagery). Lubricants may be helpful for women who are experiencing vaginal dryness, which may be contributing to low physiological arousal.

In general, however, researchers have noted a paucity of high-quality controlled trials of psychological treatments for arousal concerns (Brotto, Basson, & Luria, 2008; Heiman, 2002). The two psychological interventions that have showed some promise for the treatment of arousal problems in women are mindfulness and autogenic training. Studies from Brotto and colleagues (2008a; 2008b) have shown that mindfulness, which focuses on facilitating awareness of bodily sensations, increased self-assessed genital wetness despite little or no change in genital arousal and led to marginally significant improvements in subjective arousal and perceived genital sensations during an erotic stimulus. Mindfulness may affect sexual arousal function through improved interoceptive awareness (Silverstein, Brown, Roth, & Britton, 2011) and increased attention to sexually relevant physiological cues (de Jong, 2009). By focusing on the physical sensations of sexual activity instead of being preoccupied with current levels of desire or arousal,

women can learn to be present and attentive to both their genital sensations and their subjective feelings of arousal during sexual situations.

Autogenic training has also led to increases in sexual arousal in both sexually functional women and women with FSAD. When engaging in this training, practitioners are guided to focus on increasing certain sensations (e.g., heaviness, warmth) in different parts of the body (Linden, 1994). In two studies, genital and subjective arousal were measured before and after participants listened to an autogenic training recording (Stanton, Hixon, Nichols, & Meston, 2018; Stanton & Meston, 2016). Significant increases in both genital and subjective arousal were observed post-autogenic training in sexually functional women, whereas women with FSAD only experienced significant increases in subjective arousal. Autogenic training and mindfulness both aim to increase awareness of and attention to bodily sensations; however, autogenic training instructs participants to actively conjure these sensations, whereas mindfulness does not.

1.5. Heart rate variability

1.5.1. Definition and analysis methods

The fluctuation in the lengths of time between successive heartbeats is known as heart rate variability (HRV). Experts agree that HRV reflects both the dynamics of the autonomic nervous system (ANS) and an individual's ability to adapt to environmental and physiological challenges (for a review, see McCraty & Shaffer, 2015). An optimal level of HRV within an individual indicates a healthy, adaptive balance of the two major branches of the ANS, the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS). Too much variability (e.g., arrhythmias) is detrimental to physiological functioning, while too little variation is indicative of chronic stress, pathology, or inadequate self-regulation (Singer et al., 1988; Thayer, Hansen, Saus-Rose, & Johnsen, 2009).

Given that healthy systems are constantly in flux, an indicator of the vitality of the human body is its ability to adjust to the autonomic state that is most appropriate for its current context. Heart rate at any one time represents the net effect of the output of the parasympathetic (vagus) nerves, which act to slow down heart rate, and sympathetic nerves, which act to accelerate it (McCraty & Shaffer, 2015). Parasympathetic activity is dominant when heart rate is below 100 bpm, the intrinsic rate that is generated by the sinoatrial node (Opthof, 2000). When heart rate increases above 100 bpm, sympathetic activity becomes dominant. The inability of these physiological systems to adapt to context is associated with a variety of clinical conditions (e.g., Acharya, Joseph, Kannathal, Lim, & Suri, 2006; Palatini, 1999; Xhyheri, Manfrini, Mazzolini, Pizzi, & Bugiardini, 2012). Analysis of HRV provides insight into the relationship between autonomic balance and clinical phenomena.

Heart rate variability is typically analyzed via time domain methods or frequency domain methods. Time domain indices are relatively simple to calculate; they quantify the amount of variance in the inter-beat interval (IBI) lengths using traditional statistical measures. Most commonly reported in the literature is the standard deviation of normal-to-normal (SDNN) IBIs, which is measured in milliseconds. This measurement is a general reflection of the ebb and flow of all of the factors that contribute to HRV. For a more nuanced examination of HRV, power spectral analysis separates the HRV waveform into its component rhythms that operate within different frequency bands. The European Society of Cardiology and the North American Society of Pacing and Electrophysiology Task Force (Malik et al., 1996) divided heart rate oscillations into four primary frequency bands. The high frequency (HF) band, which includes oscillations between 0.15 Hz to 0.4 Hz, reflects parasympathetic (vagal) activity, as it corresponds to heart rate variations that are related to the respiratory cycle (Porges, Doussard-Roosevelt, & Maiti,

1994). For this reason, the HF band of HRV is sometimes referred to as respiratory sinus arrhythmia (RSA). During inhalation, the cardiorespiratory center inhibits vagal outflow, which increases heart rate; during exhalation, vagal outflow is restored, and heart rate decreases (Eckberg, 1983). The low frequency (LF) band, which is defined as oscillations that range from 0.04 Hz to 0.15 Hz, is indicative of baroreflex function when the body is at rest (Moak et al., 2007). The baroreceptors are stretch-sensitive receptors in the heart (Malliani, 1995). Some research has suggested that the LF band is influenced primarily by sympathetic activity (e.g., Montano et al., 1994; Pal et al., 2013), but this perspective is controversial (Reyes del Paso, Langewitz, Mulder, van Roon, & Duschek, 2013). The very low frequency (VLF) band, which refers to oscillations that occur between 0.0033 Hz and 0.04 Hz, appears to be associated with long-term regulatory mechanisms, such as thermoregulation and certain hormonal systems (Cerutti, Bianchi, & Mainardi, 1995). Finally, the ultra low frequency (ULF) band, which includes all oscillations below 0.0033 Hz, is associated with the circadian rhythm, core body temperature, and other slow acting systems (McCraty & Shaffer, 2015).

1.5.2. Heart rate variability, autonomic imbalance, and health

Heart rate variability is considered an index of one's capacity for self-regulation. Compared to lower resting state HRV, higher resting state HRV has been associated with adaptive self-regulation and increased social engagement during times of distress (Geisler, Kubiak, Siewert, & Weber, 2013). Another study found that HRV level is associated with self-regulation, specifically in the context of alcohol cravings (Quintana et al., 2013). In this study, alcohol-dependent outpatients with low resting HRV were more likely to experience increased alcohol cravings compared to their counterparts with higher resting HRV. These data align well with polyvagal theory (e.g., Porges, 1995, 1997, 2001), which suggests that HRV is associated

with the experience and expression of both social and emotional behavior. The theory makes an important distinction between myelinated and unmyelinated vagus nerves; according to Porges (2001), the myelinated vagus nerves are associated with changes in HRV and therefore with social engagement and approach behaviors. In combination with the sympathetic nervous system, the unmyelinated vagus nerves, which are phylogenetically older than the myelinated nerves, support the individual when the body is in danger (Kemp & Quintana, 2013), leading to what is often referred to as the "fight or flight" response. Polyvagal theory indicates that optimal self-regulation and social engagement (indexed by HRV) can only occur when the individual is perceived to be safe and secure in her surroundings.

The analysis of HRV, via both time domain and frequency domain methods, has been used to assess autonomic function and to quantify risk for a variety of both cardiac and non-cardiac disorders. It is well known that HRV decreases with age, therefore age-adjusted HRV values are typically used in the context of risk prediction for these disorders (Umetani, Singer, McCraty, & Atkinson, 1998). Age-adjusted HRV has been associated with all-cause mortality (Dekker et al., 1997; Tsuji et al., 1994), and this association has been attributed to poor autonomic cardiac control. The Framingham Heart Study revealed that, in a large community-based sample, the estimation of heart rate variability offers prognostic information beyond that provided by the evaluation of traditional risk factors (Tsuji et al., 1994). Similarly, Dekker and colleagues (1997) found that, among middle-aged men, the relative rate of total mortality was 2.1 percent higher in men with HRV <20 milliseconds (msec) compared to men with HRV between 20-39 msec. Impaired autonomic nervous system function, which is indicated by reduced HRV, increases risk for developing components of metabolic syndrome, including hypertension, diabetes, and obesity. Indeed, reduced HRV has been associated with all three of these

components (Koskinen et al., 2009; Licht, De Geus, & Penninx, 2013; Soares-Miranda et al., 2012; Windham et al., 2012). Reduced HRV has also been linked to inflammatory markers in individuals with no apparent heart disease (Sajadieh et al., 2004).

In addition, HRV has also been examined in relation to different psychological disorders that are characterized by disrupted autonomic function, including depression, anxiety, and alcohol dependence. Several meta-analyses (e.g., Kemp et al., 2010, 2012) have revealed that reduced HRV is characteristic of otherwise healthy patients who have been diagnosed with major depressive disorder (MDD). Moreover, reductions in HRV have been associated with increasing depression severity. Patients with MDD and comorbid generalized anxiety disorder (GAD) display the greatest reductions in HRV, relative to MDD patients without any notable comorbid psychological conditions and to patients with comorbid posttraumatic stress disorder (Kemp et al., 2012). Kemp and colleagues (2012) concluded that this association between low resting HRV and GAD may be particularly strong because patients with GAD are typically hypervigilant and find it difficult to disengage from perceived threats; therefore, they may have chronic withdrawal of the PNS and consistent over activation of the SNS. Alcohol dependent patients also display reductions in HRV compared to non-dependent controls, independent of cardiovascular disease and comorbid psychiatric problems (Quintana et al., 2013). Though HRV improves after prolonged abstinence from alcohol, it remains significantly reduced compared to nonalcoholic control groups (Karpyak, Romanowicz, Schmidt, Lewis, & Bostwick, 2013). Overall, these findings support the conclusion that HRV plays a key role in both physical and mental wellbeing.

1.5.3. Heart rate variability and female sexual arousal

Given the established link between the two branches of the ANS and female sexual arousal, it is reasonable to expect that heart rate variability is also related to both genital arousal

and subjective arousal in women. As a marker of heart health, HRV indexes the body's ability to alter blood flow and blood pressure in order to meet the demands of a given situation. Selective manipulation of blood pressure is particularly relevant for physiological sexual arousal in women, which results from genital vasocongestion and increased blood flow to the genitals. When blood begins to pool in the vaginal walls, the increase in blood volume leads to increased pressure inside the capillaries, which subsequently triggers lubricated plasma to transcend the vaginal epithelium onto the surface of the vagina (Levin, 1980). These platelets form droplets, creating the lubricative film that typically covers the vaginal walls during sexual activity. Increased blood flow also leads the clitoris and the vestibular bulbs to protrude and become engorged (Berman, 2005), and well-oxygenated blood is supplied to the skin and the breasts (Levin, 2002). A recent study by Lorenz and colleagues (2012) provided evidence supporting the relationship between HRV and sexual arousal function. In this study, the experimenters found a curvilinear relationship between percent change in HRV and percent change in VPA, such that small positive percent changes in HRV were associated with the highest levels of VPA, while either large positive or large negative changes in HRV were associated with the lowest levels of VPA. Although this study used HRV as a specific marker of SNS activity, more recent work has challenged the interpretation of HRV as an index of cardiac sympathetic control (Reyes del Paso et al., 2013). Instead, HRV appears to reflect the balance of the two branches.

The polyvagal theory (Porges, 1992, 2001) suggests that HRV is not only relevant to sympathovagal balance; it also may be a way of mapping arousal regulation. Relating autonomic function to behavior, the polyvagal theory specifies that the autonomic nervous system is (1) influenced by the central nervous system, (2) sensitive to afferent influences, and (3) characterized by adaptive reactivity that reflects the phylogeny of the autonomic nervous system

(Porges, 2009). The theory also speaks to the role of HRV in the experience and expression of emotional or social behavior. Lower HRV is triggered by the perception of threat, which activates the amygdala, triggers a "flight or fight" response, and activates social withdrawal, whereas higher HRV facilitates approach-related behaviors like social engagement (Kemp & Quintana, 2013). In a sexual context, HRV level may "map" arousal regulation in the sense that it provide us with information about whether an individual (a) is capable of suppressing or enhancing arousal or (b) feels the need to suppress or enhance their arousal. This mapping of arousal regulation likely applies to both genital and subjective arousal, given that physiological *and* psychological modifications must be made to meet the demands of a sexual situation.

Indirectly, HRV may also affect subjective sexual arousal in women, particularly in relation to the processing of emotional cues. Considered to be an indicator of emotional responding, HRV reflects an individual's ability to respond adaptively to emotional cues (Appelhans & Luecken, 2006). Adaptive response to emotional cues is particularly relevant to psychological sexual arousal, as the subjective processing of a sexual stimulus as "arousing" results from a conscious appraisal of that stimulus, in its context, in the presence of positive affective or emotional feedback (Basson, 2002). Emotions that are expressed with sensitivity to the situational context in which they unfold are more likely to facilitate adaptive responses (Gross, 1998). This is true for sexual situations, during which subjective arousal (feeling mentally "turned on") is healthy and adaptive.

1.6. Overview of dissertation studies

This dissertation aims to evaluate HRV level as a marker for sexual arousal problems and target for treatments to improve sexual arousal in women. The five studies presented in this document highlight the relationship between HRV and sexual arousal, examine the mechanisms

driving that relationship, and investigate the effects of HRV-targeted interventions on both physiological and psychological sexual arousal in women with and without sexual arousal concerns.

2. EXPLORING THE RELATIONSHIP BETWEEN HEART RATE VARIABILITY AND FEMALE SEXUAL AROUSAL

2.1. Overview

The two studies included in this chapter examine the relationship between heart rate variability and female sexual arousal. The first study (Study 1) assesses the feasibility of using HRV as an index of women's self-reported sexual arousal function and overall sexual function outside the laboratory. Women with below average resting HRV were significantly more likely to report sexual arousal dysfunction ($p < .001$) and overall sexual dysfunction ($p < .001$) than both women with average resting HRV and women with above average resting HRV. Based on these results, we concluded that low HRV might be a marker of female sexual arousal dysfunction and overall sexual dysfunction.

The second study (Study 2) examines the hypothesis that differences in vagal activity between sexually functional and sexually dysfunctional women may be driving the association between low HRV and sexual problems. The high frequency component of HRV, known as respiratory sinus arrhythmia (RSA), has been shown to be a reliable measure of both overall PNS activity and the strength of vagal influence on the heart (Berntson et al., 1997; Malik et al., 1996). Acute changes in RSA have been linked to positive psychological phenomena. Rapid withdrawal of vagal activity leads to quick increases in heart rate (Berntson, Cacioppo, & Quigley, 1993), which enables the body to respond effectively to environmental triggers. In this study, RSA was assessed before, during, and after physiological sexual arousal in sexually functional and dysfunctional women. The change in RSA from baseline to the erotic film was significantly different ($p < .02$) between function and dysfunctional women. Specifically, the dysfunctional group exhibited vagal activation, while the function group experienced vagal

withdrawal. These findings provided additional specificity to the recently established relationship between HRV and female sexual function while also proposing RSA, and HRV in general, as a potential treatment target.

2.2. Study 1. Heart rate variability: A marker for female sexual dysfunction[1]

2.2.1. Introduction

Heart rate variability (HRV) has emerged as a valuable non-invasive test to assess autonomic nervous system (ANS) activity (Xhyheri et al., 2012). Several studies have linked low resting HRV to mental health conditions including depression, anxiety, and alcohol dependence, indicating these disorders may be related to an imbalance in autonomic activity (Kemp et al., 2010; Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012; Quintana, Guastella, McGregor, Hickie, & Kemp, 2013). As HRV is an index of the balance of sympathetic nervous system (SNS) and parasympathetic nervous system activity (PNS), it has proven a useful tool for examining the relative role of SNS activity in female sexual arousal (Lorenz, Harte, Hamilton, & Meston, 2012). Moderate SNS dominance (relative to PNS activity) has been shown to predict women's genital arousal in the laboratory (Lorenz et al., 2012; Meston & Gorzalka, 1996a; Meston & Gorzalka, 1996b; Meston & Heiman, 1998; Meston & Gorzallka, 1995). Given these findings, it is reasonable to expect ANS activity (indexed by HRV) may be related to women's self-reported, real-life sexual arousal function outside of the laboratory. The present study is the

[1]Stanton, A.M., Lorenz, T. A., Pulverman, C.S, & Meston, C. M. (2015). Heart rate variability: A risk factor for female sexual dysfunction. *Applied Psychophysiology and Biofeedback*, *40*(3), 229–327.
Contribution statement: The first author designed the research, analyzed the data, drafted the paper, and revised the paper. The second and the third authors collected the data and revised the paper. The fourth author designed the research, drafted the paper, and revised the paper.

first to examine HRV as a potential marker of clinically relevant sexual arousal function and overall sexual function in women.

Heart rate variability refers to the variation over time between consecutive heartbeats and is one of the most sensitive and objective measures of the interplay between the SNS and the PNS, the two major branches of the ANS. Autonomic balance of these two branches creates a dynamic equilibrium of vital functions. When the body is physiologically and psychologically stable, PNS input into heart rate is greater than SNS input, resulting in a lower heart rate and relatively greater influence of breathing-related fluctuations (the respiratory sinus arrhythmia) on heart rate (i.e., higher HRV). When physiological or psychological stress is high, increased SNS activity helps coordinate increased rates of heartbeats and breathing, leading to relatively less influence of breathing-related fluctuations on heart rate (i.e., lower HRV).

Increasing evidence indicates autonomic balance, specifically SNS dominance, plays a significant role in female sexual function. In a series of studies by Meston and colleagues (Lorenz et al., 2012; Meston & Gorzalka, 1996a; Meston & Gorzalka, 1996b; Meston & Heiman, 1998; Meston, Gorzalka, & Wright, 1997; Meston & Gorzalka, 1995), moderate activation of the SNS using either exercise (Meston & Gorzalka, 1996a; Meston & Gorzallka, 1995) or ephedrine (Meston & Heiman, 1998) facilitated genital sexual arousal, and suppression of the SNS using clonidine inhibited genital arousal (Meston, Gorzalka, & Wright, 1997). In order to further examine the role of autonomic balance and to test the hypothesis that there may be an optimal level of SNS activation for facilitating genital sexual arousal, Meston and Gorzalka (1996a) induced SNS activation via exercise and measured the effect of low, moderate, and high levels of SNS activation on genital arousal by assessing arousal at 5, 15, and 30 minutes post-exercise. They found that high SNS activation (5 minutes post-exercise) inhibited genital arousal; the

opposite effect of what was seen in earlier literature. Moderate SNS activation (15 minutes post-exercise) and low SNS activation (30 minutes post-exercise) still facilitated significant increases in physiological arousal (Meston & Gorzalka, 1996b). Moreover, a recent study demonstrated an optimal level of SNS dominance for facilitating women's physiological sexual arousal (Lorenz et al., 2012).

Heart rate variability, specifically, plays both a direct and an indirect role in female sexual arousal function. Directly, HRV may index cardiovascular health, which is critical for genital sexual arousal. Sexual arousal is largely a matter of selective manipulation of blood pressure in the genitals. As HRV is a marker of heart health (for review, see Rajendra Acharya, Paul Joseph, Kannathal, Lim, & Suri, 2006), it is also a marker of the body's ability to modulate blood pressure appropriately to context. Indirectly, HRV's role in sexual arousal function relates to the processing of emotional cues. A proven indicator of emotional responding (Appelhans & Luecken, 2006), HRV reflects an individual's capacity to respond to emotional cues, which is particularly relevant to sexual arousal function (Heiman, 1980). In this context, low resting HRV may be more reflective of poor emotional health than above average resting HRV is indicative of good emotional health.

The laboratory studies by Meston and colleagues examined the relationship between women's genital sexual arousal and different levels of experimentally induced SNS activation. However, there is currently no research on the effect of variations in *resting* autonomic balance on sexual arousal function and sexual function in general. Clinical literature has shown that low resting HRV, which is generally indicative of relative SNS dominance, is a marker of various negative physical and mental health outcomes (Kemp & Quintana, 2013). The present study is the first to determine the effect of resting state autonomic balance, indexed by HRV, on validated

measures of sexual arousal function and sexual function at large. To date, there are no validated physiological markers of sexual dysfunction in women. If HRV proves to be a marker of sexual dysfunction, it could have widespread implications for developing a cost effective, objective, and empirically validated means for monitoring changes in female sexual arousal function.

In sum, based both on evidence that moderate and low levels of SNS activation facilitated genital arousal (Meston & Gorzalka, 1995; Meston & Gorzalka, 1996a) yet high levels of SNS activation inhibited genital arousal (Meston & Gorzalka, 1996b) and on a growing clinical literature indicating that low HRV (generally indicative of high SNS), is associated with negative health outcomes (Kemp & Quintana, 2013), we predicted a positive linear relationship between HRV and sexual arousal function. That is, we predicted that women with autonomic balance indicating moderate or low resting SNS activity (relative to PNS activity) would be less likely than women with autonomic balance indicating high resting SNS to report clinically relevant sexual arousal dysfunction on an empirically validated scale of sexual function. We also predicted that this relationship would hold for overall sexual function.

2.2.2. Methods

Participants

Participants were selected from three experiments, one previously published elsewhere (Lorenz et al., 2012, contributing n = 39) and two unpublished studies (contributing n = 33). No participant's data was used more than once. In each study, participants were recruited from The University of Texas at Austin psychology subject pool and from the Austin area community using flyers, online advertisements, and print advertisements that highlighted the sexual nature of the experiments. Potential participants were screened over the phone to ensure that they met the inclusion and exclusion criteria. Please see Table 1 for participant characteristics and Table 2 for

general inclusion and exclusion criteria. One of the unpublished studies recruited both women with and without histories of childhood sexual abuse; however, because differences in sexual distress and sexual satisfaction have been observed between women with and without abuse histories (Rellini & Meston, 2007), only data from women without abuse histories were used in the present sample.

Table 1

Participant Characteristics (N = 72)

	M	***SD***
Age (years)	22.7	4.3
FSFI (total score)	28.0	5.2
HRV neutral	67.5	19.8
HRV resting norm, female, age 10-29[a]	66.0	18.0
HRV resting norm, female, age 30-49[a]	58.0	13.0
	n	**%**
Race		
Caucasian	45	62.5
African American	2	2.8
Asian American	8	11.1
Other/missing	17	23.6
Relationship status		
Single/dating	40	55.6
Married or in a committed relationship	30	41.7
Divorced	1	1.4
Other	1	1.4
Sexual identity		
Exclusively or predominately heterosexual	63	87.5
Equally heterosexual and lesbian	7	9.7
Exclusively or predominately lesbian	2	2.8

[a]Normative resting HRV values established by Umetani et al. (2008).

Table 2

Inclusion and exclusion criteria

Inclusion criteria	
At least 18 years of age	
Currently sexually active	
Exclusion criteria	***N***
Lorenz et al., 2012	39
Current self-reported sexual complaints within domains of sexual desire, sexual arousal, and/or sexual pain, and/or a history of treatment for sexual dysfunction	
History of sexual trauma	
Use of medication known to affect sexual or vascular functioning, with the exception of hormonal contraceptives	
Untreated Axis I disorders	
Medical conditions likely to affect sexual arousal	
Unpublished study 1	21
History of sexually transmitted diseases	
Past pelvic surgery	
Current pelvic, vaginal, or urinary tract infection	
Neurological impairment	
Unpublished study 2	12
Current self-reported sexual complaints within domains of sexual desire, sexual arousal, and/or sexual pain, and/or a history of treatment for sexual dysfunction	
History of sexually transmitted diseases	
Past pelvic surgery	
Current pelvic, vaginal or urinary tract infection	
Neurological impairment	

Procedure

Although the studies included in this paper had different objectives, they were all conducted within the same laboratory and followed the same general procedure. Testing sessions took place in a private room with an intercom that participants used to communicate with the researcher. Participants were instructed in how to attach the wires for an electrocardiogram (ECG) before the session began. In all three studies, vaginal photoplethysmography was used to assess physiological sexual arousal; these data are not considered in the present manuscript but some of the main findings can be found in Lorenz, Harte, Hamilton, and Meston (2012). . After participants attached the wires and inserted the vaginal probe, they underwent a 5-10 minute habituation period where no measurements were taken. Participants then watched a 3-minute neutral (nonsexual) film followed by one of a set of erotic films validated to produce sexual arousal. While all participants viewed a neutral film followed by an erotic film, only HRV data collected from the entire 3-minute neutral film segments were used in analyses as our index of resting HRV. Following the neutral film, participants in all three studies viewed an 8-10 minute erotic film clip, during which HRV was also measured. The two film segments (neutral, then erotic) were always presented in the same order. All participants completed measures on demographics and sexual function (see below). Participants gave informed consent and were compensated between $10-50, depending on the number of sessions and on the study completed.

Measures

Heart Rate Variability. In the Lorenz et al. (2012) study, heart rate was measured during the neutral film segment at a rate of 80 samples/sec. In the other two studies, heart rate was measured at a rate of 200 samples/sec. These sampling rates are adequate to produce a minimally biased estimate of time domain measures of HRV, such as those presented here

(Hejjel & Roth, 2004; Ziemssen, Gasch, & Ruediger, 2008).. The three leads of the ECG were placed under the participant's right collarbone, below the lowermost left rib, and on the right ankle. The signal from the leads was collected with AcqKnowledge software, and movement artifacts were removed manually. The AcqKnowledge peak finder function was used to isolate the beat-to-beat (NN) intervals.

Heart rate variability was calculated using the standard deviation of the NN intervals (SDNN), one of the most widely used techniques to analyze HRV (Xhyheri et al., 2012). Research has shown that SDNN, a time domain index, is an effective and accurate marker of HRV and can reflect the relative contribution of the SNS to the regulation of heart rate. Specifically, a high SDNN is thought to reflect low SNS (and/or high PNS) activity, while a low SDNN is thought to reflect high SNS activity (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). After collecting all of the NN intervals for each participant, SDNN for the neutral film segment was computed using Kubios HRV Analysis Software (Biosignal Analysis and Medical Imagine Group, University of Kuopio, Kuopio, Finland).

Sexual Function. Sexual function was assessed with the Female Sexual Function Index (FSFI; Rosen et al., 2000), an empirically validated, 19-item questionnaire. The FSFI assesses six domains of sexual function: desire (2 items), arousal (4 items), vaginal lubrication (4 items), orgasm (3 items), satisfaction (3 items), and sexual pain (3 items). The clinical cutoff that reliably discriminates between women with and without a sexual dysfunction diagnosis is 26.55 (Rosen et al., 2000). In other words, women whose scores are above that cutoff are considered sexually functional, and women whose scores fall below that cutoff are considered sexually dysfunctional (Rosen et al., 2000).

2.2.3. Analysis

Regression analyses were used to test the relationship between sexual function and SDNN. Separate linear regression analyses were conducted for the sexual arousal function domain of the FSFI as well as for the FSFI total score, controlling for age as a covariate. Finally, FSFI total scores were used to dichotomize participants as either sexually functional or sexually dysfunction. A logistic regression analysis was then conducted to assess the ability of SDNN to predict sexual function status (functional or dysfunctional).

Analysis of variance (ANOVA) tests were used to test the relationship between SDNN groups and sexual function. Participants were categorized into one of three HRV groups (below average, average, and above average) based on previously published normative SDNN values (Umetani et al., 1998). Umetani and colleagues (1998) defined the effects of age and gender on the normal range of time domain HRV over nine decades in healthy subjects. They found that HRV declined with age, and HRV was lower in women than in men until age 30, when gender differences decreased. In the current study, SDNN was calculated from the neutral film segments in order to match the HRV normative values (Umetani et al., 1998), which apply to resting HRV only. Among the three groups, there were no significant differences with respect to sexual orientation and age. There were, however, significant differences in relationship status among the three groups, $F(1,71) = 4.535$, $p < .02$. Significantly more single women were in the average HRV group than in the below average and above average groups. There were also significant differences in race, $F(1,71) = 4.138$, $p < .02$. Significantly more Asian American women and women of other/unspecified racial identities were in the average HRV group than in the below average and above average groups.

All analyses were conducted with SPSS statistical software version 22.0.0 (SPSS Inc., Chicago, IL, USA). In all analyses, a two-tailed $p < .05$ was considered statistically significant.

2.2.4. Results

Sample Characteristics. The final sample included 72 women, aged 18-39 (M = 22.7, SD = 4.3; see Table 1). With respect to relationship status, 55.6% of the participants were single or dating, and 41.7% reported being married or in a committed relationship. The sample was 62.5% Caucasian, 11.1% Asian American, and 2.8% African American. Based on the FSFI, 70.8% of the participants in this sample were considered sexually functional (M = 28, SD = 5.2), and 29.2% were considered sexually dysfunctional. Please see Table 3.

Table 3

HRV (SDNN)[a] category by sexual function (FSFI)[b] status

	Below average HRV	Average HRV	Above average HRV	
	***n* (%)**	***n* (%)**	***n* (%)**	χ^2
Sexual function status				8.69[c]*
Dysfunctional	8 (11.1)	12 (16.7)	1(1.4)	
Functional	6 (8.3)	31 (43.1)	14 (19.4)	

[a]Normative resting HRV values established by Umetani et al. (2008).
[b] Sexual function status determined by empirically validated FSFI clinical cutoff score (Rosen et al., 2000).
[c]Chi-square with Fisher's Exact Text.
*$p < .05$

Resting HRV and Sexual Arousal Function. To determine if resting SDNN was associated with sexual arousal function, we performed a linear regression with FSFI arousal domain scores regressed on SDNN. The overall model was significant, $R^2 = .15$, $F(1, 71) =$

12.395, $p < .001$ (see Figure 1), with SDNN significantly correlating with sexual arousal function. As SDNN increased, sexual arousal function also increased.

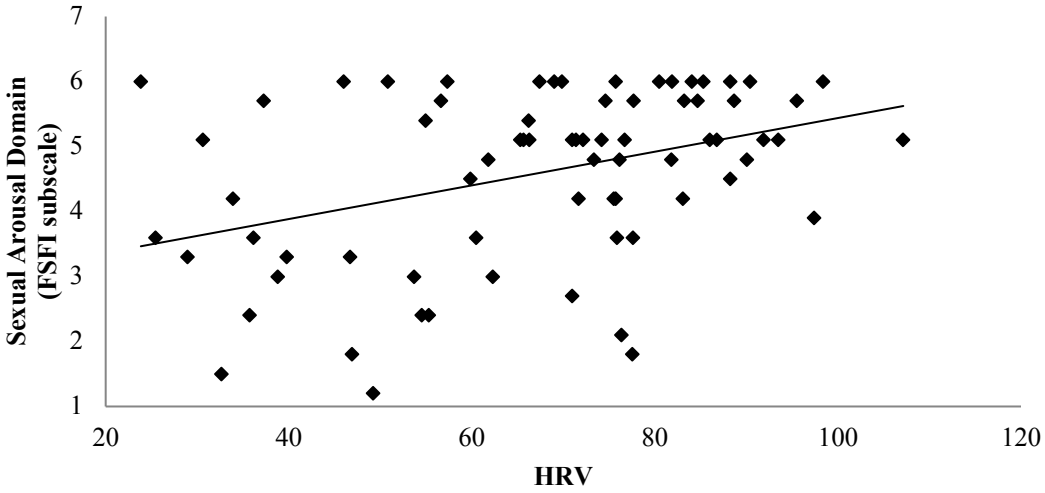

Figure 1. Linear relationship between resting HRV and sexual arousal function.

A one-way ANOVA revealed a significant effect of HRV group (below average, average, above average) on sexual arousal function, $F(2, 69) = 7.113$, $p = .003$. As a Levene statistic of 3.973, p = .023 revealed that the homogeneity of variance assumption was violated among the three groups, we used Welch's F test to correct this violation. Planned specific contrasts indicated that women with below average HRV had significantly lower scores on the FSFI sexual arousal scale (indicative of more severe arousal dysfunction) than women with average HRV and women with above average HRV combined, $t(16.109) = 2.819$, $p = .012$. This difference had a moderate effect size, $r = .57$. See Figure 2.

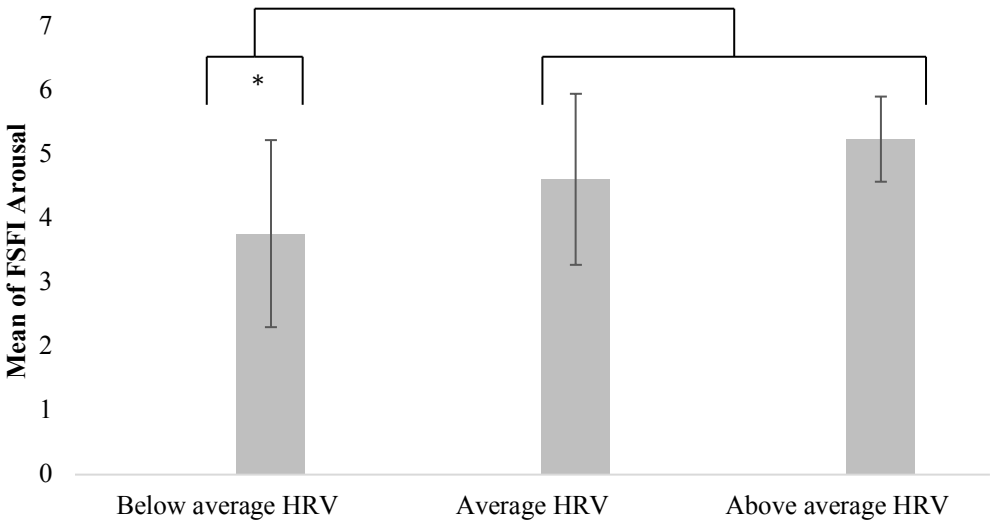

Figure 2. Mean FSFI arousal domain scores by HRV group.

Resting HRV and Overall Sexual Function. To determine whether resting SDNN was associated with overall sexual function (that is, the combined domains of desire, arousal, lubrication, orgasm, satisfaction, and pain), we performed a linear regression with FSFI total scores regressed on SDNN. The overall model was significant, $R^2 = .16$, $F(1, 71) = 13.359$, $p < .001$ (see Figure 3), with SDNN significantly correlating with overall sexual function.

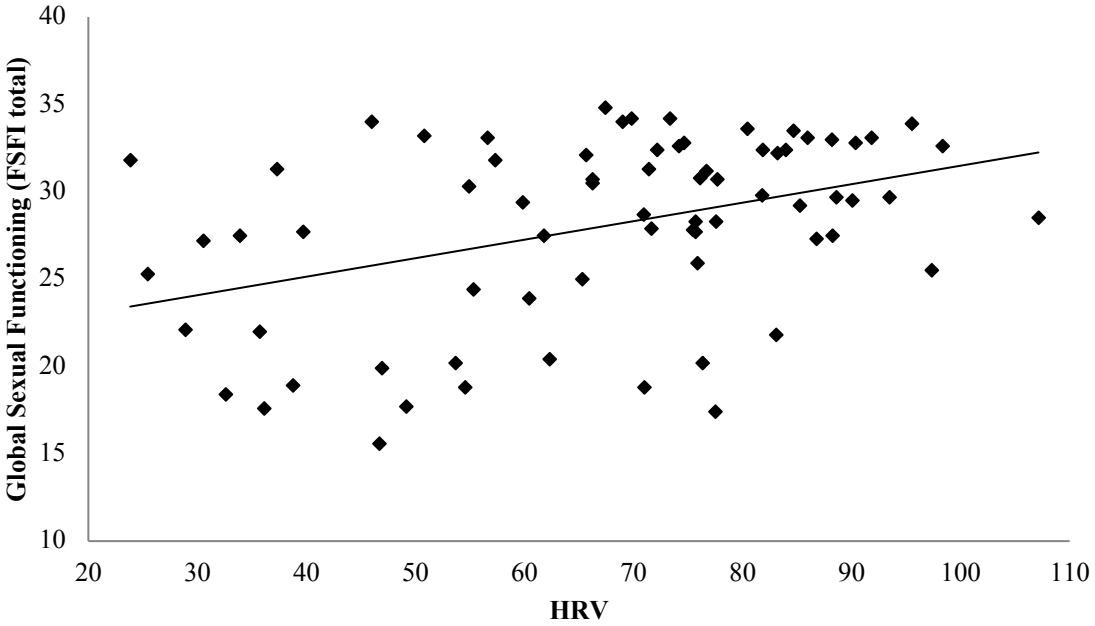

Figure 3. Linear relationship between resting HRV and overall sexual function.

A one-way ANOVA indicated that there was a significant effect of HRV group (below average, average, above average) on overall sexual function, $F(2, 69) = 6.257$, $p = .003$. As above, a Levene statistic of 4.469, p = .015 revealed that the homogeneity of variance assumption was violated among the three groups, and thus we used Welch's *F* test. Planned contrasts revealed that women with below average HRV had significantly lower total FSFI scores (indicative of poorer overall sexual function) than both women with average HRV and above average HRV combined, $t(16.015) = 3.145$, $p = .006$. This difference had a moderate to high moderate effect size, $r = 0.62$. Further, compared to women with average HRV, women with below average HRV had significantly lower total FSFI scores, $t(20.234) = 2.380$, $p = .027$. As with sexual arousal function, the effect size was moderate, $r = 0.47$. See Figure 4.

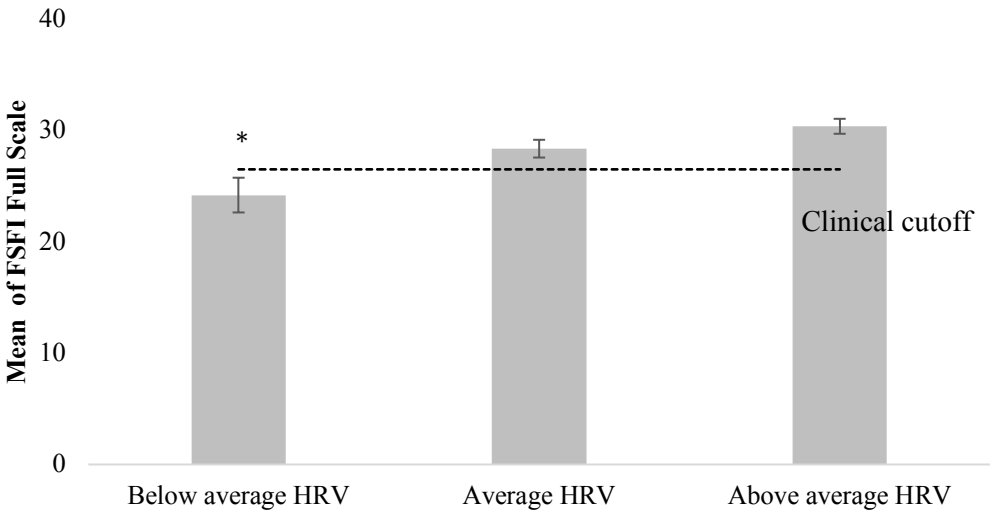

Figure 4. Mean FSFI full-scale scores by HRV group.

A logistic regression indicated that resting SDNN significantly predicted sexual function status, B = .045, Wald $\chi^2(1) = 9.091$, $p = .003$. Participants were dichotomized into two groups, a clinical sexual dysfunction group and a non-clinical sexual function group, using Rosen and colleagues' (2000) empirically validated FSFI clinical cutoff score. The lower the SDNN

measured during the neutral film, the more likely a participant's FSFI total score fell in the dysfunctional range. During the neutral film, each additional unit increase in SDNN was associated with an increased likelihood (OR = 1.046) of being categorized as sexually functional.

HRV During Erotic Film and Overall Sexual Function

There are currently no established normative values for SDNN during sexual arousal; however, we present summary statistics from our data in Table 4. A logistic regression analysis indicated that SDNN during the erotic film segment significantly predicted sexual function status, B = .049, Wald $\chi^2(1) = 11.287$, $p = .001$. Again, the lower the SDNN measured during the erotic film, the more likely the participants' FSFI total scores placed them in the dysfunctional range. During the erotic film, each additional unit increase in SDNN was associated with an increased likelihood (OR = 1.05) of being categorized as sexually functional.

Table 4

HRV during neutral and erotic films by sexual function (FSFI)[a] status

	Average HRV during neutral film		Average HRV during erotic film	
	SDNN	***sd***	***SDNN***	***sd***
Sexual function status				
Dysfunctional	55.87	19.52	51.01	19.07
Functional	72.28	18.02	71.63	20.47

[a] Sexual function status determined by empirically validated FSFI clinical cutoff score (R. Rosen et al., 2000).

2.2.5. Discussion

This study examined the relationships between SDNN, an index of resting HRV, and sexual arousal function and overall sexual function in women. Results indicated that low resting

HRV, which is indicative of a highly SNS-dominant autonomic balance, significantly predicted scores on a self-report measure of sexual arousal dysfunction and overall sexual dysfunction. Furthermore, sexual function status (functional or dysfunctional) was significantly associated with HRV group. That is, women who had below average resting HRV (relatively high SNS) had significantly lower FSFI scores compared to women who had average resting HRV (moderate SNS dominance) or above average resting HRV (low SNS dominance). These findings are consistent with both recent clinical literature on HRV and research on the effect of autonomic balance on female genital arousal. Given that low resting HRV has been associated with depression, anxiety, and alcohol dependence (Kemp et al., 2010; Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012; Quintana, Guastella, McGregor, Hickie, & Kemp, 2013), it is not surprising that low HRV may also predict female sexual dysfunction. These findings are also consistent with laboratory studies, which indicated that high levels of SNS activation inhibit (Meston & Gorzallka, 1996b) while moderate and low SNS levels facilitate genital sexual arousal (Meston & Gorzalka, 1996a; Meston & Gorzallka, 1995).

An examination of SDNN during the erotic film clip revealed that HRV during this segment was also a significant predictor of sexual function as measured by the FSFI. It is possible that physiological responses during the erotic film clip, rather than those that occurred during the neutral film clip, may better approximate physiological responses in real world situations. However, this measure may be limited in clinical utility, given the difficulty in assessing HRV during sexual arousal; as such, it is important to note that resting HRV was also a significant and robust predictor of sexual dysfunction.

The results of this study have implications for research on the relationship between HRV and sexual function in women. Although this study is the first to link resting HRV to female

sexual arousal function and overall sexual function, there is already an established relationship between resting HRV and erectile dysfunction (ED) in men. The present study indicated that low HRV, which is often linked with SNS dominance, might place women at risk for sexual arousal problems and overall sexual difficulties. Similarly, research on men has shown that sympathetic pathways play an anti-erectile role while parasympathetic pathways play a pro-erectile role (Giuliano & Rampin, 2004). In men without sexual arousal problems, an increase in PNS activity signals endothelial cells in the penis to release relaxing agents (Solomon, Man, & Jackson, 2003), which cause smooth muscle relaxation in the arteries supplying the erectile tissue. This process leads to an increase in blood flow to the penis as well as a decrease in outflow from the penis. In men with sexual arousal problems, the elevation of SNS activity negatively affects vascular functioning and disturbs the sympathovagal balance, which inhibits blood flow (McVary, 2006; Simpson, Doux, Lee, & Yun, 2006). Because SNS activity tends to be elevated in men with ED (McVary, 2006; Simpson, Doux, Lee, & Yun, 2006; Pagani, 2000), HRV has been used as a marker of ED (Pagani, 2000). HRV has been shown to be significantly lower in men with ED relative to healthy controls (Fernandez et al., 2010; Lee et al., 2011).

In women, genital arousal is mediated by some of the same mechanisms as genital arousal in men (Levin, 2002). Both male sexual function and female sexual function rely on smooth muscle relaxation and vasodilation to allow for increased blood flow to the genitals. In women, smooth muscle relaxation leads to increased blood flow into the cavernosal tissues present in the clitoral bulbs. During sexual arousal, the clitoral bulbs fill with blood and cuff the vaginal opening, which leads to an expansion of the vulva. If smooth muscle relaxation does not occur, blood flow to the cavernosal tissues is hindered and genital arousal is impaired (Levin,

2002). Given that SNS activity is elevated in both men and women with sexual arousal problems, insights from the literature on HRV and ED may apply to female sexual dysfunction.

One such insight that may be relevant to female sexual dysfunction is the relationship between ED and cardiovascular disease (CVD). ED has been shown to be a robust early indicator of CVD (Billups, Bank, Padma-Nathan, Katz, & Williams, 2005; Thompson et al., 2005). Impeded blood flow resulting from atherosclerosis initially manifests in small arteries (Roose, 2003), so the small penile artery is particularly vulnerable to blockage (Montorsi et al., 2005). Males who present with erectile dysfunction of vascular rather than psychological origin who are asymptomatic for ischemic heart disease have been shown to be at increased risk for future negative cardiovascular events (Greenstein et al., 1997; Montorsi et al., 2005). It is important to note that CVD is the leading cause of death for both men and women in the United States (Coulter, 2011). More women die each year of CVD than men, and the lifetime risk of developing CVD in women by age 50 is 39% (Coulter, 2011). Because the vascular mechanisms governing male sexual function are similar to those involved in female sexual function, it is possible that arousal dysfunction could be an early prognostic factor for CVD in women.

HRV has been associated with anxiety (Kemp, Quintana, Felmingham, Matthews, & Jelinek, 2012), depression (Kemp et al., 2010), and now with female sexual dysfunction. Female sexual dysfunction is also associated with anxiety and depression (Laurent & Simons, 2009). Heart rate variability may be a marker of some third variable, potentially automatic imbalance, which then leads to depression, anxiety, and female sexual dysfunction. Further research in this area should investigate common variables among the three disorders.

To our knowledge, these results provide the first empirical evidence for low HRV as a potential marker of sexual dysfunction in women. If this finding is replicated in future studies,

HRV may prove to be a cost effective, easy to administer, and non-intrusive index for both assessing potential sexual dysfunction and for monitoring treatment progress. This could be of interest to clinicians treating patients with female sexual arousal dysfunction, particularly in patients with co-morbid conditions relevant to cardiovascular function.

It is worth noting several limitations of this study. Given the difficulties inherent in assessing heart rate variability outside the laboratory, and the necessity of using self-report data to determine participant's sexual function, the generalizability of these findings is uncertain. Future research may benefit from a portable device that calculates HRV, which allows participants to measure their own HRV from home (Bloemers et al., 2010). Also, although the vaginal photoplethysmography is generally considered non-invasive (Janssen, Prause, & Geer, 2007) and participants were given an adequate habituation period, the insertion of a vaginal probe may have been an unusual experience which may have affected our measure of HRV, particularly in women with sexual dysfunction. Some participants in this study (n = 12) were not screened for conditions and medications that could alter sexual response and SNS activity. Specifically, because we used archival data across studies with varied sampling strategies and procedures as well as different aims, we did not have data on mental health variables such as depression or anxiety, which may be a mediating pathway between HRV and sexual function. Future research on the relationship between HRV and sexual function should control for such factors and others that could impact SNS activity, such as smoking, athleticism, and antidepressant medication use.

Despite these limitations, however, the results of this study reveal a significant relationship between HRV and sexual function, thus establishing low HRV as a potential marker of sexual dysfunction in women. Furthermore, HRV may also be a useful marker of treatment-

related improvements in sexual arousal function, and it may be used as an index of sexual arousal function in clinical trials of medications developed to treat female sexual arousal disorders.

2.3. Study 2. Vagal activity during physiological sexual arousal in women with and without sexual dysfunction[2]

2.3.1. Introduction

Heart rate variability (HRV) has recently been associated with female sexual function (Stanton, Lorenz, Pulverman, & Meston, 2015). In that study, HRV level, indexed by the standard deviation of the inter-beat interval lengths (SDNN; a time-domain measure of HRV), was a significant predictor of sexual function status. Women with below average HRV were significantly more likely to report sexual arousal dysfunction and overall sexual dysfunction than women with average HRV and women with above average HRV. In other words, low HRV may be a marker for female sexual dysfunction, as it is for depression (Kemp et al., 2010) and anxiety (Kemp et al., 2012), disorders all characterized by autonomic imbalance.

Fluctuation in HRV that occurs in the high frequency range, most often defined as .15 to .4 hertz (Hz), is a result of respiratory sinus arrhythmia (RSA), the increase and decrease in heart rate that occurs with respiration (Porges, Doussard-Roosevelt, & Maiti, 1994). RSA is primarily associated with parasympathetic nervous system (PNS) activity via the vagus (10^{th} cranial) nerve (Berntson et al., 1993). High frequency HRV, indexed by RSA, has been shown to be a reliable

[2] Stanton, A.M., Pulverman, C.S, & Meston, C. M. (2016). Vagal activity during physiological sexual arousal in women with and without sexual dysfunction. *Journal of Sex & Marital Therapy, 43*(1), 78-89.
Contribution statement: The first author designed the research, analyzed the data, drafted the paper, and revised the paper. The second author collected the data and revised the paper. The third author designed the research, drafted the paper, and revised the paper.

measure of both overall PNS activity and the strength of vagal influence on the heart (Berntson et al., 1997; Malik et al., 1996).

There is a large body of evidence indicating that the PNS modulates psychophysiological arousal. Much of the variation in heart rate derives from the PNS, which controls the brain stem regions that connect to the heart through the vagus nerve. During inhalation, heart rate increases as vagal, or PNS, influence decreases. During exhalation, heart rate decreases as vagal influence increases. This process of inhalation and exhalation, increasing and decreasing PNS influence, has regular period cycles.

The quantification of RSA provides an opportunity to dynamically monitor vagal regulation of the heart in a variety of conditions. The vagus responds rapidly to changing metabolic demands due to emotional arousal, environmental triggers, or even simple changes of posture (Salata & Zipes, 1991). Optimally, during physical and emotional challenges that demand physiological mobilization, there is an acute withdrawal of vagal inhibition of the heart, which leads to increased heart rate. During these moments of physiological and psychological stress, sympathetic nervous system (SNS) activity becomes dominant relative to parasympathetic nervous system (PNS) activity. The dominance of the SNS allows for increased physiological arousal to help the body respond to challenges (Appelhans & Luecken, 2006).

The sympathetic nervous system (SNS) has been shown to play an important role in female sexual arousal. Moderate SNS dominance (relative to PNS dominance) has been shown to predict women's level of genital arousal in the laboratory (Lorenz & Meston, 2012; Meston & Gorzalka, 1995, 1996a, 1996b; Meston & Heiman, 1998). Research has consistently indicated that moderate SNS activation facilitates genital sexual arousal in women (Meston & Gorzalka, 1995, 1996a, 1996b). By contrast, there has been little direct examination of the role of the

parasympathetic nervous system (PNS) in female sexual function. As differences in vagal activity have been shown to discriminate between individuals with disorders characterized by autonomic imbalance and individuals without those disorders, it is possible that differences in vagal activity between sexually functional and sexually dysfunctional women may help account for the association between low HRV and female sexual dysfunction.

With regard to the PNS, there are two commonly used methods of assessing vagal activity—measuring resting RSA and measuring acute changes in RSA due to stressful situations or demanding tasks. Most relevant here, acute changes in RSA have been linked to positive psychological phenomena. In healthy individuals, rapid withdrawal of vagal activity, or rapid decrease in RSA, occurs in response to stressful situations (Berntson et al., 1994). Rapid withdrawal of vagal activity leads to quick increases in heart rate (Berntson et al., 1993) and enables the body to respond effectively to environmental triggers. In other words, rapid vagal withdrawal in demanding situations is healthy and adaptive. Smaller acute differences, or slower vagal withdrawal, in response to challenging psychological and physiological tasks has been associated with disorders characterized by autonomic imbalance, including major depressive disorder (Rottenberg, Salomon, Gross, & Gotlib, 2005), generalized anxiety disorder (McLeod, Hoehn-Saric, Porges, Kowalski, & Clark, 2000), and posttraumatic stress disorder (Sack, Hopper, & Lamprecht, 2004). Following the stressful situation, rapid vagal rebound is also typical of healthy populations (Mezzacappa, Kelsey, Katkin, & Sloan, 2001). Poor vagal rebound has been shown to predict autonomic imbalance, specifically poor response to physiological stress (Cole, Blackstone, Pashkow, Snader, & Lauer, 1999) and risk for cardiovascular disease (La Rovere, Bigger, Marcus, Mortara, & Schwartz, 1998).

In the field of sexual medicine, researchers have examined the relationship between vagal activity and orgasm. Komisaruk, Gerdes, and Whipple (1997) studied vaginal and cervical self-stimulation in a sample of women with traumatic spinal cord injury at various levels of the spinal column and determined that vagal pathways can convey sensory activity from the cervix, independent of the spinal cord. Studies using both positron emission tomography (PET; Whipple & Komisaruk, 2002) and functional magnetic resonance imaging (fMRI; Komisaruk & Whipple, 2005) confirmed that the vagus nerves convey genital sensory activity from the cervix to the brain in women with and without spinal cord injury. Moreover, Frangos, Ellrich, and Komisaruk (2015) recently indicated that stimulation of vagal afferents in the external ear activates genital sensations. This body of evidence suggests an important role for vagal pathways in the orgasm domain of female sexual function.

Even though vagal pathways have been shown to facilitate the communication of sensory activity from the vagina to the brain, to our knowledge, there have been no investigations of the relationship between vagal activity and sexual dysfunction in women beyond the orgasm domain. The present study is the first to examine vagal activity before, during, and after physiological sexual arousal in women with and without clinically relevant sexual dysfunction. Based both on evidence that SNS activation, which is inversely correlated with PNS activation, facilitates female sexual arousal (Lorenz & Meston, 2012; Meston & Gorzalka, 1995, 1996a, 1996b; Meston & Heiman, 1998) and that HRV (SDNN) is associated with female sexual function (Stanton, Lorenz, et al., 2015), we predict that women with sexual dysfunction would show higher RSA during sexual arousal, slower vagal withdrawal, and slower vagal recovery, than sexually functional women.

2.3.3. Methods

Participants

Participants with and without sexual dysfunction were recruited from the Austin area community using flyers, online advertisements, and print advertisements that highlighted the sexual nature of the experiment. Potential participants were screened over the phone to ensure that they met the inclusion criteria. Inclusion criteria were as follows: at least 18 years of age, currently sexually active, fluent in English, heterosexual or bisexual, and current sexual dysfunction or no current sexual dysfunction. Exclusion criteria included currently breastfeeding or pregnant; current diagnosis of posttraumatic stress disorder, major depressive disorder, or generalized anxiety disorder; history or current diagnosis of sexually transmitted disease; history of major pelvic surgery; currently taking medications likely to affect sexual arousal, such as anxiolytics or beta blockers; and current diagnosis of psychosis (e.g. bipolar disorder or schizophrenia). Women currently taking alprazolam (Xanax) were permitted to participate in the study if they agreed to refrain from taking it the day of their study session.

Procedure

The experimenter greeted the participants and invited them to read and sign a consent form. Testing sessions took place in a private room with an intercom that participants used to communicate with the researcher. Vaginal photoplethysmography was used to assess physiological sexual arousal, but these data are not considered in the present manuscript. An electrocardiogram (ECG) was used to isolate HRV, specifically high frequency HRV, during the session. Participants were instructed in how to use the vaginal photoplethysmograph and attach the ECG wires before the session began. Once the participants had the equipment in place, they underwent a three to five minute habituation period where no physiological measurements were

taken. They then viewed a 9-minute film composed of neutral (3 minute) and erotic (6 minutes) content while their genital sexual arousal and HRV were measured. The erotic film featured a heterosexual couple engaging in foreplay, cunnilingus, and vaginal intercourse. Baseline HRV measurements were collected during the neutral film segment, arousal HRV measurements were collected during the erotic film segment, and recovery HRV measurements were collected in the three minutes following the erotic film segment. All participants completed measures on demographics and sexual function (see below). Participants were compensated monetarily for their time. This procedure was approved by the Institutional Review Board of the University of Texas at Austin.

Measures

High frequency heart rate variability (respiratory sinus arrhythmia). Heart rate was measured at a rate of 200 samples/sec. This sampling rates was adequate to produce a minimally biased estimate of frequency domain measures of HRV, such as those presented here (Hejjel & Roth, 2004; Ziemssen et al., 2008). The three leads of the ECG were placed under the participant's right collarbone, below the lowermost left rib, and on the right ankle. The signal from the leads was collected with AcqKnowledge software, and movement artifacts were removed manually. The AcqKnowledge peak finder function was used to extract the beat-to-beat (NN) intervals.

Power spectral densities of the NN-interval variability were determined via the Fast Fourier Transform using Kubios HRV Analysis Software (Biosignal Analysis and Medical Imagine Group, University of Kuopio, Kuopio, Finland). Following the guidelines established by the North American Society of Pacing and Electrophysiology (Malik et al., 1996), this software isolates spectral power into low frequency (LF; .04-.15 Hz) and high frequency (HF; .15-.4 Hz)

bands. For the present study, only HF HRV was examined, as it is associated exclusively with PNS activity (Berntson et al., 1993). Respiratory sinus arrhythmia, defined as HF HRV, was transformed via the natural logarithm to reduce the skewness of its distribution. This natural logarithm-transformed measure of RSA was then used as an index of vagal activity.

Sexual function. Sexual function was assessed with the Female Sexual Function Index (FSFI; Rosen et al., 2000), an empirically validated, 19-item questionnaire. The FSFI is a widely used measure of female sexual function. The clinical cutoff that reliably discriminates between women with and without a sexual dysfunction diagnosis is 26.55 (Rosen et al., 2000). In the present study, women whose scores were above that cutoff were considered sexually functional, and women whose scores fell below that cutoff were considered sexually dysfunctional. The FSFI assesses six domains of sexual function: desire (2 items), arousal (4 items), vaginal lubrication (4 items), orgasm (3 items), satisfaction (3 items), and sexual pain (3 items). However, only FSFI total scores were used in the present study.

Subjective sexual arousal. Subjective sexual arousal was assessed with the 3 original subjective sexual arousal items from Heiman and Rowland's (1983) Film Scale, which assesses sexual arousal as well as positive and negative affect in response to an erotic film. These 3 items include: "sexual arousal", a sense of "mental sexual arousal", and one reverse-scored item on feeling "sexually turned off". Participants rated the degree to which they experienced each of the three items on a 7-point Likert scale. Subjective sexual arousal was used to ensure that the sexually functional group and the sexually dysfunctional group found the erotic film to be comparably arousing.

2.3.5. Analysis

To determine the overall trajectory of RSA before, during, and after physiological sexual arousal, we applied a linear mixed effects model, a form of hierarchical linear modeling, to the data. The term "mixed effects" refers to the use of both fixed and random effects in the same analysis. Mixed effects models are essential tools for the analysis of longitudinal data, as they provide a flexible approach to the analysis of repeated measurements on each subject over time (Peng & Lu, 2012). Although these data are not longitudinal in the traditional sense, they do map three distinct time points (before, during, after the erotic film) across a 12-minute period.

To examine potential differences in vagal withdrawal and recovery between sexually functional and sexually dysfunctional women, RSA difference scores (between baseline and erotic, and erotic and recovery) were calculated for each participant. Welch's t-tests were applied to these difference scores.

2.3.6. Results

Sample characteristics. The final sample included 84 women, aged 18-47 (M = 26.9, SD = 6.8). With respect to relationship status, 51.2% of the sample was in a committed relationship. The majority of the sample was Caucasian (65.5%), 10.7% were Asian American, 8.3% were African American, 1.2% were American Indian or Native Alaskan, 1.2% were Pacific Islanders, and 10.7% listed "other". In terms of sexual function status, 42.9% of the participants were categorized as sexually functional based on the FSFI (see Table 5 for full demographics). Between the sexually functional and sexually dysfunctional groups, there were no significant differences with respect to age, relationship status, or race.

Table 5

Participant Characteristics (N = 84)

	M	***SD***
Age (years)	26.9	6.8
FSFI (total score)	24.6	6.3
Sexually functional group[a]	30.2	2.3
Sexually dysfunctional group[a]	20.9	4.3
	n	**%**
Race[b]		
American Indian/Alaska Native	1	1.2
African American/Black	7	8.3
Caucasian/White	55	65.5
Asian American	9	10.7
Pacific Islander	1	1.2
Other	9	10.7
Relationship status		
Single, not dating	14	16.7
Single, dating	10	11.9
In a committed relationship	43	51.2
Married	17	20.2
Sexual function[a]		
Sexually functional	36	42.9
Sexually dysfunctional	40	47.6
Invalid FSFI score	8	9.5

[a]As defined by the FSFI (R. Rosen et al., 2000).
[b]Participants could identify as belonging to more than one race.

Respiratory sinus arrhythmia and sexual function. The fixed effects considered in these analyses were time and sexual function group (functional or dysfunctional), and the random effect was an intercept value that applied to the subject identification number. The time variable violated the homogeneity of variance assumption, so a correction was applied. There was a trend toward a significant interaction effect between sexual function group and time (before, during, after the erotic film) on RSA, $F(2, 140) = 2.76$, $p = 0.07$.

With respect to vagal reactivity from the baseline segment to the erotic segment, a Welch's t-test revealed that the change in RSA from baseline to erotic was significantly different between the two groups ($t = -2.35$, $p = .02$). As is evident in Figure 5, the dysfunctional group exhibited activation, rather than withdrawal, between baseline measurements and erotic measurements. The functional group had some, though limited, RSA withdrawal. With respect to RSA rebound, the change in RSA from erotic to recovery was not significantly different between the two groups.

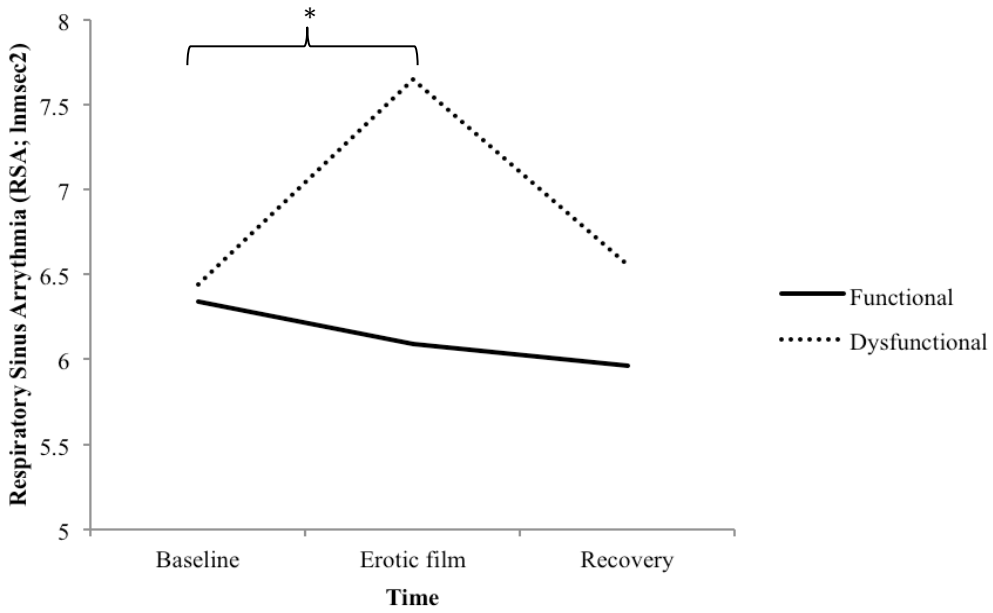

Figure 5. Relationship between time and RSA in sexually functional and sexually dysfunctional women.

Subjective sexual arousal. A Welch's t-test revealed that level of subjective sexual arousal did not differ significantly between the sexually functional group and the sexually dysfunctional group ($t = 0.04$, $p = .97$). The two groups of participants found the stimulus film to be comparably arousing.

2.3.7. Discussion

This study examined the relationship between vagal activity and sexual function during physiological sexual arousal in the laboratory in women. Results revealed a trend toward a statistically significant difference in RSA based on sexual function group across baseline, arousal, and recovery. Most importantly, the shift in RSA from the baseline time segment to the erotic time segment significantly differed between the sexually functional women and the sexually dysfunctional women. Sexually functional women exhibited vagal withdrawal (evidenced by a decrease in RSA), as would be expected, yet sexually dysfunctional women showed vagal activation (evidenced by an increase in RSA). In other words, differences in vagal activity from baseline to the presentation of an erotic stimulus may be contributing to the association between low HRV and female sexual dysfunction. To our knowledge, this is the first study to measure RSA during sexual arousal in women with clinically-relevant sexual dysfunction. This study adds additional specificity to our understanding of the relationship between HRV and female sexual function, indicating that vagal pathways may be worth targeting in treatments for sexual dysfunction.

The finding that sexually dysfunctional women showed vagal activation from the baseline to the erotic segment is consistent with research on autonomic function during sexual arousal in sexually healthy women. Laboratory studies have indicated that moderate SNS activation contributes to increased genital sexual arousal in sexually functional women (Meston

& Gorzalka, 1995, 1996a). Considering that SNS activation is associated with increases in sexual arousal in healthy women, it is not surprising that sexually dysfunctional women exhibit vagal activation, which is indicative of PNS dominance over the SNS, during sexual arousal.

The results of this study also align with previous research on vagal activity in both healthy and clinical populations. In healthy individuals, vagal activity is highest when the body is unchallenged or at rest (Rottenberg, 2007). The vagal pathway slows heart rate below its autonomous rhythm, allowing the body to conserve energy until environmental conditions become more demanding. This pattern was evident in the sexually functional group, who showed a slight drop in RSA from baseline to the erotic film segment (see Figure 1). According to polyvagal theory (Porges, 1995), the inability to withdraw the vagal break and to allow for sympathetic activation in the face of environmental demands prevents optimal engagement and coping with challenging tasks. Diminished vagal reactivity and lack of vagal withdrawal in response to environmental demands has been associated with different forms of psychopathology, including major depressive disorder (Rottenberg, Salomon, Gross, & Gotlib, 2005), generalized anxiety disorder (McLeod et al., 2000), and posttraumatic stress disorder (Sack et al., 2004). Now, based on this data, we may be able to apply polyvagal theory to female sexual dysfunction, which, like the disorders mentioned above, is associated with autonomic imbalance. In the sexual dysfunction group, there was no withdrawal of the vagal break to allow for sympathetic activation, thus preventing healthy sexual function.

It is worth noting that the observed differences in vagal activity between sexually functional and sexually dysfunctional women cannot be attributed to differences in subjective sexual arousal. In other words, the erotic stimulus was comparably arousing to both groups of women. Using the same measurement instrument as the current study, past studies have also not

found significant differences in subjective sexual arousal between sexually functional and sexually dysfunctional women (Meston & Gorzalka, 1996a; 1996b).

This examination of vagal activity, indexed by RSA, during sexual arousal in women with and without sexual dysfunction has a number of important clinical implications. It is possible that lack of vagal withdrawal during sexual arousal, which requires physiological mobilization, contributes to the precipitation and maintenance of female sexual dysfunction. Future research may point to effective methods of facilitating vagal withdrawal during sexual arousal as a potential treatment for female sexual dysfunction. Such treatments may feature physiological awareness training, mindfulness components, and intentional manipulation of RSA. HRV biofeedback may be helpful to increase resting state HRV in women with sexual dysfunction, which may in turn reduce vagal activation during sexual arousal. Although pre-existing HRV interventions, which are designed to take place when patients are at rest, may be effective for treating sexual dysfunction, it is also possible that targeted physiological awareness interventions that specifically decrease vagal activation *during* sexual arousal may need to be developed.

Furthermore, it would be clinically beneficial for the field to clarify the relationship between vagal activity and sexual function in different populations of women, such as women with sexual dysfunction related to childhood sexual abuse (CSA) and women with antidepressant medication-induced sexual dysfunction. Women with CSA histories are known to have unique disruptions in autonomic nervous system activity (Putnam, 2003), and they are less responsive to standardized sex therapy treatments than non-abused women (L. a. Berman, Berman, Bruck, Pawar, & Goldstein, 2001; Maltz, 2002, 2012). A better understanding of vagal activity during sexual arousal in women with CSA histories would be an integral first step in developing

effective physiological awareness-based treatments for this population. Women with antidepressant-induced sexual dysfunction may have a different trajectory of vagal activity during sexual arousal than women who are not on antidepressants, as two years of antidepressant medication use has been shown to significantly decrease RSA and cardiac vagal control (Licht et al., 2008). An estimated one in six American women has been prescribed an antidepressant (Rosen, Lane, & Menza, 1999), and all antidepressants are associated with sexual side effects. However, there are few treatments for these sexual side effects that do not interfere with therapeutic efficacy, and the treatments that have shown some promise are entirely pharmacologic in nature (Taylor, Rudkin, & Hawton, 2005). More recent evidence indicates that acute exercise may improve antidepressant-related genital problems (Lorenz & Meston, 2012), therefore it may be worth examining other physiological-based treatments for this vulnerable population. If women who are prescribed antidepressants stop taking their medication due to sexual side effects, they may be at risk of having a major depressive episode. Developing effective non-pharmacologic, physiologically oriented treatments for this sub-group of women may help prevent the onset of a new episode.

This study underscores an important clinical distinction between male sexual function and female sexual function. In men, parasympathetic pathways have been shown to facilitate sexual arousal (Giuliano & Rampin, 2004). An increase in PNS activity during sexual arousal activates endothelial cells in the penis to relax the smooth muscle in the arteries supplying the erectile issue (Solomon et al., 2003). Based on the findings of the present study, it seems that, in women, rapid vagal activation is characteristic of sexual dysfunction rather than sexual function. Clinicians, particularly primary care physicians, gynecologists, sex therapists, and other sexual

medicine specialists, need to be sensitive to this difference when treating female patients with sexual problems.

It is important to note some limitations of the present study. First, we relied on the FSFI, a self-report measure, to dichotomize participants into either the sexually functional group or the sexually dysfunctional group. Although this index has been extensively validated and translated into over 30 languages worldwide (Sun, Li, Jin, Fan, & Wang, 2011), the FSFI does not differentiate among the different female sexual dysfunction disorders, which may have led to a fairly heterogeneous collection of sexual dysfunctions in the sexually dysfunctional group of the present study. On the other hand, the potential for heterogeneity within the sexual dysfunction group adds strength to our findings, indicating that the observed difference in vagal activity between the two groups is not specific to a certain type of dysfunction. Second, the use of vaginal photoplethysmography may have altered our overall measurement of HRV, especially for those women in the sexual dysfunction group who may have become anxious or concerned about the insertion of the probe. However, vaginal photoplethysmography is generally considered non-invasive (Janssen et al., 2007), and participants were given a standardized habituation period to adjust to the presence of the plethysmograph prior to the collection of physiological data. Finally, though we did exclude participants who reported a current diagnosis of major depressive disorder or generalized anxiety disorder, we did not collect data on trait or state anxiety or depressive symptoms, which may mediate the relationship between vagal activity and sexual function. Vagal activity is known to be blunted in anxious populations (Thayer, Friedman, & Borkovec, 1996), and there have been mixed reports on the relationship between vagal activity and depression (for review, see Rottenberg, 2007). Future research on the relationship between vagal activity and sexual function should assess these variables.

Despite these limitations, the results of this study provide more specificity to our understanding of the recently established relationship between low HRV and clinically-relevant female sexual dysfunction by pointing to vagal pathways as a potential target for future treatment. This study also lends additional support to the suggestion that HRV and its component frequency bands may play a mechanistic role in female sexual function (Stanton, Lorenz, et al., 2015). High frequency HRV, indexed by RSA and mediated entirely by vagal pathways, may be an important internal marker of individual differences in physical responsiveness and healthy adaptation to sexual situations. Given this possibility, interventions that target changes in RSA may be a valuable option for women with sexual dysfunction.

3. EXPERIMENTALLY INCREASING HEART RATE VARIABILITY IN THE LABORATORY

3.1. Overview

The two studies included in this chapter attempted to experimentally increase HRV in the laboratory to facilitate increases in sexual arousal. In both studies, the HRV manipulation was autogenic training. A relaxation technique that restores the balance between the activity of the sympathetic and the parasympathetic branches of the autonomic nervous system, autogenic training has been shown to significantly increase HRV (Miu, Heilman, & Miclea, 2009). The first of these two studies (Study 3) assessed vaginal pulse amplitude and subjective sexual arousal before and after a short session of autogenic training in sexually functional women. Post-autogenic training, significant increases in both VPA ($p < .05$) and subjective sexual arousal ($p < .005$) were observed. Moreover, change in HRV from pre to post manipulation significantly moderated changes in subjective sexual arousal ($p < .05$), when it was measured continuously during the erotic stimulus.

In the second study (Study 4), the same experimental paradigm was tested on a sample of women who met diagnostic criteria for FSAD. Marginally significant increases in discrete subjective sexual arousal ($p = .051$) and significant increases in perceived genital sensations ($p = .018$) were observed. In addition, degree of change in HRV significantly moderated increases in subjective arousal measured continuously over time ($p < .0001$). There were no significant increases in genital arousal following autogenic training. The results of these two studies suggested that experimentally increasing HRV could yield promising results for women with sexual arousal problems.

3.2. Study 3. Single session of autogenic training increases acute subjective and physiological sexual arousal in sexually functional women[3]

3.2.1. Introduction

Below average resting heart rate variability (HRV) has recently been associated with sexual arousal dysfunction and overall sexual dysfunction in women (Stanton, Lorenz, et al., 2015). Low resting HRV has also been linked with a variety of negative physical outcomes, namely poor cardiovascular health, and negative psychophysiological health outcomes beyond female sexual dysfunction, including, but not limited to, depression (Kemp et al., 2010) and anxiety (Kemp et al., 2012). Given these established relationships between low HRV and poor mental health outcomes, researchers have attempted to manipulate HRV typically through biofeedback, in order to decrease symptoms (e.g., Karavidas et al., 2007; Kudo, Shinohara, & Kodama, 2014; Nolan et al., 2005). Another type of manipulation, known as autogenic training, has been shown to significantly increase HRV (Mishima, Kubota, & Nagata, 1999; Miu et al., 2009) and to reduce symptoms associated with a wide variety of psychophysiological conditions, including depression and anxiety (for review, see Stetter & Kupper, 2002). The present study is the first to assess changes in genital sexual arousal and subjective sexual arousal due to HRV manipulation via autogenic training.

In general, HRV is a useful signal for understanding the state of the autonomic nervous system (ANS). Normal variability in heart rate is governed by autonomic neural regulation of the heart (Saul, 1990). Specifically, the balancing action of the two branches of the ANS, the

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[3] Stanton, A.M. & Meston, C. M. (2016). A single session of autogenic training increases acute physiological and subjective sexual arousal in sexually functional women. *Journal of Sex & Marital Therapy, 43*(7): 601-617.
Contribution statement: The first author designed the research, collected the data, analyzed the data, drafted the paper, and revised the paper. The second author designed the research, drafted the paper, and revised the paper.

sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS), controls heart rate. The SNS is typically associated with energy mobilization, while the PNS controls the body's restorative functions. When SNS activity increases, PNS activity decreases, leading to cardio-acceleration. Therefore, when SNS activity decreases, PNS activity increases, resulting in cardio-deceleration. The degree of variability in the lengths of time between successive heartbeats (HRV) provides important information about the regulation of these systems and about the heart's ability to respond. Higher HRV is reflective of organized variability, rather than static levels of SNS or PNS input, which enables the body to adapt to constantly changing environmental demands (Thayer et al., 2010).

In the past 30 years, numerous studies have pointed to the significant relationship between autonomic imbalance and physiological, specifically cardiovascular, health. When one branch of the ANS dominates over the other, researchers believe that dynamic flexibility and physiological health are compromised. This most commonly occurs when the sympathetic system is hyperactive and the parasympathetic system is hypoactive (Thayer et al., 2010). When the SNS dominates for long periods of time, the body cannot keep up with the branch's energy demands. The inability to meet these demands increases the risk of mortality from a variety of conditions and diseases, most notably cardiovascular disease (CVD). Measures of HRV, including the standard deviation of the normal heartbeat interval (SDNN, which is used in the present study), can be used to assess autonomic imbalance and the activity of the vagus nerve, which is a key component of the PNS. The vagus nerve regulates organ systems that do not involve conscious operation, including the heart. Findings from several epidemiological studies (e.g. Schroeder et al., 2003; Singh et al., 2000) provide strong evidence that vagal activity, indexed by HRV, is lower in individuals with cardiometabolic disease.

There is also a significant relationship between autonomic imbalance and female sexual dysfunction. A series of studies by Meston and colleagues has indicated that moderate SNS dominance (relative to parasympathetic dominance) predicts women's level of genital arousal in the laboratory (Meston & Gorzalka, 1995, 1996; Meston & Heiman, 1998). Specifically, there is evidence for a curvilinear relationship between sympathetic nervous system activation and women's physiological sexual arousal (Lorenz et al., 2012). Using decreases in HRV as a specific marker of increased SNS activity, Lorenz and colleagues (2012) found that moderate increases in SNS activity were associated with higher genital arousal, while very low or very high SNS activation was associated with lower genital arousal. Based on these results, they concluded that there is likely an optimal level of SNS activation for women's physiological sexual arousal.

These laboratory studies examined the relationship between women's genital sexual arousal and different levels of experimentally induced SNS activation, but they did not investigate the effect of variations in resting state autonomic balance on sexual arousal function and overall sexual function. To investigate the possibility that resting state autonomic balance may also be related to sexual arousal function and overall sexual function, Stanton and colleagues (2015) measured resting state HRV and sexual function using the Female Sexual Function Index (FSFI; Rosen et al., 2000) in 72 women aged 18-39. In this study, women with below average resting HRV were more likely to report sexual arousal problems and overall sexual problems than women with average and above average resting HRV. In addition, HRV measured during an erotic film clip (rather than during a neutral film clip, during which resting HRV was measured) was also a significant predictor of sexual function. Based on these findings, the authors concluded that low resting HRV could be a marker for female sexual dysfunction. As

there few established physiological markers for female sexual dysfunction, this relationship between low resting state HRV and sexual dysfunction is particularly notable.

Given that low resting state HRV is now associated with sexual arousal concerns and overall sexual dysfunction in women, it is logical to consider the manipulation of resting HRV as a means to increase arousal. Research has indicated that autogenic training is an effective way to manipulate HRV. Autogenic training is a psychophysiological relaxation technique that is based on passive concentration of bodily perceptions, such as heaviness and warmth in the legs or the arms, which are conjured through verbal self-suggestions (Stetter & Kupper, 2002). Established by Schultz and Luthe (1959), the theory underlying autogenic training suggests that the modulation of physiological functions can be achieved through changes in mental processes (Mitani, Fujita, Sakamoto, & Shirakawa, 2006). There is a recognized association between autogenic training and changes in HRV. One study reported that healthy volunteers who were taught how to engage in autogenic training over a period of three months showed increased variability in inter-beat interval lengths (Mishima et al., 1999). Another study indicated that, in comparison to mental stress, brief autogenic training facilitated increased HRV and vagal control of the heart (Miu et al., 2009). Unlike Mishima and colleagues, Miu and colleagues developed an autogenic training protocol that fit into a single session, and all of their subjects were naïve to the training procedure. The present study builds upon the work of Miu and colleagues by investigating the effect of a single-session of autogenic training on different outcome variables, acute VPA and subjective sexual arousal.

A large body of research has shown that autogenic training improves physiological *and* psychophysiologcal health, not just HRV. Physiological health generally refers to the health and vitality of the body, which includes both individual organs and body systems. A meta-analysis

revealed that autogenic training has a medium-size effect on clinical outcomes in patients who have been diagnosed with coronary heart disease (Stetter & Kupper, 2002). Autogenic training has also led to improvements in symptoms associated with irritable bowel disease (Shinozaki et al., 2010) and in motor performance among individuals with Parkinson's disease (Ajimsha, Majeed, Chinnavan, & Thulasyammal, 2014). Psychophysiological health is characterized by an interaction of physiological (body systems) and psychological (mental) processes. Female sexual arousal, for example, is a psychophysiological phenomenon, as it involves both physical responsiveness (e.g. vasocongestion, vaginal lubrication and expansion, swelling of the genitalia) and subjective ratings (e.g. being mentally "turned on") of a stimulus. Other psychophysiological processes include emotions such as joy or anxiety, or states of mental arousal that are associated with stress or pain. At an extreme, psychophysiological processes also contribute to psychopathologies such as depression, via chronic recruitment of the autonomic nervous system. Autogenic training can influence these psychopathologies, increasing positive aspects of arousal and decreasing negative aspects. For example, research has demonstrated that autogenic training is associated with reductions in anxiety (e.g. Kanji, White, & Ernst, 2006), pain (e.g. Kanji, 2000), and depression (Krampen, 1999).

To our knowledge, there have been no investigations of the effect of HRV manipulation on acute genital and subjective sexual arousal in women. Based both on evidence that low resting state HRV predicts female sexual dysfunction (Stanton, Lorenz, et al., 2015) and that autogenic training can significantly increase HRV (Miu et al., 2009), we predict that raising resting state HRV via autogenic training will increase both acute genital sexual arousal and acute subjective sexual arousal in sexually functional women.

3.2.2. Methods

Participants

Participants were female undergraduate students recruited from the psychology student subject pool of a large university using flyers and print advertisements that explained the sexual nature of the experiment. Prospective participants were instructed to read about the study's inclusion/exclusion criteria online and then sign up for an available time slot if they met all of the inclusion criteria and none of the exclusion criteria. Once they arrived in the lab for their scheduled study sessions, prospective participants were given an eligibility screener to ensure that they met the inclusion criteria. Only women aged 18 to 30 who scored above a 26.55 on the FSFI (Rosen et al., 2000), the clinical cutoff for healthy sexual function in women, were included in the study. Exclusion criteria included history of sexually transmitted diseases; current active or untreated pelvic, vaginal, or urinary tract infections; history of major pelvic surgery; history of neurological impairment; history of or current psychotic disorder; and currently taking medications that are known to affect genital sexual arousal in women, such as antidepressants, beta blockers, or benzodiazepines.

In exchange for university credit, 40 women signed up via the online portal to participate in the study. Of these 40 women, 7 women were excluded from participation based on the results of the eligibility screener. Four women were excluded because they had not been sexually active over the past month (which was necessary in order to obtain a valid FSFI score); 2 women were excluded because they were taking antidepressant medications; and one woman was excluded because her FSFI score fell below the clinical cutoff. The final sample included 33 women aged 18-27, with an average age of 19.3 (SD = 1.7). For full demographics, please see Table 6.

Table 6

Participant Characteristics (N = 33)

	M	***SD***
Age (years)	19.3	1.7
FSFI (total score)	30.9	2.3
	n	**%**
Race[a]		
African American/Black	3	9.1
Caucasian/White	24	72.7
Asian American	4	12.1
Other	1	3.0
Relationship status		
Single, not dating	5	15.2
Single, dating	8	24.2
In a committed relationship	20	60.6
Sexual orientation		
Exclusively heterosexual	19	57.6
Predominantly heterosexual	13	39.4
Bisexual	1	3.0

[a]Participants could identify as belonging to more than one race or choose to not identify any race.

Measures

Heart rate variability. Heart rate was measured at a rate of 200 samples/sec via electrocardiography (ECG). This sampling rate is adequate to produce a minimally biased estimate of time domain measures of HRV used in the present study (Hejjel & Roth, 2004;

Ziemssen et al., 2008). The research administrator positioned disposable electrodes on the participant's upper right chest, lowermost left rib, and inner right ankle, and then the participant attached the leads after the administrator left the room. The signal from the ECG leads was detected using an MP100 data acquisition unit that was equipped with AcqKnowledge 3.9.1 software (Biopac Systems, Inc., Santa Barbara, CA).

Genital sexual arousal. Genital sexual arousal was assessed with vaginal photoplethysmography (Sintchak & Geer, 1975), which consists of a tampon-shaped device, known as the vaginal plethysmograph, that is inserted into the vagina. The vaginal plethysmograph transmits a beam of light into the vaginal canal, which is then detected by photocells in the vaginal wall. This process produces two physiological measurements: vaginal blood volume (VBV) and vaginal pulse amplitude (VPA). Vaginal blood volume, the direct signal, highlights slow changes in the pooling of blood in the vaginal tissue (Hatch, 1979). Vaginal pulse amplitude, the indirect signal, reflects short-term changes in the engorgement of blood in the vaginal tissue (Rosen & Beck, 1988). Considered to be the more sensitive of the two indices of change in vaginal blood volume (Heiman, 1977), VPA has been shown to be a reliable index of women's physiological, or genital, arousal (Ellen Laan, Everaerd, Van Aanhold, & Rebel, 1993) and was therefore used in the present study. Sampled at a rate of 200 samples/sec throughout both of the erotic films, VPA data were recorded in millivolts and collected by an MP100 data acquisition unit equipped with AcqKnowledge 3.9.3 software (Biopac Systems, Santa Barbara).

Subjective sexual arousal. Subjective sexual arousal was measured both discretely and continuously. Discrete measurement of the construct was calculated by summing the scores of the 3 original subjective sexual arousal items from Heiman and Rowland's (1983) Film Scale,

which assesses sexual arousal as well as positive and negative affect in response to an erotic film. These 3 items include: an assessment of overall "sexual arousal", a sense of "mental sexual arousal", and one reverse-scored item on feeling "sexually turned off". On two occasions during the experiment (immediately following the first neutral-erotic film sequence and immediately following the second neutral-erotic film sequence), participants rated the degree to which they experienced each of the three items on a 7-point Likert scale, and then the three scores were combined into a single subjective sexual arousal score for each of the two time points. Subjective sexual arousal was also measured continuously during the film presentation with an arousometer (Rellini, McCall, Randall, & Meston, 2005). The arousometer is a computer mouse attached to a lever, which is numbered from 0 to 7. During the neutral-erotic film sequences, the participant is instructed to move the mouse up or down as she feels her mental sexual arousal changing. The device is placed on a small table to the right of the participant's chair for ease of access during the film sequences.

Stimulus materials

Two 8-min audiovisual films were used as stimulus materials in this study. Both films included a 2-min neutral segment followed by a 6-min erotic segment. The neutral segments of both films depicted different images of landscapes accompanied by classical music. The erotic segments of both films featured different heterosexual couples engaging in 2 min each of foreplay, cunnilingus, and penetrative sexual intercourse. Both films have been found to be arousing to women in past studies conducted in our laboratory. The films were presented counterbalanced order and matched for content.

Procedure

A female research administrator oriented participants to the study procedures and obtained informed consent. Testing sessions took place in a private room equipped with an intercom that participants used to communicate with the researcher. Participants were first instructed in how to use the vaginal photoplethysmograph and attach the ECG wires before the testing session began. Then, after the researcher applied the electropads and left the room, the participants inserted the vaginal probe and then attached the ECG wires. After a 2-4 min habituation period where no physiological measurements were taken, participants viewed the first 8-min stimulus film, during which their VPA and HRV were measured.

After the first film, the participants completed a few questionnaires, which typically took them 5-10 minutes, and then listened to a 14-min autogenic training recording. The recording was adapted from an autogenic training manual developed by Linden (1990). Participants were instructed to close their eyes and listen to a relaxation exercise. They were also asked to follow along with the recording and to try to remain as still as possible. The recording focused specifically on repeatedly inducing sensations of heaviness and heat in the arms and legs. Following the autogenic training, participants watched the second 8-min film while their VPA and HRV were measured. After the second film, participants completed measures on subjective sexual arousal and provided demographic information. Participants were compensated for their time in university course credit.

3.2.3. Analysis

Data reduction. Heart rate variability data was collected using AcqKnowledge 3.9.3 software. The AcqKnowledge peak finder function was used to isolate the inter-beat (NN) intervals, which were then exported to Microsoft Excel for processing. The Excel documents

were converted to Text files, which were then imported to the Kubios HRV Analysis Software (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Kuopio, Finland). This software calculates the standard deviation of the normal heartbeat intervals (SDNN), which was used as an index of HRV in the present study. SDNN has been shown to be an accurate marker of HRV, and, as such, it is one of the most widely used measures of HRV (Xhyheri et al., 2012).

Vaginal pulse amplitude data was exported from AcqKnowledge 3.9.3 to Microsoft Excel for processing. Movement artifacts in the data were identified and removed by an automatic processing procedure (Pulverman, Meston, & Hixon, 2015) that has been shown to effectively remove outliers more accurately than visual inspection. This automatic processing procedure uses the R software environment (R Foundation, 2014). For a more comprehensive explanation of this data reduction procedure, please see Pulverman et al. (2015).

Resting heart rate variability. A paired-samples t-test was used to determine the effect of autogenic training on resting HRV. Measurements of baseline (resting) SDNN, collected during the 2-minute neutral segment before the first erotic film, were compared to SDNN measurements collected during the 2-minute neutral segment immediately following the 14 minutes of autogenic training, prior to the start of the second erotic film.

Vaginal pulse amplitude. After movement artifacts were removed from the VPA data via the automatic processing procedure, a paired-samples t-test was used to determine the effect of autogenic training on VPA. Pre-manipulation VPA was measured during the 2-minute neutral segment and the 6-minute erotic segment of the first film, and post-manipulation VPA was measured during the 2-minute neutral segment and the 6-minute erotic segment of the second film, which followed the 14 minutes of autogenic training. For each participant, the mean VPA level during the pre-manipulation neutral film segment was subtracted from the mean VPA level

during the pre-manipulation erotic film segment to obtain a mean VPA difference score ($VPA_{eroticfilm1mean} - VPA_{neutralfilm1mean}$) for the pre-manipulation phase of the experiment. This difference score was divided by mean VPA during the first neutral film and then multiplied by 100 to yield a percent change score for the pre-manipulation film sequence. The same procedure was carried out for the post-manipulation phase, resulting in a post-autogenic training mean VPA difference score ($VPA_{eroticfilm2mean} - VPA_{neutralfilm2mean}$) and then finally in a percent change score for the post-manipulation film sequence.

Subjective sexual arousal. A paired-samples t-test was used to determine the effect of autogenic training on subjective, or psychological, sexual arousal. Immediately following the presentation of the first neutral-erotic film sequence, participants completed the subjective sexual arousal items from Heiman and Rowland's (1983) film scale. Participants then listened to the autogenic training recording, after which they watched another neutral-erotic film sequence. Then, participants answered the same subjective arousal items from the Heiman and Rowland (1983) scale, and the two subject arousal scores were compared.

Change in HRV as a moderator of change in vaginal pulse amplitude. Hierarchical linear modeling software (HLM7; Raudenbush, Bryk, Cheong, Congdon, & Du Toit, 2011) was used to examine HRV as a moderator of change in continuous vaginal pulse amplitude from pre to post manipulation. A statistical technique that models parameters that vary at more than one level, hierarchical linear modeling (HLM) is particularly useful when examining VPA because baseline VPA differs by individual. This technique allows for each participant to act as her own control, as individual slopes and intercepts at Level 1 become outcome variables at Level 2.

A Level 1 analysis was conducted to evaluate the relationship between continuous VPA and film (where 0 = pre-manipulation, 1 = post-manipulation). Here, film is treated as a simple level 1 fixed effect. The equation for this analysis is listed below:

$$VPA = \beta_{0j} + \beta_{1j}(FILM) + r_{ij}, \qquad \text{(Level 1)}$$

In the above equation, β_{0j} represents the intercept, or the expected VPA, for participant *j* when film equals 0; β_{1j} represents the slope, or the expected change in VPA, that is associated with change in film from pre to post manipulation for participant *j*; and r_{ij} is an error term.

A Level 2 moderation analysis was conducted to determine if raw change in HRV from pre to post manipulation accounted for change in the relationship between film and VPA. Raw change in HRV was centered around the grand mean. The equation for this analysis is listed below:

$$VPA = \beta_{0j} + \beta_{1j}(FILM) + r_{ij}, \qquad \text{(Level 1)}$$

$$\beta_{0j} = \gamma_{00} + \gamma_{01j} + u_{0j} \qquad \text{(Level 2)}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11j}(RAW\ CHANGE\ IN\ HRV) + u_{1j},$$

In the above equations, γ_{00} and γ_{10} are the mean intercepts for all participants adjusted for film; γ_{01j} represents the association between film and VPA for participant *j*; γ_{11j} is the association between film and VPA moderated by change in HRV, and u_{0j} and u_{1j} are the error terms.

Change in HRV as a moderator of change in subjective sexual arousal. Similarly, hierarchical linear modeling software (HLM7; Raudenbush et al., 2011) was used to examine HRV as a moderator of change in continuous subjective sexual arousal from pre to post manipulation.

A Level 1 analysis was conducted to evaluate the relationship between arousometer scores, or continuous subjective arousal, and film (where 0 = pre-manipulation, 1 = post-

manipulation). Film was treated as a simple level 1 fixed effect. The equation for this analysis is listed below:

$$\text{Arousometer} = \beta_{0j} + \beta_{1j}(FILM) + r_{ij}, \qquad \text{(Level 1)}$$

In the above equation, β_{0j} represents the intercept, or the expected subjective arousal for participant j when film equals 0; β_{1j} represents the slope, or the expected change in subjective arousal, that is associated with change in film from pre to post manipulation for participant j; and r_{ij} is an error term.

A Level 2 moderation analysis was conducted to determine if raw change in HRV from pre to post manipulation accounted for change in the relationship between film and subjective sexual arousal. Raw change in HRV was centered around the grand mean. The equation for this analysis is listed below:

$$\text{Arousometer} = \beta_{0j} + \beta_{1j}(FILM) + r_{ij}, \quad \text{(Level 1)}$$

$$\beta_{0j} = \gamma_{00} + \gamma_{01j} + u_{0j} \qquad \text{(Level 2)}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11j}(RAW\ CHANGE\ IN\ HRV) + u_{1j},$$

In the above equations, γ_{00} and γ_{10} are the mean intercepts for all participants adjusted for film; γ_{01j} represents the association between film and subjective sexual arousal for participant j; γ_{11j} is the association between film and subjective sexual arousal moderated by change in HRV, and u_{0j} and u_{1j} are the error terms.

3.2.4. Results

Heart rate variability

Average resting HRV (i.e. HRV during the neutral film segments) across participants differed significantly from pre-autogenic training to post-autogenic training, $t = -4.83$, $p < .0001$ (Table 2). Specifically, SDNN levels measured during the neutral film that followed the

autogenic training intervention were significantly greater (M = 64.13, SE = 4.04) than SDNN levels measured at baseline (M = 52.32, SE = 3.61), indicating that the manipulation may have targeted and increased HRV. The Welch degrees of freedom modification was applied, as the t-test function in R assumes unequal variance. Since the number of samples was relatively large (n > 30), the assumption of normality was likely satisfied. This difference had a large effect size (d = 0.840). See Table 7.

Table 7

Results of Paired Samples t-tests

	M	SD	SDE	n	95% CI for Mean Difference	t	df
Pre-manipulation HRV to post-manipulation HRV	-11.80	14.05	2.45	33	-16.78, -6.82	-4.83***	32
Pre-manipulation percent change in VPA to post-manipulation percent change in VPA	-13.57	35.36	6.16	33	-26.11, -1.03	-2.21*	32
Pre-manipulation subjective sexual arousal to post-manipulation subjective sexual arousal	-1.61	2.41	0.42	33	-2.46, -0.75	-3.83**	32

*p < .05; **p < .01; ***p < .0001

Vaginal pulse amplitude

There was a significant difference between percent change in VPA before the autogenic training manipulation and percent change in VPA following the manipulation, t = -2.06, p < .05 (Figure 6). In other words, increasing HRV may have facilitated a significant increase in genital sexual arousal. Again, the t-test function in R assumes unequal variance and applies the Welch degrees of freedom modification. Based on the number of samples, the assumption of normality

was likely satisfied. This difference in VPA pre- to post-manipulation had a small effect size (d = 0.365).

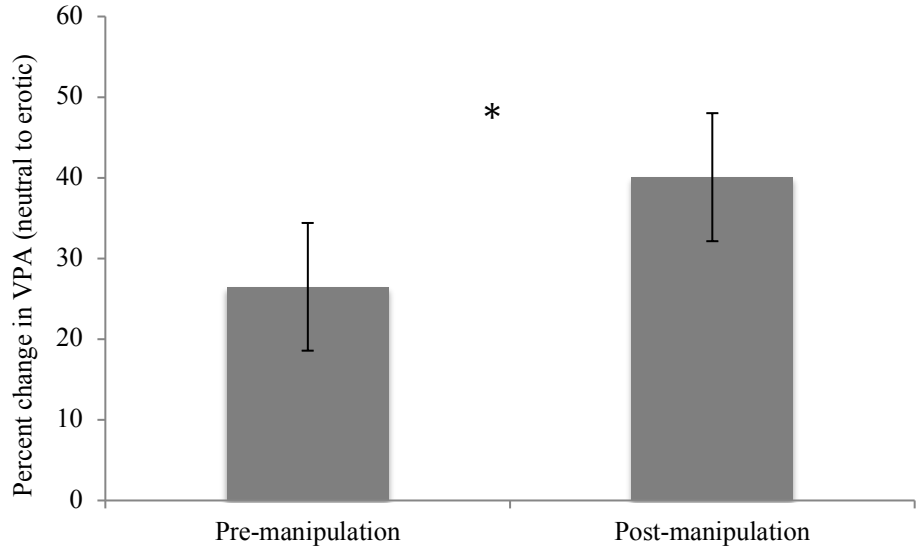

Figure 6. Percent change in VPA before and after HRV manipulation.

Subjective sexual arousal

There was also a significant difference between mean subjective arousal score before the manipulation and mean subjective arousal score after the manipulation, t = -3.83, p < .001 (Figure 7). Overall, after listening to the autogenic training recording, participants experienced a significant increase in subjective sexual arousal, as measured by the combined score of the three subjective arousal questions on the Heiman and Rowland (1983) film scale. The Welch degrees of freedom modification was applied, and, due to the sample size, we assumed the data to be normally distributed. The pre-to-post difference in subjective sexual arousal scores had a medium to large effect size (d = 0.666).

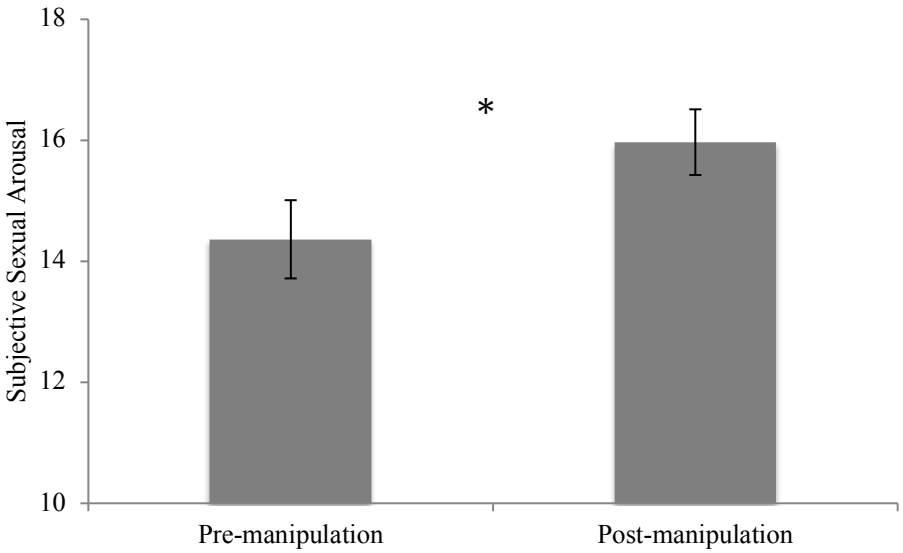

Figure 7. Mean subjective sexual arousal, measured via Heiman and Rowland's (1983) film scale, before and after HRV manipulation.

Change in HRV as a moderator of change in vaginal pulse amplitude.

The null model (model with no predictors) was significant ($X^2 = 9361.12$, $p < .001$), which suggested that multilevel modeling was warranted. Within the multilevel model, film significantly predicted VPA, $\beta = 0.56$ $t = 8.18$, $p < 0.001$. That is, prior to the manipulation (film = 0), a participant could be expected to have a mean VPA of 7.67 mV. After the manipulation (film =1), a participant could be expected to have a mean VPA of 8.23mV. In other words, there was a 0.56 mV increase in VPA on average from pre- to post-manipulation. When raw change in HRV was added to the model, it did not moderate the relationship between film and VPA, $\beta = 0.0068$, $t = 1.39$, $p = .16$.

Change in HRV as a moderator of change in subjective sexual arousal.

The null model (model with no predictors) was significant ($X^2 = 2060.80$, $p < .001$), which suggested that multilevel modeling was warranted. Within the multilevel model, film significantly predicted subjective sexual arousal, $\beta = 0.076$, $t = 9.78$, $p < 0.001$. This model shows that the predicted mean of subjective sexual arousal pre-manipulation (film = 0) was 0.35

units; post-manipulation (film = 1), the predicted mean of subjective sexual arousal increased to 0.43 units. Therefore, there was a 0.076 until increase in subjective sexual arousal on average following the manipulation. When raw change in HRV was added to the model, it significantly moderated the relationship between film and subjective arousal, $\beta = 0.0012$, $t = 2.151$, $p = .031$. Greater change in HRV from pre- to post-manipulation was associated with larger increase in continuous subjective arousal.

3.2.5. Discussion

This study examined the effect of HRV manipulation on acute genital and subjective sexual arousal in sexually healthy women. It only took 14 minutes of autogenic training, a relaxation technique known to restore the balance between the parasympathetic and sympathetic branches of the autonomic nervous system, to generate significant increases in both physiological and subjective indices of sexual arousal. Moreover, change in HRV from pre-manipulation to post-manipulation significantly moderated changes in continuous subjective arousal from the first neutral-erotic film sequence to the second neutral-erotic film sequence. These findings may have implications for facilitating increases in sexual arousal, particularly subjective sexual arousal, in women.

Heart rate variability manipulation may increase genital sexual arousal via direct vascular mechanisms. Physiological sexual arousal depends on a specific degree of blood pressure in the clitoris and the vaginal walls. In women, smooth muscle relaxation and vasodilation facilitate increased blood flow to the genitals. Diminished pelvic blood flow can lead to decreased inflow to the clitoris and the vagina, potentially resulting in fibrosis of the vaginal wall and clitoral smooth muscle (Park et al., 1997). Although there are other physiological and psychological factors that contribute to female sexual dysfunction, arterial insufficiency and other vascular

problems can affect the development and maintenance of sexual problems. Heart rate variability is considered to be a marker of heart health and is thought to reflect the heart's ability to quickly adapt to changing external triggers (Acharya et al., 2006). In other words, HRV can indicate the body's ability to coordinate increased blood flow to certain regions as warranted by environmental demands, which is particularly relevant to sexual situations as the body responds to both internal and external sexual cues.

Heart rate variability manipulation may also indirectly affect female sexual arousal, specifically subjective sexual arousal, by targeting the processing of emotional cues. Research suggests that HRV level is an index of emotional responding. Higher levels of respiratory sinus arrhythmia, the high frequency band of HRV, have been linked to greater self-reported emotion regulation in adults (Fabes & Eisenberg, 1997) and to active coping strategies in recently bereaved individuals (O'Connor, Allen, & Kaszniak, 2002). Generally, it is accepted that higher HRV reflects a greater capacity for regulation of emotional responses (Appelhans & Luecken, 2006). The ability to regulate emotional expression is considered to be critical for adaptive functioning (Baumeister & Vohs, 2004), and a lack of adequate control over emotion may be a contributing catalyst to the development of psychopathology (Calkins, 1994). Emotion regulation may be particularly germane to female sexual arousal function (Heiman, 1980), as emotional bonding is considered to be an important cue for sexual activity (McCall & Meston, 2006) and thus perhaps for sexual arousal as well. This conclusion, however, is tentative; future studies should directly examine the relationship among changes in affect, changes in subjective sexual arousal, and changes in HRV.

The present study was conducted with sexually functional women without sexual arousal problems. An important next step is to test the autogenic training protocol on women who are

distressed by diminished and/or lacking mental sexual arousal or by a reduction in pleasurable genital sensations. If the findings of this study are replicated among these women, then autogenic training may prove to be a valuable tool for clinicians who work with this population. Women with clinically-relevant sexual dysfunction have been shown to report lower subjective sexual arousal during the presentation of an erotic stimulus compared to their sexually functional counterparts (Morokoff & Heiman, 1980). Given that changes in HRV moderated changes in continuous subjective sexual arousal, HRV manipulation may be beneficial for women who are struggling to feel mentally "turned on." Though vaginal photoplethysmography has not been shown to differentiate between women with and without sexual arousal dysfunction (e.g., Laan, Van Driel, & Van Lunsen, 2008), it is possible that higher levels of vaginal blood flow are associated with increased vaginal sensations compared to lower levels of vaginal blood flow. Unfortunately, higher levels of sexual arousal, up to and during orgasm, are not often obtained during laboratory experiments (Laan, Everaerd, Van der Velde, & Geer, 1995), which makes it challenging to test the association between increased genital arousal, measured by VPA, and increased self-reported genital sensations.

Currently, there are no FDA-approved drugs for genital arousal problems in women. When women report having diminished genital sensations, their providers typically offer them topical lubricants, which help mask impairments in vaginal lubrication, even when lubrication is not their primary concern. Anecdotally, many women do report an increase in genital sensations with lubricant use; however, lubricants may not enhance all genital sensations, which, in addition to genital wetness, include genital pulsing or throbbing, genital or clitoral fullness, and genital warmth. There is some evidence from limited placebo-controlled studies that indicates that Viagra increases genital engorgement in healthy, premenopausal women (Ellen Laan, Smith,

Boolell, & Quirk, 2002) and in postmenopausal women with genital arousal problems (Basson & Brotto, 2003); however, studies in general have not shown that this drug increases psychological sexual arousal. The EROS clitoral therapy device (Urometrics, St. Paul, MN), approved by the FDA in 2000 to treat sexual arousal and orgasmic disorders, increases vasocongestion in the clitoral and labial region via a suction mechanism, which has been shown to increase genital sensations (Billups et al., 2001) but not subjective sexual arousal.

Psychological treatments of sexual arousal problems generally include elements from traditional sex therapy, such as sensate focus and masturbation training, as well as mindfulness-based exercises (for a review, see Brotto, Bitzer, Laan, Leiblum, & Luria, 2010). However, there is a lack of clear treatment protocols for this population, and, according to Brotto and colleagues (2010), there is also "great need for controlled efficacy studies in this area." The few studies that have examined the effects of certain psychological treatments on arousal function have involved multiple sessions, which involve a relatively large time commitment for both the provider and the patient, and have generally shown increases in subjective but not physiological sexual arousal (e.g., Brotto et al., 2008; Brotto et al., 2012).

It is important to note some limitations of the present study. Given that we did not include a control group, we cannot definitively conclude that the autogenic training, rather than repeated testing (i.e., repeated exposure to erotic material), led to increases in acute physiological and subjective sexual arousal. However, participants' mean VPA during the neutral segment of the second film sequence, which followed the manipulation, did not significantly differ from their mean VPA during the neutral segment of first film sequence. This suggests both that there was enough time between the presentations of the two erotic stimuli for women to return to baseline levels of genital responsiveness and that there was no carry-over of increased genital

blood flow from the first film sequence to the second film sequence. In addition, participants in this study were undergraduate women who were enrolled in a psychology course at a large university. Therefore, the findings of this study may not generalize to the larger population of sexually functional women. Finally, we did not measure indices of compliance or attentiveness to the autogenic training recording; therefore, we must assume that participants followed the instructions provided to them by the experimenter. The assumption that participants are listening to and following an experimenter's instructions is not uncommon in psychological research. In future studies, it may be beneficial to assess level of attentiveness to autogenic training recordings, as this variable may act as a treatment moderator.

Another limitation of the current study was the timing of the autogenic training recording in reference to the two neutral-erotic film sequences. The design of the study situated the autogenic training recording between the two neutral-erotic film sequences, such that the first film sequence was always the "pre manipulation" sequence and the second sequence was always the "post manipulation" sequence. Based on this design, we cannot definitively determine that the autogenic training recording, rather than the effect of time, facilitated the observed changes in acute physiological and subjective sexual arousal. If the mechanism of action driving the effects of the autogenic training is indeed its ability to manipulate autonomic balance, then the timing of the autogenic training should not impact study findings. To conclusively rule out the effect of timing as a causal factor, future research may randomize the order of the autogenic training recording, such that participants would first listen to the autogenic training recording, watch a neutral-erotic film sequence (which, in this case, would be the "post manipulation" sequence), return to baseline arousal, and then watch another neutral-erotic film sequence (which would be the equivalent of the "pre manipulation" sequence).

Though one session of autogenic training has been shown to increase HRV (Miu et al., 2009), autogenic training protocols are typically 4-8 weeks long (e.g. Jain et al., 2007; Mitani et al., 2006). Our brief 14-minute intervention cannot be considered a complete, comprehensive round of autogenic training. Rather, it was an introduction to the procedure that was intended to produce acute increases in resting HRV. It would be useful for future research to increase the number of autogenic training sessions, as additional sessions will likely be necessary in order for skills to be acquired and to generalize and for gains in subjective and physiological sexual arousal to be maintained. In addition, it may also be worthwhile to compare HRV-related changes in sexual arousal due to prolonged autogenic training with HRV-related changes in sexual arousal due to HRV biofeedback, another form of HRV manipulation. Briefly, HRV biofeedback involves learning to breathe at a resonance frequency of the cardiovascular system. At this frequency, respiratory sinus arrhythmia and baroreflex gain are maximized. Generally, HRV biofeedback protocols range from 5 sessions (e.g., Lehrer, Vaschillo, & Vaschillo, 2000) to 10 sessions (Lehrer et al., 2013), although some clinicians may choose to extend the length of the protocols depending on the severity of the symptoms. Regular practice of this technique has resulted in clinically significant improvement for a variety of disorders, and, given the findings of the present study, it is possible that HRV biofeedback may also increase sexual arousal, particularly mental sexual arousal.

In summary, our finding that autogenic training acutely increased both subjective and physiological components of sexual arousal is notable in that it differs from past research examining drug or psychotherapy treatments which generally increase only one or the other of these components of sexual arousal. In addition, the finding that change in HRV moderated changes in continuous subjective arousal suggests that increases in HRV may help account for

increases in mental sexual arousal. Autogenic training is easy to learn in a single session with a psychologist or another behavioral health provider, and it has the advantage of being free or very cheap. Recordings of the procedure can be downloaded from online platforms, which provide easy access to patients who cannot afford therapy. In addition, patients who are reluctant to seek out therapy for their sexual concerns due to shame or discomfort discussing sexual issues will be able to listen to the autogenic training protocol from their privacy of their own homes. Though preliminary, the present study highlights the importance of continued examinations of the effects of HRV manipulation on sexual arousal in women.

3.3. Study 4. The effect of a single session of autogenic training on acute subjective and physiological sexual arousal in women with female sexual arousal disorder[4]

3.3.1. Introduction

Low resting-state heart rate variability (HRV) has been associated with decreased sexual arousal and poor overall sexual function (Stanton, Lorenz, et al., 2015). An index of the modification of heart rate over time, HRV has become a widely used measure of autonomic control of the heart and the relative contributions of the sympathetic and parasympathetic nervous systems to that process. In addition to sexual arousal dysfunction, other psychological conditions have been associated with below average resting HRV; these include depression (Kemp et al., 2010), anxiety (Licht, de Geus, van Dyck, & Penninx, 2009), and post-traumatic stress disorder (Chalmers, Quintana, Abbott, & Kemp, 2014). More broadly, reductions in

[4] Stanton, A.M., Hixon, J. G., Nichols, L. M., & Meston, C. M. (2018). One session of autogenic training increases acute subjective sexual arousal in pre-menopausal women with sexual arousal problems. *Journal of Sexual Medicine, 15*(1): 64-76.
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resting state HRV reflect cardiac autonomic dysfunction, which plays a critical role in the development of cardiovascular disease as well as the maintenance of psychological states that are characterized by poor self-regulation (Chalmers, Heathers, Abbott, Kemp, & Quintana, 2016).

An expanding literature has documented the positive effects of experimentally increasing HRV on psychological health. Several interventions have led to significant increases in HRV and improvements in various psychological measures. Heart rate variability biofeedback is one such intervention; a number of HRV biofeedback studies have documented that biofeedback training to increase HRV produces both acute and chronic gains (Lehrer et al., 2003; Nolan et al., 2005). These biofeedback protocols have led to significant decreases in symptoms of the following disorders: perinatal depression (Beckham, Greene, & Meltzer-Brody, 2013), chronic fatigue (Windthorst et al., 2017), and post-traumatic stress disorder (Zucker, Samuelson, Muench, Greenberg, & Gevirtz, 2009), among others. A recent meta-analysis found that HRV biofeedback training is associated with a large reduction in self-reported stress and anxiety (Goessl, Curtiss, & Hofmann, 2017).

Although HRV biofeedback effectively decreases symptoms of disorders that are characterized by autonomic imbalance, the intervention requires a considerable time investment. Biofeedback protocols typically involve four to five visits with an experienced provider (Lehrer et al., 2013), which may not be feasible for certain patients or clinical populations. An intervention that has led to significant increases in HRV, but over a shorter period of time, is autogenic training. Autogenic training is a psychophysiological relaxation technique that is thought to improve self-regulatory functions and increase bodily resistance to stress (Nasim Kanji et al., 2006). The rationale for autogenic training is centered on the maintenance of autonomic balance or homeostasis, and the practice is designed to promote the recuperative

processes that oppose the physiological changes typically induced by stress (Schultz & Luthe, 1959). Developed by Schulz in 1932, autogenic training consists of six standard exercises which use verbal instructions to achieve specific goals (Kanji, 1997). The first exercise targets muscular relaxation, which the practitioner achieves by repeating a specific phrase that focuses on heaviness ("My right arm is heavy"); the second exercise targets feelings of warmth ("My right arm is warm"). The third exercise isolates cardiac activity ("My heartbeat is calm and regular"), and the fourth emphasizes steady respiration ("It breathes me"). Finally, the fifth and the sixth exercises focus on warmth in the abdomen ("My solar plexus is warm") and coolness in the cranial region ("My forehead is cool"), respectively. Autogenic training is based on three core principles: (1) reducing internal and external stimulation; (2) mental repetition of specific verbal instructions; and (3) 'passive concentration,' or total, effortless immersion in the task (Kanji, 1997) This training has been associated with increases in HRV, both after long-term practice (Mishima et al., 1999) and after a single session (Miu et al., 2009; Stanton & Meston, 2016).

In light of the established relationship between depressed HRV and low sexual arousal (Stanton, Lorenz, et al., 2015), a recent study attempted to experimentally increase HRV in order to facilitate increases in both physiological sexual arousal (i.e., genital arousal, measured via vaginal photoplethysmography) and subjective sexual arousal (i.e., the degree to which one feels mentally "turned on") in a sample of sexually healthy women (Stanton & Meston, 2016). In this study, women's physiological sexual arousal and subjective sexual arousal were measured before and after they listened to a 14-minute autogenic training recording. There were significant increases in resting HRV post-autogenic training compared to pre-autogenic training, indicating that the manipulation may have effectively targeted the mechanism of interest. Most importantly, physiological and subjective sexual arousal were significantly higher when measured after the

autogenic training recording than when measured prior to the manipulation, which suggests that increasing HRV may lead to acute increases in both types of arousal among women without sexual arousal concerns. Moreover, change in HRV from pre to post-manipulation significantly moderated changes in subjective sexual arousal; greater change in HRV was associated with larger increases in subjective sexual arousal. These findings suggest that interventions that increase HRV could be promising therapeutic options not only for sexually functional women but also for women who are having trouble feeling mentally "turned on" at the prospect of sexual activity or during sexual activity.

The current study extends the findings of Stanton and Meston (2016b) to a population of women who met DSM-IV-TR criteria for female sexual arousal disorder (i.e., recurrent or persistent inability to attain or maintain an adequate physiological genital response (e.g., vasocongestion, lubrication, swelling of the genitalia) during or until completion of sexual activity). Based on previous studies (Stanton, Lorenz, et al., 2015; Stanton & Meston, 2016), we had reason to believe that increasing HRV would specifically target arousal and not desire mechanisms. For this reason, we chose to use DSM-IV-TR (American Psychiatric Association, 2000) criteria as opposed to the DSM-5 (Association, 2013) diagnostic criteria for female sexual interest/arousal disorder, which encompasses symptoms of both arousal and desire. Though the inclusion criteria for this study focused only on physiological arousal of the genitals, women with low or absent genital arousal may also have difficulties feeling mentally "turned on" during sexual activity due to problems with recognizing, processing, or appraising genital responses or due to a general lack of subjective excitement. Recently, researchers have argued for the return of separate diagnostic categories for inadequate genital arousal and low desire (Parish et al.,

2016), and they have suggested that female sexual arousal disorder should include both a genital arousal subtype and a subjective arousal subtype (Althof et al., 2017).

Prevalence estimates for sexual arousal concerns vary. When arousal problems are assessed via scores on the arousal domain of the Female Sexual Function Index (FSFI; Rosen et al., 2000), a well-validated and widely-used self-report index that assess six domains of female sexual function (arousal, lubrication, desire, pain, orgasm, and satisfaction), rates range from 11.4 % in the UK (Burri & Spector, 2011) to 44.9% in Turkey (Çayan et al., 2016). Even though arousal concerns are relatively common among women, there are no FDA-approved pharmacological treatments that specifically target female sexual arousal, and only a few psychological interventions have led to clinically meaningful increases in arousal.

We hypothesize that, among women with sexual arousal problems, an acute increase in HRV via autogenic training will lead to acute increases in subjective sexual arousal but not in physiological sexual arousal. Given the brief length of the intervention, we do not believe that there will be a significant increase in genital arousal among women who are suffering from clinically low levels of arousal. In addition, based on the results of previous research (Stanton & Meston, 2016), we hypothesize that the degree of change in HRV from pre to post-intervention will significantly moderate changes in subjective sexual arousal. If Stanton and Meston's findings are replicated in this sample of premenopausal women with sexual arousal problems, the results of this study may have implications for the treatment of sexual arousal problems. Furthermore, this study may help clarify the relationship between HRV and female sexual arousal, offering insight that may shape the development of HRV-targeted interventions for the treatment of sexual arousal concerns.

3.3.3. Methods

Participants

Participants were recruited from the community using flyers as well as print and online advertisements. These advertisements instructed potential participants to call the laboratory and complete a phone screen with a trained research assistant in order to determine eligibility. All potential participants completed a thorough phone screen, which included the FSFI (Rosen et al., 2000), a 19-item self-report questionnaire that assesses desire, arousal, lubrication, pain, orgasm, satisfaction, and overall sexual function. Total scores range from 2 to 36, with higher scores indicating greater sexual function. The FSFI has good internal reliability (r = .89-.97), test-retest reliabilities (α = .79-.88), and has been shown to discriminate between women with and without sexual problems (Rosen et al., 2000). Only premenopausal women who scored below a 26.55 on the FSFI, the clinical cut-off for sexual function (Wiegel, Meston, & Rosen, 2005), were included in the study.

In addition to meeting the FSFI cut-off, participants were required to report decreased or diminished genital sensations and to respond in the affirmative to the following question: "Do you think that you have an arousal problem?" An adapted version of the Female Sexual Dysfunction Diagnosis (FSDD) questionnaire, which was originally developed to identify women who have acquired sexual arousal problems, was also used to determine eligibility with respect to the genital sensations criterion. The adapted FSDD assesses participants' past and current levels of genital sexual arousal by referencing five specific genital sensations (pleasurable sexual feeling in your genitals; genital pulsing or throbbing; genital/clitoral fullness, pressure, or engorgement; genital warmth; genital wetness or lubrication) that are typically experienced during sexual activity. Women who identified experiencing at least two of these

genital sensations in the past and stated that these sensations were currently diminished or absent (for at least six months) were eligible to participate. The adapted FSDD also evaluates the level of importance associated with these specific genital sensations during sexual activity with 7-point Likert scale, which ranges from 1 (not at all important) to 7 (extremely important). However, the level of importance attributed to the sensations was not used to determine eligibility for this study.

Other inclusion criteria were as follows: generalized low genital arousal; currently sexually active with a partner; heterosexual or bisexual sexual orientation; and fluency in English. Generalized low arousal was defined as arousal concerns that are *not* situational (i.e., low arousal regardless of context, no matter the setting, the partner, the time of day, etc.). Exclusion criteria included: history of sexually transmitted diseases; current active or untreated pelvic, vaginal, or urinary tract infections; history of sexual abuse; history of major pelvic surgery; history of neurological impairment; history of or current psychotic disorder; and currently taking medications that are known to affect genital sexual arousal in women, such as antidepressants, beta blockers, or benzodiazepines. Participants were compensated $50 for their time.

The final sample included 25 women, aged 20 to 44, with an average age of 31.16 (SD = 6.71). The sample was mostly Caucasian (64%), 28% were African American, 4% were Asian American, and 4% were Pacific Islander. The majority of the sample considered themselves to be exclusively heterosexual (64%); 36% of the sample considered themselves to be predominantly heterosexual. With respect to relationship status, most women in the sample were single and dating (52%), some women were in committed relationships (36%), and a minority was single but not dating (12%). All participants met the clinical cut-off for sexual dysfunction established

by the FSFI (M = 18.25, *SD* = 5.36). The average domain scores were as follows: 2.74, *SD* = 1.13 (desire); 2.77, *SD* = .866 (arousal); 3.10, *SD* = 1.04 (lubrication); 3.04, *SD* = 1.14 (orgasm); 3.00, *SD* = 1.30 (satisfaction); and 4.29, *SD* = 1.48 (pain).

Measures

Heart rate variability. Heart rate was measured at a rate of 200 samples/sec via electrocardiography (ECG). The signal from the ECG leads was detected using an MP100 data acquisition unit that was equipped with AcqKnowledge 3.9.1 software (Biopac Systems, Inc., Santa Barbara, CA). During the experimental sessions, the research administrator placed disposable electrodes on the participant's upper right chest, lowermost left rib, and inner right ankle to triangulate the signal. Then, after the administrator left the room, the participant attached the leads to the electrodes.

Physiological sexual arousal. Physiological sexual arousal was assessed via a vaginal photoplethysmograph (Sintchak & Geer, 1975), a photo-receptive diode which produces two measurements: vaginal blood volume (VBV) and vaginal pulse amplitude (VPA). Vaginal pulse amplitude, which reflects short-term changes in the engorgement of blood in the vaginal tissue (Rosen & Beck, 1988), is considered to be the more sensitive of the two indices (Heiman, 1977) and has been shown to be a reliable index of women's physiological, or genital, arousal (Ellen Laan, Everaerd, & Evers, 1995). Sampled at a rate of 200 samples/sec throughout both of the neutral and erotic films, VPA data were recorded in millivolts, band-pass filtered (0.5-30 Hz), and collected by an MP150 data acquisition unit equipped with AcqKnowledge 3.9.3 software (Biopac Systems, Santa Barbara).

Subjective sexual arousal. Subjective sexual arousal was measured both discretely and continuously. Discrete subjective arousal scores were calculated by summing the scores of the

three original subjective sexual arousal items from Heiman and Rowland's Film Scale (1983). This 15-item self-report questionnaire features a 7-point Likert scale with answer choices ranging from 1 (not at all) to 7 (intensely). On two occasions during the experiment (immediately following the first neutral-erotic film sequence and immediately following the second neutral-erotic film sequence), participants were asked to rate the degree to which they experienced each of the three items on a 7-point Likert scale, and then the three scores were combined into a single subjective sexual arousal score for each of the two time points. Subjective sexual arousal was also measured continuously during the two neutral-erotic film sequences with an arousometer (Rellini et al., 2005a), a computer mouse mounted on a lever which is numbered from 0 (no mental sexual arousal) to 7 (maximum mental sexual arousal). The experimenter instructed the participant to move the mouse up or down as she felt her mental sexual arousal increasing or decreasing during the course of the films.

Perceived genital arousal. Perceived genital arousal was calculated by summing the scores of the five perceived genital arousal items from Heiman and Rowland's Film Scale (1983). Immediately following the first and second neutral-erotic film sequences, participants rated the intensity of their genital sensations (e.g., genital pulsing or throbbing; genital/clitoral fullness, pressure, or engorgement) on a 7-point Likert scale.

Stimulus materials

Two nine-minute audiovisual films were used as stimulus materials. They were presented in counterbalanced order and matched for content. Both films included a three-minute neutral segment followed by a six-minute erotic segment. The neutral segments of both films depicted different images of natural landscapes alongside classical music. The erotic segments of both films featured different heterosexual couples engaging in two minutes of foreplay, two minutes

of cunnilingus, and two minutes of penetrative sexual intercourse. Both films have been found to be arousing to women in previous studies that have been conducted in our laboratory.

Procedure

The Institutional Review Board at The University of Texas at Austin approved the study protocol and all study materials. Eligible participants were greeted and oriented to the study procedures before providing informed consent. After the female experimenter left the room, the participants inserted the vaginal photoplethysmograph and attached the ECG wires. The experiment took place in a private room equipped with an intercom, which the participants used to communicate with the experimenter during the duration of the study session. The experimenter allowed the participant's data to normalize for one to three minutes. After this brief habituation period, participants watched the first nine-minute stimulus film, while their VPA and heart rate date was collected. During the film, participants were asked to move the arousometer up as they felt their mental sexual arousal increasing and down as they felt their mental sexual arousal decreasing.

After watching the first nine-minute neutral-erotic film sequence, participants were asked to complete the Film Scale as well as a demographics form, which typically took five to ten minutes. They were then instructed to stay seated, close their eyes, remain as still as possible, and listen carefully to a 22-minute autogenic training recording, which was adapted from an autogenic training manual written by Linden (1990). The recording focused on the first two of the six standard autogenic training exercises (i.e., inducing sensations .of heaviness and warmth). It is worth noting that the length of the autogenic training recording was increased from what was 14 minutes in a prior study conducted among sexually healthy women (Stanton & Meston, 2016) to 22 minutes in the current study, which assessed women with sexual arousal concerns.

This change was made to allow for the possibility that women with sexual concerns may take longer to acclimate to a laboratory environment than sexually healthy women. After listening to the recording, participants watched a second neutral-erotic film sequence as their VPA and heart rate data was collected. During the second film, participants were again asked to move the arousometer in concert with changes in their mental sexual arousal.

3.3.4. Analysis

Data reduction. Heart rate data was collected using electrocardiography via AcqKnowledge 3.9.3 software. The AcqKnowledge peak finder function isolated the inter-beat intervals (NN intervals), which were exported to Microsoft Excel for artifact removal. Artifacts were visually detected, and then a correction level was applied. The resulting Excel files from the data processing phase were converted to text files and then imported into Kubios HRV Analysis Software (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Kuopio Finland), a program that offers both time domain and frequency domain analyses for HRV data.

Two indices of HRV were used in this study: a time domain measurement, the standard deviation of the normal heart beat interval lengths (SDNN), and a frequency domain measurement, the natural log of the high frequency (HF) band. The Kubios software calculates time domain measurements, including SDNN, and isolates the various components of the HRV signal for frequency domain analyses. SDNN is considered one of the most widely used measures of HRV (Xhyheri et al., 2012); it provides information about all components contributing to HRV during the recording period and is thus a more global measure than the HF band and the other power-spectrum derived measures. When measured across shorter time spans, SDNN values can be compared only with other SDNN measures derived from recordings of a

similar length, as SDNN tends to increase (up until a point) with longer recording periods (Ponnusamy, Marques, & Reuber, 2012). For the analysis of parameters in the frequency domain, Kubios derives the intervals between successive normal QRS complexes (i.e., NN intervals) using a fast Fourier transform and then generates a power distribution as a function of frequency. The two spectral components that can be isolated from brief recordings are the low frequency band (LF, 0.04-0.15 Hz) and the high frequency band (HF, 0.15-0.4 Hz). It has been suggested that the LF band reflects sympathetic activity (Pagani et al., 1986; Pal et al., 2013), but a number of researchers have challenged this view, arguing that this band actually indexes baroreflex activity (MacKinnon, Gevirtz, McCraty, & Brown, 2013; Porges, 2007). The HF band is thought to reflect the magnitude of parasympathetic (i.e., vagal) influence on the heart (Malliani, Lombardi, & Pagani, 1994). It is frequently referred to as the "respiratory band" because it corresponds to heart rate variations that are related to respiration, known as respiratory sinus arrhythmia (McCraty & Shaffer, 2015). The power of the HF band is a commonly used measure of vagally-influenced HRV. In short term recordings, the primary source of variation that contributes to HRV is mediated by the parasympathetic nervous system; therefore, SDNN is correlated with higher frequency rhythms (McCraty & Shaffer, 2015).

Resting heart rate variability. A paired-samples *t*-test was used to determine the effect of autogenic training on resting HRV. Measurements of baseline (resting) SDNN and baseline HF-HRV, collected during the 4-minute neutral segment before the first erotic film, were compared to SDNN and HF-HRV measurements collected during the 4-minute neutral segment immediately following the 22 minutes of autogenic training, prior to the start of the second erotic film.

Vaginal pulse amplitude. These data were analyzed in two ways, with percent change scores and with hierarchical linear modeling (HLM). For the percent change score analyses, a mean VPA score was calculated for the pre-manipulation film sequence by averaging VPA during the first neutral film and then separately averaging VPA values for the first erotic film. Then, a mean VPA difference score ($VPA_{eroticfilm1mean} - VPA_{neutralfilm1mean}$) for the pre-manipulation phase of the experiment was determined for each participant. This difference score was used to calculate a percent change score for the pre-manipulation film sequence: each difference value was divided by mean VPA during the neutral film, and then multiplied by 100. The same procedure was carried out for the post-manipulation phase, resulting in a post-autogenic training mean VPA difference score ($VPA_{eroticfilm2mean} - VPA_{neutralfilm2mean}$) and then in a percent change score for the post-manipulation film sequence. A paired-samples *t*-test was used to determine the effect of autogenic training on VPA percent change.

These data were also analyzed via HLM, a sensitive statistical technique accounts for individual variability by estimating coefficients based on the unique slopes and intercepts of each participant (Snijders & Bosker, 2012). This technique is particularly well suited for the analysis of continuous, multilevel data, and it has been effectively applied to VPA data in previous research (Meston, Rellini, & McCall, 2010). The VPA analyses using HLM were conducted in R 3.2.3 (Team, 2016) with the NLME package (Pinheiro, Bates, DebRoy, Sarkar, & Team, 2017).

Discrete subjective sexual arousal and perceived genital arousal. A paired-samples t-test was used to determine the effect of autogenic training on discrete subjective, or psychological, sexual arousal as well as on perceived genital arousal. Pre-manipulation subjective arousal scores were compared to post-manipulation subjective arousal scores, and pre-

manipulation perceived genital arousal scores were compared to post-manipulation perceived genital arousal scores.

Change in HRV as a moderator of change in vaginal pulse amplitude and in continuous subjective arousal. Several moderation models were tested using hierarchical linear modeling (HLM) in the R software environment (Team, 2016) with the NLME package (Pinheiro et al., 2017). These moderation models examined the degree to which change in HRV from pre- to post-manipulation influences genital and continuous subjective sexual arousal following the manipulation.

The following four models assessed the relationship between change in HRV (indexed by SDNN and HF-HRV) and either VPA or continuous subjective arousal during the film sequences:

$$Y(VPA)_{ij} = \beta_0 + \beta_1(\Delta SDNN)_{ij} + \beta_2(Film)_{ij} + \beta_3(Time)_{ij} + \beta_4(\Delta SDNN * Time)_{ij} + \beta_5(\Delta SDNN * Film)_{ij} + \beta_6(Film * Time)_{ij} + \beta_7(\Delta SDNN * Film * Time)_{ij} + r_{ij}$$

$$Y(VPA)_{ij} = \beta_0 + \beta_1(\Delta HF\text{-}HRV)_{ij} + \beta_2(Film)_{ij} + \beta_3(Time)_{ij} + \beta_4(\Delta HF\text{-}HRV * Time)_{ij} + \beta_5(\Delta HF\text{-}HRV * Film)_{ij} + \beta_6(Film * Time)_{ij} + \beta_7(\Delta HF\text{-}HRV * Film * Time)_{ij} + r_{ij}$$

$$Y(Arousometer)_{ij} = \beta_0 + \beta_1(\Delta SDNN)_{ij} + \beta_2(Film)_{ij} + \beta_3(Time)_{ij} + \beta_4(\Delta SDNN * Time)_{ij} + \beta_5(\Delta SDNN * Film)_{ij} + \beta_6(Film * Time)_{ij} + \beta_7(\Delta SDNN * Film * Time)_{ij} + r_{ij}$$

$$Y(Arousometer)_{ij} = \beta_0 + \beta_1(\Delta HF\text{-}HRV)_{ij} + \beta_2(Film)_{ij} + \beta_3(Time)_{ij} + \beta_4(\Delta HF\text{-}HRV * Time)_{ij} + \beta_5(\Delta HF\text{-}HRV * Film)_{ij} + \beta_6(Film * Time)_{ij} + \beta_7(\Delta HF\text{-}HRV * Film * Time)_{ij} + r_{ij}$$

$Y(VPA)_{ij}$ and $Y(Arousometer)_{ij}$ are the $_i$th participant's VPA and continuous subjective arousal, respectively, at the $_j$th time point. In these models, β_1 represents the main effect of change in HRV from pre- to post-manipulation on either genital or subjective sexual arousal, β_2 represents the main effect of film (where 0 = the pre-manipulation film, 1 = the post-manipulation film), β_3 highlights the main effect of time, and $\beta_{5\text{-}7}$ represent the various two-way interactions effects and the three-way interaction effect among HRV, film, and time. The time variable refers to the course of each of the neutral-erotic film segments; both the pre-manipulation film and the post-manipulation film were 540 seconds in duration. Finally, β_0 represents the participant-specific intercept and r_{ij} are the individual error terms.

To account for the clustering of observations within subject, these analyses included a random intercept on subject. All other variables were treated as fixed effects. For all analyses, we used an alpha level of 0.05 to determine statistical significance.

3.3.5. Results

Heart rate variability

Resting HRV, measured by SDNN and HF-HRV, differed significantly from pre-autogenic training to post-autogenic training. Both SDNN and HF-HRV were significantly greater during the neutral film that followed the manipulation ($t(24) = -2.93$, $p = .007$; $t(24) = -3.56$, $p = .002$) than during the pre-manipulation neutral film segment, which indicates that the autogenic training likely contributed to increased HRV, as was expected. These differences had medium effect sizes ($d = 0.59$ and $d = 0.71$, respectively). Please see Tables 8 and 9 for a comparison of means and paired samples t-test results.

Table 8

Pre-autogenic training and post-autogenic training means

	M_1	SD (M_1)	SE (M_1)	M_2	SD (M_2)	SE (M_2)	*n*
HRV (SDNN)	46.56	19.29	3.86	58.54	26.47	5.29	25
HRV (LnHF)	5.94	1.42	0.28	6.50	1.38	0.28	25
VPA percent change	30.31	33.16	6.63	29.15	32.11	6.41	25
Discrete subjective sexual arousal	12.64	4.45	0.89	13.80	5.10	1.02	25
Perceived genital sensations	15.68	7.25	1.47	18.20	9.30	1.86	25

Note. M_1 = pre-autogenic training means; M_2 = post-autogenic training means; HRV = heart rate variability; SDNN = standard deviation of the N-N intervals; LnHF = natural log of the high frequency HRV band (0.15-0.40 Hz); VPA = vaginal pulse amplitude.

Table 9

Results of paired samples t-tests

Pre-manipulation to post-manipulation	M	SD	SE	*n*	95% CI for Mean Difference	*t*-ratio	df
HRV (SDNN)	-11.98	20.37	4.07	25	[-20.39, -3.58]	-2.94**	24
HRV (LnHF)	-.57	.89	.18	25	[-.89, -.24]	-3.56**	24
VPA percent change	1.16	30.81	6.16	25	[-11.56, 13.87]	.19	24
Discrete subjective sexual arousal	-1.16	2.82	.565	25	[-2.33, .006]	-2.05•	24
Perceived genital sensations	-2.52	4.95	.99	25	[-4.56, -.48]	-2.55*	24

Note. CI = confidence interval; HRV = heart rate variability; SDNN = standard deviation of the N-N intervals; LnHF = natural log of the high frequency HRV band (0.15-0.40 Hz); VPA = vaginal pulse amplitude.
• p = .05; *p < .05; **p < .01

Vaginal pulse amplitude

The intervention did not lead to significant increases in VPA percent change from pre- to post-autogenic training ($t(24) = .188$, p = ns). Similarly, the HLM analyses did not reveal a significant main effect for film (pre or post-manipulation), indicating that VPA did not significantly change from film one, which was shown before the presentation of the autogenic training recording, to film two, which followed the autogenic training intervention. That is, in line with our hypothesis, listening to the brief autogenic training recording was not associated

with increased physiological sexual arousal post-recording. See Tables 1 and 2 for a comparison of means and results.

Discrete subjective sexual arousal

There was a marginally significant difference in mean discrete subjective arousal, measured by the Film Scale, following the autogenic training manipulation ($t(24) = -2.05$, $p = .051$). See Tables 1 and 2 for results. Participants experienced an increase in subjective sexual arousal after listening to the autogenic training recording. This increase had a small to medium effect size ($d = 0.41$). Please see Figure 8.

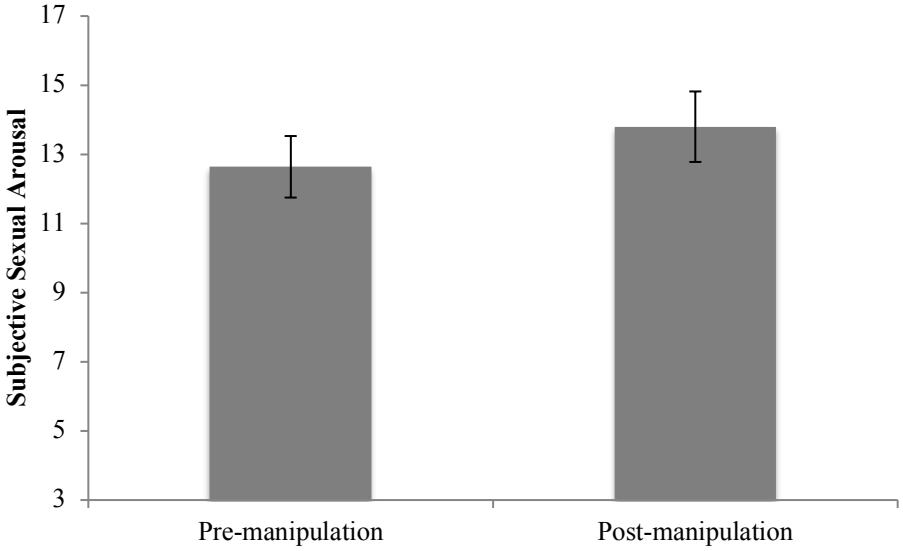


Figure 8. Mean subjective sexual arousal, measured via Heiman & Rowland's (1983) Film Scale, before and after HRV manipulation.

Perceived genital arousal

Participants experienced a significant acute increase in perceived genital arousal following the 22-minute autogenic training recording ($t(24) = -2.55$, $p = .018$). That is, participants reported increased genital warmth, wetness or lubrication, pulsing or throbbing, and

tenseness or tightness. This difference in perceived genital arousal had a medium effect size (d = 0.51). See Tables 10 and 11 for results and Figure 9 for a visualization of this increase.

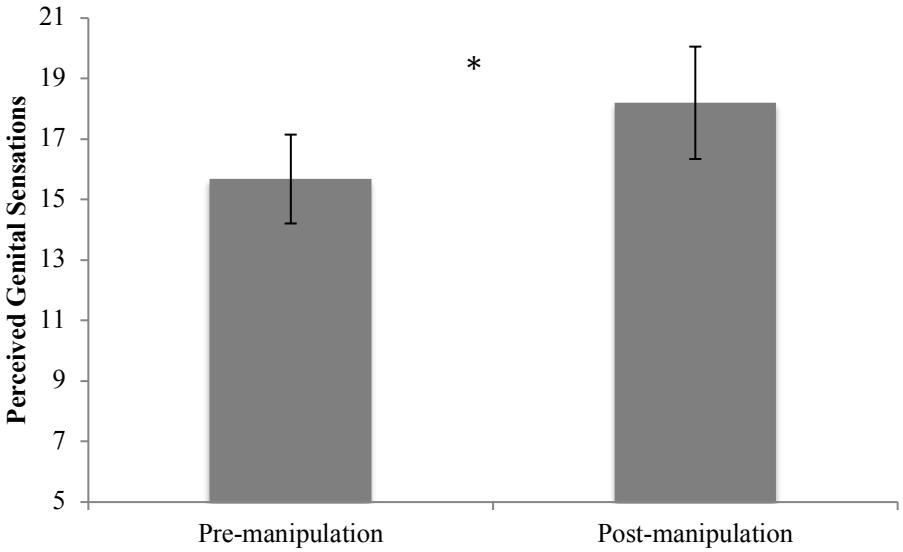


Figure 9. Mean perceived genital sensations, measured via Heiman & Rowland's (1983) Film Scale, before and after HRV manipulation.
*p < .05

Change in HRV as a moderator of change in vaginal pulse amplitude

Regardless of HRV index used, there was no significant three-way interaction among change in HRV, film (pre or post-manipulation), and time. Therefore, change in HRV was not a significant moderator of changes in VPA. See Table 10.

Table 10

Results from an HLM analysis examining the relationship among film, time, and change in SDNN (HRV) from pre- to post-manipulation

Predictor	β	SE	df	*t*-ratio	*p*-value
(Intercept)	0.25	0.03	5369	7.56	0.000
ΔSDNN	-0.003	0.002	23	-1.56	0.13
Film	0.07	0.005	5369	13.15	0.000
Time	0.001	0.0002	5369	61.42	0.000
ΔSDNN*Film	0.001	0.0003	5369	5.51	0.000
ΔSDNN*Time	-0.000009	0.0000008	5369	-10.37	0.000
Film*Time	0.0001	0.00003	5369	3.06	0.002
ΔSDNN*Film*Time	0.00001	0.000002	5369	6.10	0.000

ΔSDNN = Change in resting SDNN (HRV) from pre-manipulation neutral film to post-manipulation neutral film; Film = pre- or post- manipulation (0 = pre, 1 = post); SE = standard error; df = degrees of freedom.

Change in HRV as a moderator of change in continuous subjective sexual arousal

When SDNN was used as an index of HRV, there was a significant three-way interaction among change in SDNN, film (pre or post-manipulation), and time, $\beta = .0001$, $t(5393) = 6.10$, $p < .0001$ (see Table 10, Figure 10). That is, women who experienced greater changes in resting SDNN from pre to post-autogenic training had the greatest increases in continuous subjective sexual arousal from the first neutral-erotic film segment to the second neutral-erotic film segment. The same significant three-way interaction emerged when the natural log of the high frequency band of the HRV signal was used to index HRV, $\beta = .0001$, $t(5393) = 4.60$, $p < .0001$ (see Table 11, Figure 11). Therefore, increased change in SDNN and HF-HRV may be helping to

account for the increase in subjective sexual arousal from the first film sequence to the second film sequence. Figures 10 and 11 highlight the differences in subjective sexual arousal from pre to post-autogenic training at three different levels of HRV change: HRV change minus one standard deviation, mean HRV change, and HRV change plus one standard deviation.

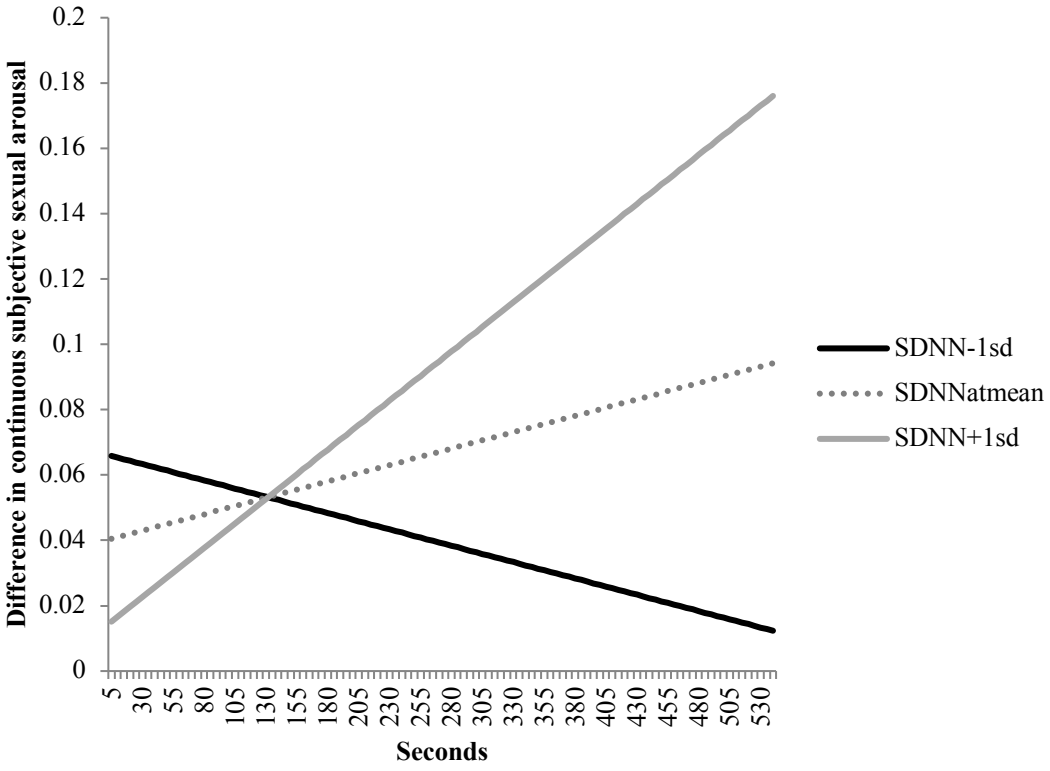


Figure 10. Difference in continuous subjective sexual arousal from pre- to post-autogenic training at three levels of change in SDNN. All three groups experienced increases in subjective sexual arousal following the intervention. However, the women who had the lowest increases in HRV (SDNN) following the intervention experienced the smallest gains in subjective sexual arousal.

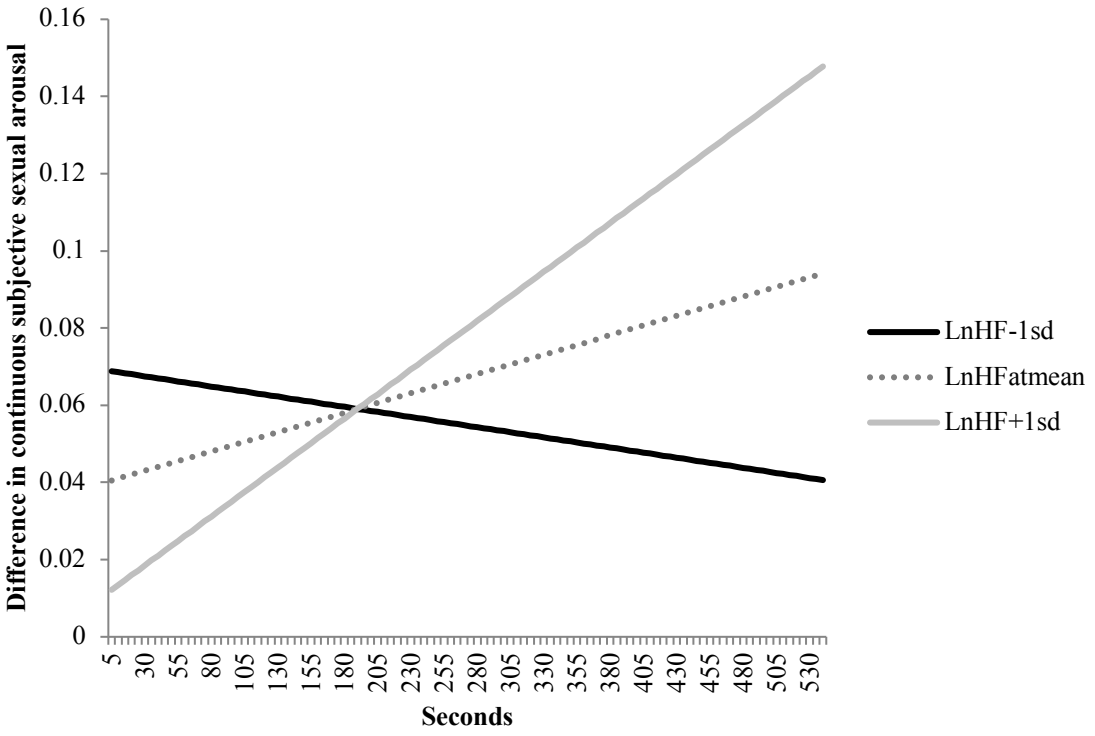


Figure 11. Difference in continuous subjective sexual arousal from pre- to post-manipulation at three levels of change in LnHF-HRV. All three groups experienced increases in subjective sexual arousal following the intervention. However, the women who had the lowest increases in HRV (LnHF) following the intervention experienced the smallest gains in subjective sexual arousal.

Table 11

Results from an HLM analysis examining the relationship among film, time, and change in LnHF (HRV) from pre- to post-manipulation

Predictor	β	SE	df	*t*-ratio	*p*-value
(Intercept)	0.82	2.13	5369	0.39	0.69
ΔLnHF	0.99	0.35	23	2.86	0.009
Film	2.23	0.23	5369	9.51	0.000
Time	0.002	0.0008	5369	2.09	0.04
ΔLnHF*Film	-0.37	0.04	5369	-9.63	0.000
ΔLnHF*Time	0.0005	0.0001	5369	4.18	0.000
Film*Time	0.008	0.002	5369	5.47	0.000
ΔLnHF*Film*Time	-0.001	0.0002	5369	-5.76	0.000

ΔLnHF = Change in the natural log of the high frequency HRV band (0.15-0.40 Hz) from pre-manipulation neutral film to post-manipulation neutral film; Film = pre- or post- manipulation (0 = pre, 1 = post); SE = standard error; df = degrees of freedom.

3.3.6. Discussion

This study assessed the effect of increasing HRV via autogenic training on both genital and subjective sexual arousal, as well as on perceived genital sensations (e.g., warmth, fullness, pressure), in premenopausal women with diminished or absent sexual arousal. The 22-minute autogenic training recording led to marginally significant increases in discrete subjective sexual arousal and significant increases in both continuous subjective arousal and perceived genital sensations, but not in genital sexual arousal as indexed by VPA. Importantly, change in HRV, measured by both SDNN and the natural log of the HF band, moderated changes in subjective sexual arousal when it was measured continuously throughout the film. In other words, larger

increases (i.e., increases greater than one standard deviation above the mean) in resting HRV from the pre-manipulation neutral film segment to the post-manipulation neutral film segment were associated with the greatest increases in subjective sexual arousal over time.

Heart rate variability may be related to subjective sexual arousal due to its role in the processing of emotional cues and regulation of emotional responses. Adaptive emotional processing and regulation involve the flexible modulation of emotional experiences, expressions, and physiological responses (Aldao, 2013). Emotional responses that are consistent with a given situation (e.g., sexual activity) are indicative of adaptive emotional regulation, which is critical for overall functioning and well-being (Baumeister & Vohs, 2004). It has been suggested that HRV can be considered an index of emotional regulation because of its relationship to the inhibitory pathways that are regulated by the parasympathetic branch of the autonomic nervous system (ANS; Williams et al., 2015). The heart and other peripheral organs are under the control of the ANS, and this process is characterized by the relative dominance of the parasympathetic system over the sympathetic system (Thayer, Åhs, Fredrikson, Sollers, & Wager, 2012; Thayer & Lane, 2009). The regulation of physiological functions via parasympathetic pathways is influenced by psychological processes like emotion regulation (Thayer & Lane, 2000; Thayer & Sternberg, 2010), and emotion regulation is likely relevant for adaptive "mental" sexual arousal function (Heiman, 1980). When women are in a sexual situation, effective regulation of emotional responses "in the moment" will at least partially contribute to the success of the overall experience. That is, feeling mentally turned on during sexual activity may be considered adaptive emotion regulation, as this feeling integrates psychological and physiological responses to meet the demands of a sexual situation.

Barlow's model of sexual dysfunction (1986) provides another possible explanation for these findings. According to this model, the locus and quality of the individual's attention and, relatedly, the degree of one's cognitive distraction are maintaining factors of sexual problems. During sexual activity, individuals with sexual dysfunction tend to show decreased focus on erotic cues and increased focus on non-erotic cues (Purdon & Holdaway, 2006), such as negative thoughts about their own level of physical attraction. Similarly, spectatoring, which occurs when individuals focus on their arousal only to judge its adequacy during sexual intercourse, has been associated with sexual problems (Meston, 2006). The autogenic training intervention draws the practitioner's attention to specific areas of the body for extended periods of time, potentially reducing cognitive distraction. Spending over twenty minutes channeling feelings of warmth and heaviness in different limbs may help women direct their attention to similar sensations in their genitals and to other erotic cues during the sexual film, ultimately leading to increases in both subjective sexual arousal and perceived genital sensations.

It is notable that the autogenic training manipulation failed to result in significant VPA increases over time. In a previous study, the same protocol was applied to a group of pre-menopausal women *without* sexual arousal concerns, and there was a significant increase in VPA from pre- to post-manipulation (Stanton & Meston, 2016). It is possible that the intervention may not be applicable to women with a clear genital arousal disorder, such as women with medical comorbidities that affect the neurovascular system. Or, it may be that a 22-minute, single-session intervention was not long enough or intense enough to translate into statistically meaningful gains in genital arousal in among women who have been suffering from low arousal for at least six months. To test this hypothesis, researchers could consider titrating the dose of the intervention in future studies (i.e., longer sessions or multiple sessions) or altering the protocol to

enable women to listen to the autogenic training recording from the privacy of their own homes. The contradictory VPA findings are not unusual, as the literature documenting the effects of both psychosocial and pharmacologic interventions on genital sexual arousal is mixed. Some pharmacologic agents have been shown to increase VPA response relative to placebo; these include combined L-arginine glutamine plus yohimbine (Meston & Worcel, 2002), ginkgo biloba (Meston, Rellini, & Telch, 2008), tibolone (Laan, van Lunsen, & Everaerd, 2001), and sildenafil (Laan, van Lunsen, et al., 2002; Marca L Sipski, Rosen, Alexander, & Hamer, 2000). Other studies, particularly those examining the effects of sildenafil and other phosphodiesterase inhibitors on genital arousal in women, have *not* shown promising results with respect to VPA and/or similar physiological indices of female genital arousal (Chivers & Rosen, 2010; Foster, Mears, & Goldmeier, 2009).

Likewise, there is no clear consensus on the effect of psychosocial interventions, such as traditional cognitive-behavioral therapy (CBT) and mindfulness, on genital arousal in women with self-reported arousal concerns. As of 2013, when a meta-analysis of psychosocial interventions for female sexual dysfunction was published, there were no randomized-controlled studies on female sexual arousal disorder (FSAD) to include in the analysis (Frühauf, Gerger, Schmidt, Munder, & Barth, 2013). Some studies have examined the efficacy of CBT for improving other domains of sexual function, such as desire (Ravart, Marchand, & Trudel, 1996) and pain (Van Lankveld et al., 2006), but increases in female sexual arousal (and VPA, in particular) have yet to be the target of a randomized-controlled CBT trial. This lack of CBT-based options for women with arousal concerns has been somewhat remedied in recent years with the increase in studies examining mindfulness-based interventions for female sexual dysfunction. In 2003, Brotto and colleagues began a series of studies on the application of

mindfulness-based approaches for sexual dysfunction (Brotto, 2013). Brotto et al. developed a three-session, mindfulness-based group psychoeducational intervention for women with FSAD. Though the intervention had a significant positive effect on self-assessed genital wetness and led to marginally significant increases in subjective and self-reported physical arousal, it did not result in any changes in physiological arousal measured by VPA (Brotto et al., 2008). Similarly, when they tested their intervention on a sample of women with gynecologic cancer, Brotto and colleagues found a significant effect of the program on self-reported arousal (and other sexual function domains, including desire, orgasm, satisfaction, and sexual distress), but only a trend toward significantly improved physiological genital arousal (VPA) and perceived genital arousal (Brotto et al., 2008). Therefore, the lack of significant VPA findings in the current study are consistent with previous research on mindfulness-based interventions.

Autogenic training, the intervention used in this study to increase HRV, and mindfulness have some similarities but also a few critical differences. Mindfulness has been defined as a purposeful, nonjudgmental awareness of the present moment or one's present experience (Kabat-Zinn, 2005). In mindfulness-based practices, patients are invited to attend to and accept their present experience without judging it or attempting to change it in any way. Autogenic training also emphasizes nonjudgmental attention to the present moment, but it directs practitioners to conjure sensations throughout the body via verbal self-suggestions (Schultz & Luthe, 1959; Stetter & Kupper, 2002). Whereas mindfulness discourages any attempts to alter one's physical sensations, autogenic training facilitates autonomic self-regulation through these self-suggestions. Some women may find it difficult or frustrating to sit with their sensations without attempting alter them; for these women, autogenic training could be a viable option. Other women may be attracted to mindfulness-based protocols because they build curiosity, openness,

and, perhaps most importantly, acceptance of the body and the environment. If a future randomized-controlled study demonstrates that autogenic training (and/or other interventions that increase HRV) is associated with significant increases in sexual arousal among women with sexual arousal problems, then it may be worth considering this protocol as an alternative or a complement to mindfulness-based practices.

The main contribution of the current study is the demonstrated effect of the autogenic training recording on acute subjective sexual arousal and perceived genital arousal. It is arguable that subjective sexual arousal and perceived genital arousal are more important to a woman's individual experience of sexual activity than her VPA. Laboratory studies have shown low correlations between subjective and physiological measurements of sexual arousal in women.[60] That is, women are less likely than men to report feeling aroused when their physiological arousal is elevated. It may therefore be more clinically meaningful to look for changes in *perceived* genital sensations and subjective sexual arousal, rather than changes in VPA, when testing psychosocial interventions aimed to increase arousal.

Importantly, we do not believe that these increases are a result of repeated presentation of erotic material. The two films were separated by a 22-minute recording, which is likely a long enough period of time for participants to return to their baseline levels of VPA and subjective arousal. Indeed, the results of a paired samples *t*-test comparing average VPA during the first three-minute neutral film and average VPA during the second three-minute neutral film did not reach statistical significance, which indicates that participants returned to their baseline VPA before the presentation of the second erotic film. Other studies have demonstrated that presenting multiple erotic films in a single session, with sufficient time in between the films for the participants to return to their baseline levels of arousal, does not lead to increased subjective

sexual arousal. For example, Pulverman and colleagues showed heterosexual and lesbian women three different films (featuring heterosexual, lesbian, and gay male couples, respectively), in counterbalanced order, during a single laboratory visit (Pulverman, Hixon, & Meston, 2015). Subjective sexual arousal differed significantly based on the content of the films, not on the order in which the films were presented. That is, subjective sexual arousal was not significantly greater during the third film compared to the first film or the second film.

There are several limitations of this study that warrant explanation. First, the study had a small sample size and did not include a control group or a "sham" intervention. To more accurately determine the efficacy of autogenic training and other similar interventions in improving sexual arousal among women who meet ICD-10 criteria for Female Sexual Arousal Disorder (FSAD) or DSM-5 criteria for Female Sexual Interest/Arousal Disorder (FSIAD), it will be crucial to conduct a randomized-controlled trial on a larger sample that includes either a placebo or a wait-list control group. Before such a study is conducted, the generalizability of our results to clinical populations is limited. Second, to minimize the number of visits required to complete the study, we did not randomize the order of the autogenic training recording. Rather than having each participant come to the lab twice, once to establish a baseline VPA reading and once to play the autogenic training recording prior to presenting the neutral-erotic film sequence, we included both the pre-manipulation VPA recording and the post-manipulation VPA recording in a single visit. Though we recognize that a multi-visit study design may have more effectively isolated the relative contribution of the autogenic training recording to the arousal response, separating the study into two visits may have led to decreased compliance, increased dropout rates, and/or variability in the placement of the vaginal photoplethysmograph. Third, lesbian women were excluded from participation. The stimulus films that were used in this study have

been demonstrated to increase arousal among heterosexual and bisexual women in previous studies. We chose to limit potential sources of variability by using (1) only two films and (2) films that that had been piloted on other women. Given that there were no lesbian women in our sample, we cannot claim that these results generalize to that population. It is critical that future research test the efficacy of this intervention and other sexual arousal interventions on women who are sexually attracted to women.

In addition, we did not use a validated instrument to assess for sexual arousal concerns during the screening phase, nor did we inquire about deficits in subjective sexual arousal. The FSDD was originally developed from the ICD-10/DSM-IV-TR diagnostic criteria for FSAD to highlight potential deficits in genital arousal. It was adapted for this study to assess specific genital sensations that are typically thought to be associated with physiological sexual arousal (e.g., genital warmth, clitoral fullness, etc.). We do not have information on the validity and reliability of the adapted FSDD. Women were only allowed to participate if they reported decreased or absent genital arousal; they were not asked about subjective arousal during the phone screen. A broad understanding of arousal incorporates both physical and mental readiness for sexual activity. Indeed, Janssen and colleagues have proposed that arousal can be broken down into two key components: (1) conscious and unconscious mental processing leading to an automatic genital response (i.e., physiological arousal) and (2) a cognitive process appraising the sexual content of the stimulus (i.e., subjective sexual arousal; Janssen et al., 2000; Spiering et al., 2003) There are women who report diminished subjective sexual arousal but no decrements in physiological arousal (Meston et al., 2010), and these women may benefit from the autogenic training intervention.

Finally, based on these results, we cannot definitively conclude that change in HRV has a causal effect on sexual arousal or that autogenic training uniquely targets HRV. It is also possible that autogenic training modulates the entire autonomic nervous system, and one of the consequences of this modulation is increased HRV. Another consequence of this modulation may be increased arousal, such that increased HRV and increased arousal occur in parallel. The timing and nature of these effects should be further investigated in future research.

Overall, our finding that autogenic training increased acute subjective sexual arousal and perceived genital arousal among women with sexual arousal concerns suggests that this intervention may be a welcome addition to the small group of psychosocial interventions that have shown efficacy in treating sexual arousal concerns. The fact that women who experienced the greatest changes in resting HRV had the greatest increases in subjective sexual arousal indicates that HRV level may be an important mechanism fueling the effects of the autogenic training intervention. Autogenic training is easy to learn, and recordings can be downloaded from the Internet at little to no cost. Given the wide-scale availability of the intervention and its potential to improve sexual arousal in women with *and* without arousal concerns (Stanton & Meston, 2016), it is worthwhile to continue investigating the effects of HRV interventions on sexual arousal.

4. A RANDOMIZED-CONTROLLED TRIAL OF HEART RATE VARIABILITY BIOFEEDBACK FOR THE TREATMENT OF FEMALE SEXUAL AROUSAL DISORDER

4.1. Introduction and hypotheses

Studies 3 and 4 examined the effect of autogenic training, a brief HRV manipulation, on both genital sexual arousal and subjective sexual arousal in sexually functional women and women with sexual arousal problems, respectively. The results of these studies revealed that, in small samples of women, autogenic training effectively increased HRV, subjective sexual arousal (for women with and without sexual arousal dysfunction), and genital sexual (for women without sexual arousal problems). However, autogenic training did not lead to improvements in genital arousal among women with FSAD, and these studies did not follow up with participants after their laboratory visits to determine if the autogenic training intervention had long-term effects on their sexual arousal function.

The aim of this randomized-controlled trial of HRV biofeedback and the combination of HRV biofeedback with autogenic training (Study 5) was to strengthen the findings of Study 4 by increasing the intensity and duration of the HRV manipulation in order to provide long-term rather than acute gains in sexual arousal function. To that end, I designed a three-armed randomized-controlled trial with two active arms and a control group. Instead of using autogenic training alone as the method to increase HRV, which I did in Studies 3 and 4, I chose HRV biofeedback and a combination of HRV biofeedback with autogenic training as the two active arms. A method of controlling one's breathing to the resonant frequency of about five to six breaths per minute, HRV biofeedback consists of feeding back beat by beat heart rate data to the participant while she is engaging in this slow breathing in order to maximize respiratory sinus

arrhythmia (RSA) and match RSA to heart rate patterns. The comparison of biofeedback alone against the combination of biofeedback and autogenic training was intended to test the hypothesis that the combination might be associated with greater increases in HRV and ultimately greater gains in arousal over the course of the intervention.

Heart rate variability biofeedback has been linked to improvements in overall autonomic function (Lehrer et al., 2003; Vaschillo et al., 2006). The procedure is designed to produce increases in HRV, improve autonomic reactivity, and increase voluntary control over the physiological processes that are otherwise outside of one's awareness. In recent years, HRV biofeedback has also shown promise in the treatment of several disorders that are specifically associated with autonomic imbalance, including depression, anxiety, and PTSD (e.g., Beckham, Greene, & Meltzer-Brody, 2013; Henriques, Keffer, Abrahamson, & Horst, 2011; Siepmann, Aykac, Unterdörfer, Petrowski, & Mueck-Weymann, 2008; Tan, Dao, Farmer, Sutherland, & Gevirtz, 2011). The key mechanism believed to be responsible for the beneficial effects of this form of cardiorespiratory feedback training is the strengthening of homeostasis in the baroreceptor (Lehrer et al., 2003). Some researchers have suggested that the positive effects of HRV biofeedback may also be driven by stimulation of the vagal afferent pathways (Brown, Gerbarg, & Muench, 2013; Brown & Gerbarg, 2005; Porges, 2011). These pathways affect brain areas known to be involved in affect regulation and mood, specifically the locus coeruleus, orbitofrontal cortex, hippocampus, insula, and amygdala (Grundy, 2002). Biofeedback protocols have been tested on a variety of clinical populations, and in general, findings suggest that this practice improves psychomotor performance, cognitive and psychological states, and physiological functioning.

It is evident that HRV biofeedback is particularly helpful for clinical populations whose autonomic balance shifts too far toward a sympathetic-predominant state. Depression, anxiety, and PTSD are all associated with over-activation of the SNS (e.g., Blechert, Michael, Grossman, Lajtman, & Wilhelm, 2007; Carney, Freedland, & Veith, 2005). Female sexual arousal disorder likely falls into this category as well, as female sexual arousal has been consistently linked with autonomic balance. Research has indicated that there is an optimal level of SNS activation for the facilitation of physiological sexual arousal in women, such that too much (or too little) activation inhibits sexual arousal function (Lorenz et al., 2012; Meston & Gorzalka, 1996b). Women who have over-active SNS activity at baseline (e.g., women with a history of CSA and/or PTSD) do not experience increases in sexual arousal after SNS activation (Rellini & Meston, 2006). Similarly, women with high state anxiety show lower increases in physiological sexual arousal in response to an erotic film compared to women with state anxiety scores in the moderate range (Bradford & Meston, 2006).

Autogenic training, a psychophysiological relaxation technique, has also demonstrated effectiveness compared to control conditions in alleviating symptoms of disorders that are associated with autonomic dysregulation. In a meta-analyses, autogenic training reduced symptoms of anxiety, mild-to-moderate depression, and functional sleep disorders (Stetter & Kupper, 2002). Although no experiments have directly compared autogenic training to cognitive or exposure-based therapies, one study did demonstrate that depressed patients who received a combination of psychotherapy and autogenic training had better outcomes at follow-up than did patients who received psychotherapy alone (Krampen, 1999). Autogenic training has received far less attention in the literature than HRV biofeedback, but it has been demonstrated to increase HRV over short term and long term periods (Mishima et al., 1999; Miu et al., 2009).

The objective of Study 5 was to examine the effectiveness of (1) HRV biofeedback and (2) the combination of HRV biofeedback and autogenic training in increasing sexual arousal among women who report problems with genital and/or psychological sexual arousal. Based on the preliminary results of Study 4, I hypothesized that one-month of HRV biofeedback, with and without autogenic training, would improve subjective sexual arousal and perceived genital arousal, possibly leading to clinically relevant improvements in sexual arousal function. I also hypothesized that women receiving both HRV biofeedback and autogenic training would experience the greatest gains in arousal compared to the women randomized to the other two groups. Finally, I hypothesized that HRV biofeedback, with and without autogenic training, would lead to marginal increases in genital sexual arousal.

4.2. Methods

4.2.1. Experimental design

This study involved three laboratory sessions and a one-month follow up survey. After participating in a phone screen with a research assistant to determine eligibility, eligible participants were randomized into one of three conditions: HRV biofeedback (HRVB), HRV biofeedback plus autogenic training (HRVB+A), and a wait-list control condition (WL). Participants were stratified across the three groups based on baseline FSFI scores, which were determined during the phone screen. Then, participants were invited to the Sexual Psychophysiology Laboratory for their first study session.

Women in the two active conditions (HRVB, HRVB+A) received guided HRV biofeedback from the experimenter during their first study session. They were also given a Polar H7 Bluetooth Heart Rate Sensor & Fitness Tracker, as well as access to Elite HRV software. Using this software, they connected the Polar H7 sensor to their smart phones via Bluetooth.

Women in the HRVB condition were asked to complete at-home HRV biofeedback two-three 20-minute biofeedback sessions per week.[5] Women in the HRVB+A condition completed the same number of biofeedback sessions as their counterparts in the HRVB condition, but they were instructed to listen to a 14-minute autogenic training recording before doing so. Women in the WL condition were told that their sexual arousal needed to be monitored while they waited for availability in the experimental condition. After the one-month follow-up period, participants in WL condition were offered the opportunity to attend one session of guided HRV biofeedback with the experimenter. Although two women expressed interest in this option, they did not respond to follow up requests.

4.2.2. Participants

Participants were recruited from the local community via brochures, fliers, and online advertisements. These materials instructed potential participants to call the laboratory to complete a phone screen with a trained research assistant. Eligible women were randomized into one of the three groups and invited to schedule their first laboratory session.

The final sample included 78 adult women, aged 18-50 (M = 25.42, SD = 7.96), split among the three conditions. The conditions were matched on age, plus or minus a few years, and participants were stratified based on FSFI scores. There were no statistically significant differences in age, age of sexual debut, baseline FSFI scores, relationship status, race/ethnicity, educational attainment, drop out rates, or follow up rates among the three groups (see Table 12).

[5] We acknowledge that the requirement of a smart phone will be a significant limitation of the study, as it will decrease the likelihood that women of lower socioeconomic status will be able to participate and therefore limit the ecological validity of our findings.

Table 12. Participant characteristics

	HRVB (n = 31)	HRVB + A (n = 26)	WL (n = 21)		Entire Sample (n = 78)
	M (SD)	*M (SD)*	*M (SD)*	*F*	*M (SD)*
Age	25.10 (8.15)	25.46 (8.15)	25.86 (7.72)	.06[a]	25.42 (7.96)
Age of sexual debut	16.91 (2.49)	19.30 (3.29)	17.33 (1.98)	.31[a]	16.99 (2.46)
Baseline FSFI score	19.49 (3.12)	19.30 (4.84)	18.50 (3.76)	.43[a]	19.16 (3.90)
	n	*n*	*n*	χ^2	*n*
Relationship status				5.99[a]	
Single (not dating)	7	6	3		16
Single (casually dating)	8	6	8		22
In a committed relationship	11	9	10		30
Married	5	5	0		10
Race/Ethnicity				6.12[a]	
African American/Black	6	1	4		11
Asian	3	5	3		11
Caucasian/White	14	9	6		29
Hispanic/Latin American	7	10	7		24
Other	1	1	1		3
Highest level of education				6.71[a]	
High school degree/GED	3	4	6		13
Some college	17	14	10		41
College degree	8	4	5		17
Advanced degree	3	4	0		7
Drop out status				2.30[a]	
Completed all lab visits	26	25	18		69
Follow up status				.90[a]	
Completed all lab visits and follow up survey	14	15	11		40

[a] = $p > 0.05$

4.2.2.1. Inclusion/exclusion criteria

Inclusion criteria:

1. Premenopausal women (aged 18-40 years): Women under the age of 18 were not tested due to ethical issues. The upper age range was included to facilitate age-matching among the three groups and to ensure that all participants were pre-menopausal.
2. Fluent in English: The majority of the self-report measures that were selected for this study are only available in English. Therefore, women needed to be fluent in English in order to participate.
3. Heterosexual or bisexual: This criterion was established in order to limit potential variability in the data. Women in this study watched watch three different erotic film clips in each of the three experimental sessions, and these film clips featured a heterosexual couple engaging in sexual activity. By limiting our participants to women who report some sexual attraction to men, we were able to use the same erotic film clips for all participants.
4. Score of 26.55 or below on the Female Sexual Function Index (FSFI; Rosen et al., 2000): Women with sexual dysfunction disorders have been demonstrated to score at or below 26.55 on this validated self-report index (Wiegel et al., 2005). Therefore women needed to score below 26.55 in order to be eligible for participation.
5. Current sexual arousal dysfunction: As FSAD was the focus of the current study, only women who reported problems with sexual arousal were eligible to participate. Phone screeners used an expanded version of the DSM-IV-TR criteria for FSAD, which includes diminished/absent genital sensations *and/or* diminished/absent psychological arousal. To determine if women met these expanded criteria, phone screeners assessed

for arousal concerns with an adapted version of the Female Sexual Dysfunction Diagnosis (FSDD) questionnaire. The adapted FSDD assesses participants' current level of genital arousal by referencing specific genital responses typically experienced during sexual activity (e.g., genital warmth, fullness, pressure) and asks participants to rank how important it is for them to experience these specific genital responses during sexual activity. The questionnaire also assesses for diminished/absent psychological/mental sexual arousal.

6. Ownership of an iPhone 4s, 5, 5 C/S/SE, 6, 6S, 6 plus, or newer; iPad 3rd generation, 4th generation, Air, Air 2, Mini, Mini 2, Mini 3, or newer; or an Android device that runs Android 4.3 or newer: The at-home biofeedback software (Elite HRV app) is only compatible with the hardware listed above. Therefore, women who did not have access to any of the above hardware were not eligible to participate in the study.

Exclusion criteria:

1. Pregnant or breastfeeding: Sexual function is affected by the physiological and hormonal changes that occur as a result of pregnancy, and these changes persist into the postpartum period (Serati et al., 2010). Therefore, women who fit this criterion were excluded from the study.
2. History or current diagnosis of sexually transmitted disease(s): Although our protocol for sterilizing the vaginal photoplethysmograph removes risk of transmission of all sexually transmitted diseases, the Sexual Psychophysiology Laboratory excludes participants who report current or past sexually transmitted diseases from all psychophysiological studies as an additional preventative measure.

3. History of major pelvic surgery (e.g., hysterectomy, vulvectomy, or serious rectal, bladder, or abdominal surgery): Pelvic surgery may lead to nerve damage in the pelvic area, and pelvic nerve damage has been shown to affect sexual arousal in women (Vlug et al., 2010). Therefore, we excluded women with a history of these procedures.
4. History of childhood sexual abuse (CSA): CSA will be defined as unwanted oral, anal, or vaginal intercourse, penetration of the vaginal or anus, or genital touching or fondling before age 16 (Rellini, 2008). A large body of literature indicates that CSA has negative effects on women's sexual health. In this population, sexual arousal may be associated with negative feelings and traumatic memories (e.g., Meston, Rellini, & Heiman, 2006). To reduce the variability in our data, we attempted to focus on sexual arousal problems that were independent of a history of CSA.
5. Currently taking any androgens/estrogens (other than hormonal contraceptives) or any other medical treatments to enhance sexual response: As the aim of the present study was to examine the effects of a potential *treatment* for sexual arousal problems, women who were already receiving other treatments to enhance their sexual response were not be eligible to participate.
6. Currently taking benzodiazepines or beta blockers: These medications have been shown to significantly dampen physiological sexual arousal (Ghadirian, Annable, & Bélanger, 1992). Therefore, women taking these medications were excluded from the study.
7. If currently taking antidepressants or anti-hypertensives, must be stabilized on the medications for at least 3 months: These medications have been shown to have potential sexual side effects (e.g., Rosen & Kostis, 1985; Serretti & Chiesa, 2009). However, the use of these medications, particularly antidepressants, is common among

women. Indeed, an estimated 1 in 6 women has been prescribed an antidepressant (Rosen et al., 1999). Therefore, women who are taking these medications needed to be stabilized on their current dose for at least 3 months prior to enrolling in the study.

8. No current diagnosis of psychosis (e.g., bipolar disorder or schizophrenia): Sexual arousal patterns are affected by periods of psychosis (Marques et al., 2012). For this reason, women who reported diagnoses of disorders that are characterized periods of psychosis, including bipolar disorder and schizophrenia, were excluded from the current study.

4.2.3. Measures

4.2.3.1. Primary measures

1. Heart rate variability: Baseline heart rate was measured at a rate of 200 samples/sec via electrocardiography (ECG) during the neutral segment of each neutral-erotic film. The signal from the ECG leads was detected using an MP100 data acquisition unit that was equipped with AcqKnowledge 3.9.1 software (Biopac Systems, Inc., Santa Barbara, CA). The ECG data was extracted to Microsoft Excel for processing and artifact removal. The final Excel files were converted to text files and analyzed by Kubios HRV Analysis Software (Biosignal Analysis and Medical Imaging Group, University of Kuopio, Kuopio Finland). The standard deviation of the normal heart beat interval lengths (SDNN), a time domain measurement, was used as the index of HRV in this study. SDNN is considered one of the most widely used measures of HRV (Xhyheri et al., 2012); it provides information about all components contributing to HRV during the recording period
2. Genital sexual arousal: Genital sexual arousal was assessed via vaginal photoplethysmography (Sintchak & Geer, 1975), which produces two measurements:

vaginal blood volume (VBV) and vaginal pulse amplitude (VPA). Vaginal pulse amplitude, which reflects short-term changes in the engorgement of blood in the vaginal tissue (Rosen & Beck, 1988), is considered to be the more sensitive of the two indices (Heiman, 1977) and has been shown to be a reliable index of women's genital arousal (Laan, Everaerd, Van Aanhold, & Rebel, 1993). Vaginal pulse amplitude data was sampled at a rate of 200 samples/sec throughout the erotic films during each of the three laboratory sessions. These data were recorded in millivolts and collected by an MP100 data acquisition unit equipped with AcqKnowledge 3.9.3 software (Biopac Systems, Santa Barbara).

3. Subjective arousal (discrete and continuous): Discrete subjective arousal was assessed via 3 items on the modified version of the Film Scale (Heiman & Rowland, 1983), which measures perception of physiological arousal and psychological arousal in response to a sexual film. Participants completed the Film Scale after watching the erotic film during each of the three laboratory sessions. Continuous subjective arousal was measured with the Arousometer (Rellini, McCall, Randall, & Meston, 2005). The arousometer is a computer mouse attached to a lever, which is numbered from 0 to 7. During the erotic films at each of the three laboratory sessions, participants were instructed to move the mouse up or down as they felt their mental sexual arousal changing.
4. Perceived genital arousal: Perceived genital arousal was assessed via 5 items on the modified version of the Film Scale (Heiman & Rowland, 1983).. Participants completed the Film Scale after watching the erotic film during each of the three laboratory sessions.

5.

4.2.3.2. Other measures

1. Demographics: Demographic characteristics were assessed at laboratory session 1 with a questionnaire on age, gender, educational history, race, ethnicity, country of heritage, relationship status, and sexual orientation. This information was used to test for potential differences between participants in each of the three conditions.
2. Affect: Affect was measured by the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988) before and after the erotic film at each of the three visits.
3. Depression symptoms: Depression symptoms were measured by the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996), a 21-item self-report inventory, at the first laboratory visit, the third laboratory visit, and at one-month follow up.
4. Anxiety symptoms: Anxiety symptoms were measured by the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988), a 21-item questionnaire, at the first laboratory visit, the third laboratory visit, and at one-month follow up.
5. Interoceptive awareness: Interoceptive awareness was measured by the Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al., 2012), a 32-item self-report questionnaire. Participants completed this measure at the first laboratory visit, the third laboratory visit, and at one-month follow up.
6. Mindfulness: Mindfulness was measured by the Five-Facet Mindfulness questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006), a 39-item self-report questionnaire that assesses five facets of mindfulness (observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience).

Participants completed this measure at the first laboratory visit, the third laboratory visit, and at one-month follow up.

7. Sexual distress: Sexual distress will be measured by the Female Sexual Distress Scale Revised (FSDS-R), an extended version of the 12-item Female Sexual Distress Scale (FSDS; Derogatis, Rosen, Burnett, & Heiman, 2002). This measure is designed to assess distress related to sexual dysfunction in women. Participants will complete this measure at the first laboratory visit, the third laboratory visit, and at one-month follow up.
8. Sexual activity: Sexual activity throughout the course of the study will be measured with a daily diary of sexual activity, which was adapted from a study that examined the effects of ginko biloba on sexual dysfunction in women (Meston et al., 2008). Participants will be asked to complete the measure, which assesses the two components of arousal as well as orgasm, after every sexual activity during the active phase of the trial.
9. Sexual function: Overall sexual function was assessed with the Female Sexual Functioning Index (FSFI; Rosen et al., 2000). The FSFI is a widely used index that assesses female sexual function over the past month. The FSFI includes 19-items composing 6 subscales: desire, arousal, lubrication, orgasm, satisfaction, and pain. Participants completed the FSFI during the phone screen, during laboratory visit 1, during laboratory visit 3, and at one-month follow up.
10. Overall function: Overall function will be assessed with the Sheehan Disability Scale (SDS; Sheehan, 1983). The SDS assesses function impairment in three inter-related domains: work/school, social life, and family life. Participants will complete this measure at the first laboratory visit, the third laboratory visit, and at one-month follow up.

4.2.5. Procedure

4.2.5.1. Approximate study timeline

Table 13

Approximate study timeline

	Day 1	Days 2-11	Day 12-13	Days 14-27	Day 28	Day 58
Phone screen and Randomization	**Laboratory Visit 1** (90 mins for HRVB and HRVB+A groups; 50 minutes for WL group)	**At-home biofeedback** (HRVB and HRVB +A groups only)	**Laboratory Visit 2** (50 mins for all three groups)	**At-home biofeedback** (HRVB and HRVB +A groups only)	**Laboratory Visit 3** (50 mins for all three groups)	**1-month follow up** (online survey; 20-30 mins for all three groups)

4.2.5.2. Determining eligibility

Women interested in participating in the study called the laboratory to speak with a trained research assistant and complete a phone screen. In the phone screen, the research assistant provided a standardized introduction to the study and answered questions about the study procedures. After receiving information about the study, participants were offered the opportunity to complete a confidential verbal phone screen to assess inclusion and exclusion criteria. As in Study 4, phone screeners used adapted version of the Female Sexual Dysfunction Diagnosis (FSDD) questionnaire to determine if callers meet criteria for FSAD. The adapted FSDD assesses participants' current level of genital arousal, by referencing specific genital responses typically experienced during sexual activity, and asks participants to rank how important it is for them to experience these specific genital responses during sexual activity. During the phone screen, the research assistant also assessed the caller's overall sexual function using the Female Sexual Function Index (FSFI; Rosen et al., 2000) and past history of CSA with a single question. As mentioned in section earlier, CSA was defined as unwanted oral, anal, or

vaginal intercourse, penetration of the vaginal or anus, or genital touching or fondling before age 16 (Rellini, 2008). If eligible, the participant was randomized and invited to the laboratory for her first study session. Eligible participants were asked to refrain from unaccustomed or strenuous exercise for at least 6 hours prior to every study session, given that sympathetic nervous system activation via acute exercise has been shown to facilitate genital sexual arousal in women (e.g., Lorenz et al., 2012; Meston & Gorzalka, 1996b). Eligible participants were also asked to refrain from consuming caffeine, a central nervous system stimulant, for at least 5 hours prior to every study session, as the range of the half-life of caffeine in non-pregnant females is 2-5 hours (Knutti, Rothweiler, & Schlatter, 1982).

4.2.5.3. Laboratory sessions

Laboratory session 1. At the first laboratory session, the experimenter greeted the participant and oriented her to the study procedures. The experimenter explained how to use the vaginal photoplethysmograph, ECG, and the Arousometer. Following this explanation, participants read and signed the consent form. The experimenter placed the ECG electropads on the participant's body and then left the room, locking it from the inside so that the participant enjoyed complete privacy during the study session. The experimenter communicated with the participant with an intercom during the rest of the study session. First, participants were asked to complete a battery of self-report measures (demographics, affect, depression symptoms, anxiety symptoms, interoceptive awareness, mindfulness, sexual distress, and overall functioning) on an iPad. After completing these questionnaires, participants were instructed to attach the ECG wires to the electropads and insert the vaginal probe. They then watched a 10- minute film composed of neutral (4 minutes) and erotic (6 minutes) content. During the neutral stimuli, baseline HRV was measured; genital and subjective sexual arousal were measured continuously during both the

neutral and the stimuli. Then, participants in all three conditions completed an affect measure (the PANAS) and the Film Scale to retrospectively assess their subjective sexual arousal and perceived genital sensations during the erotic stimulus.

The three films selected for this study's three laboratory visits were matched for content, and they have been shown to elicit sexual arousal in heterosexual and bisexual women in previous studies conducted in our laboratory. All of the films featured a heterosexual couple engaging in foreplay (2 minutes), cunnilingus (2 minutes), and vaginal intercourse (2 minutes). The order in which these films were presented across the three laboratory visits was randomized.

After completing the Film Scale, participants in the WL condition were compensated $25 for their time and reminded of their next visit. Participants in the HRVB and HRVB+A conditions received one session of guided HRV biofeedback from the experimenter (See section 4.2.4.4 for a detailed overview of the biofeedback procedure). The experimenter then helped participants download the Elite HRV app, provided participants with the at-home biofeedback sensor, and offered detailed instructions on how to use the sensor and the app. Participants in the HRVB+A condition were informed that they needed to listen to an autogenic training recording, which was provided to them via email, before completing their biofeedback. After ensuring that participants understood the protocol, the experimenter compensated them for their time and reminded them of the date of their next laboratory sessions.

During all laboratory visits, the experimenter and the research assistants involved in the study carefully reviewed all self-report measures before the participant left the laboratory. If the participant failed to complete any items, the experimenter or the research assistant asked the participant if she intended to leave the specified items blank. If the participant did not intend to leave the items blank, she was invited to complete them at that time. In addition, the online

survey collector that was used to collect follow-up data required survey completers to select an answer for every item, which minimized missing data.

Laboratory session 2. The second laboratory session took place approximately 14 days after the first laboratory session. During this second session, all participants watched a neutral-erotic film sequence; similar to laboratory session 1, resting state HRV was measured during the neutral segment of the film; genital and subjective sexual arousal were measured continuously during both the neutral and the erotic segments. Following the film, participants completed the film scale. To incentivize women in the HRVB and HRVB+A conditions to complete the study and return the biofeedback sensors (valued at $50), they were not compensated for this laboratory session until laboratory session 3. Women in the WL condition were compensated $25 for this session.

Laboratory session 3. The third laboratory session took place approximately two weeks after the second laboratory session. At the beginning of the session, participants completed self-report questionnaires (affect, depression symptoms, anxiety symptoms, interoceptive awareness, mindfulness, sexual distress, and overall functioning) on an iPad. Following the questionnaires, participants watched a third neutral-erotic film sequence. Again, resting state HRV was measured during the neutral segment of the film, and both genital and subjective arousal were measured during the erotic segment of the film. Women in the WL condition were compensated $25 for this session.

Upon returning the biofeedback sensor, women in the HRVB and the HRVB+A conditions were compensated $50 for this session ($25 for laboratory visit 2 and $25 for laboratory visit 3). At this time, participants in these two conditions also received $5 for every self-guided HRV biofeedback session completed between laboratory visits 1 and 2 (a maximum

of $30) and $5 for every self-guided HRV biofeedback session completed between laboratory visits 2 and 3 (again, a maximum of $30). Therefore, at laboratory visit 3, women in the two active conditions had the opportunity to earn as much as $110.

The study was registered with ClinicalTrials.gov (NCT02958176).

4.2.5.4. Biofeedback procedure

During laboratory session 1, participants in the experimental condition will receive guided HRV biofeedback training (adapted from Lehrer et al., 2013) from the experimenter.

1. Provide the following instructions: "*Today, I am going to introduce you to a method that may help you control your symptoms. We will be using a sensor, and wearing it may feel a little strange in the beginning. This introduction will allow you to become familiar with what it feels like to wear the sensor, and to watch the body signals they are measuring on the screen, before we start your biofeedback training. I will attach the sensor to your body and then you will see what it is measuring on the monitor. The sensor will simply be measuring your physiological activity and will not cause any harm to you. I will briefly explain what each measurement is."*
2. Attach sensor that will be used. Begin display of physiological data.
3. Explain what each graph or number represents on the screen. The exact description may differ, depending on the particular hardware and software used and the particular array of physiological measures.
    a. For example: "*In this top graph, the red line is your heart rate in terms of beats per minute, and the blue line shows your breathing. You'll notice that the blue line moves up as you breathe in and down as you breathe out*."
4. Provide rationale for six minute breathing pace.

a. People are able to produce very large increases in heart rate variability (HRV), the variability in the lengths of time between successive heartbeats, through biofeedback because of "resonance" characteristics of the cardiovascular system. Actually, this system resonates the same way that a musical instrument does. HRV biofeedback simulates a particular reflex in the cardiovascular system that has a certain rhythm to it. It is called the "baroreflex" and it helps to control blood pressure. It also helps to control emotional reactivity and promotes breathing efficiency. When blood pressure goes up, the baroreflex causes heart rate to go down, and when blood pressure goes down, heart rate goes up. This causes a rhythm in heart rate fluctuations. When a person breathes at this exact rhythm (which varies among people, but is typically about six breaths per minute), the system resonates, much like the sound of a vibrating string resonates in the box of a violin, creating a big sound. Six breaths per minute is the frequency that produces the biggest swings in heart rate between inhaling and exhaling. When people breathe at this frequency, the baroreflex system is stimulated and strengthened, and through projections to other systems in the body (e.g., inflammatory and limbic systems), other events occur that produce the many beneficial effects of HRV biofeedback.

5. Connect the participant to the biofeedback instrument.

6. Begin by pacing breathing at 6 breaths per minute for several minutes. Coach the participant to breathe with a pacing stimulus, as evenly as possible. This rate of breathing is the average resonance frequency of the cardiovascular system for adults. If the individual feels

uncomfortable breathing at this rate, choose one that is slightly faster or slower. Adjust the Elite HRV app accordingly.

7. Ask the participant about hyperventilation symptoms (primarily lightheadedness, dizziness, heart pounding) and instruct her to breathe less deeply if needed.
8. After the participant is breathing regularly at this frequency, pause and tell the participant to relax, and stop doing paced breathing for a minute or two (or until the participant is relaxed and ready to start a new task). Ask the participant how it felt.
9. After doing some paced breathing, start biofeedback. Instruct the participant to breathe with the heart rate signal, to inhale when heart rate goes up and exhale as it goes down, and to try to maximize the peak-to-trough heart rate swings.
    a. Example: "*Breathe easily and comfortably rather than deeply. Be sure to breathe out longer than you breathe in. Inhale through your nose; exhale through your mouth with pursed lips as if you were blowing through a straw. This will help to slow down the flow of air as you breathe out and will help you exhale longer. Try to relax and feel comfortable*."
    b. Also note that some individuals find paced breathing to be aversive and difficult, while they may find HRV biofeedback to be easy and comfortable.
10. Assist participant in setting up Elite HRV app on her phone, and provide instructions on using the Polar H7 sensor at home.

4.2.5.5. At home data collection

During the two-week period in between laboratory sessions 1 and 2, participants in the HRVB and HRVB+A conditions were asked to complete at least 4 total sessions of self-guided HRV biofeedback (2-3 per week; 20 minutes per session) using a Polar H7 chest strap sensor and

the EliteHRV app, which was downloaded onto their smartphones during laboratory session 1. These biofeedback sessions were not conducted in a sexual context. That is, participants did not engage in the training immediately prior to becoming aroused/attempting to engage in sexual activity. Data from these sessions was transmitted to the experimenter via the Elite HRV app. Participants in these two conditions were also asked to complete at least 4 total sessions of self-guided HRV biofeedback in between laboratory sessions 2 and 3. Therefore, in between laboratory session 1 and laboratory session 3, participants in the HRVB and HRVB+A conditions were asked to complete at least 8 total sessions of self-guided HRV biofeedback.

The experimenter and/or research assistants checked the Elite HRV web dashboard daily to ensure that participants in the HRVB and HRVB+A groups were track to complete 2-3 sessions of self-guided HRV biofeedback per week. If participants were not on track to complete the required number of at-home biofeedback sessions, they were sent email reminders highlighting the importance of completing the intervention. They were also reminded that each completed session of at-home biofeedback was worth an extra $5 in cash at the end of the study. If the participants did not respond to the email reminders, a research assistant called them to verify that they were still interested in participating in the study. Participants who did not complete any self-guided biofeedback between laboratory visits 1 and 2 were disqualified. Participants who completed less than 4 biofeedback sessions between laboratory visits 1 and 2 were allowed to continue participating if they agreed to complete at least 4 biofeedback sessions between laboratory visits 2 and 3.

In addition, women in all three conditions were asked to complete the daily diary of sexual activity throughout the course of the month-long trial. Participants were reminded to bring their daily diaries to laboratory session 2, so that the experimenter could collect the completed

pages. Participants were also instructed to bring their daily diaries to the final laboratory session, laboratory session 3.

4.2.5.6. One-month follow up

At laboratory session 3, participants were told that they would receive an email in one month with a link to several online measures (see Measures for more details). Participants were asked to complete a battery of self-report questionnaires (affect, depression symptoms, anxiety symptoms, interoceptive awareness, mindfulness, sexual distress, and overall functioning) one month after their third laboratory visit. Once they completed the online measures, women who were in the WL condition were invited to the Sexual Psychophysiology laboratory for one session of experimenter-guided HRV biofeedback. Although several participants expressed interest in this option, no one responded to the experimenter's attempts to schedule these sessions.

4.2.6. Subject flow

Recruitment for this study took approximately 1.5 academic years (October 2016-December 2017). The target sample size for this study was 65 women (25 for the HRVB condition, 25 for the HRVB+A condition, and 15 for the wait-list control condition). It is common practice to recruit slightly more than the target number in case some participants fail to provide complete data, as some participants will likely not complete all three laboratory sessions or will be lost to follow up. Ultimately, we recruited 78 women; nine women dropped out of the study after laboratory visit 1. Of the 69 women who completed all three laboratory visits, 29 were lost to follow up (see Figure 12).

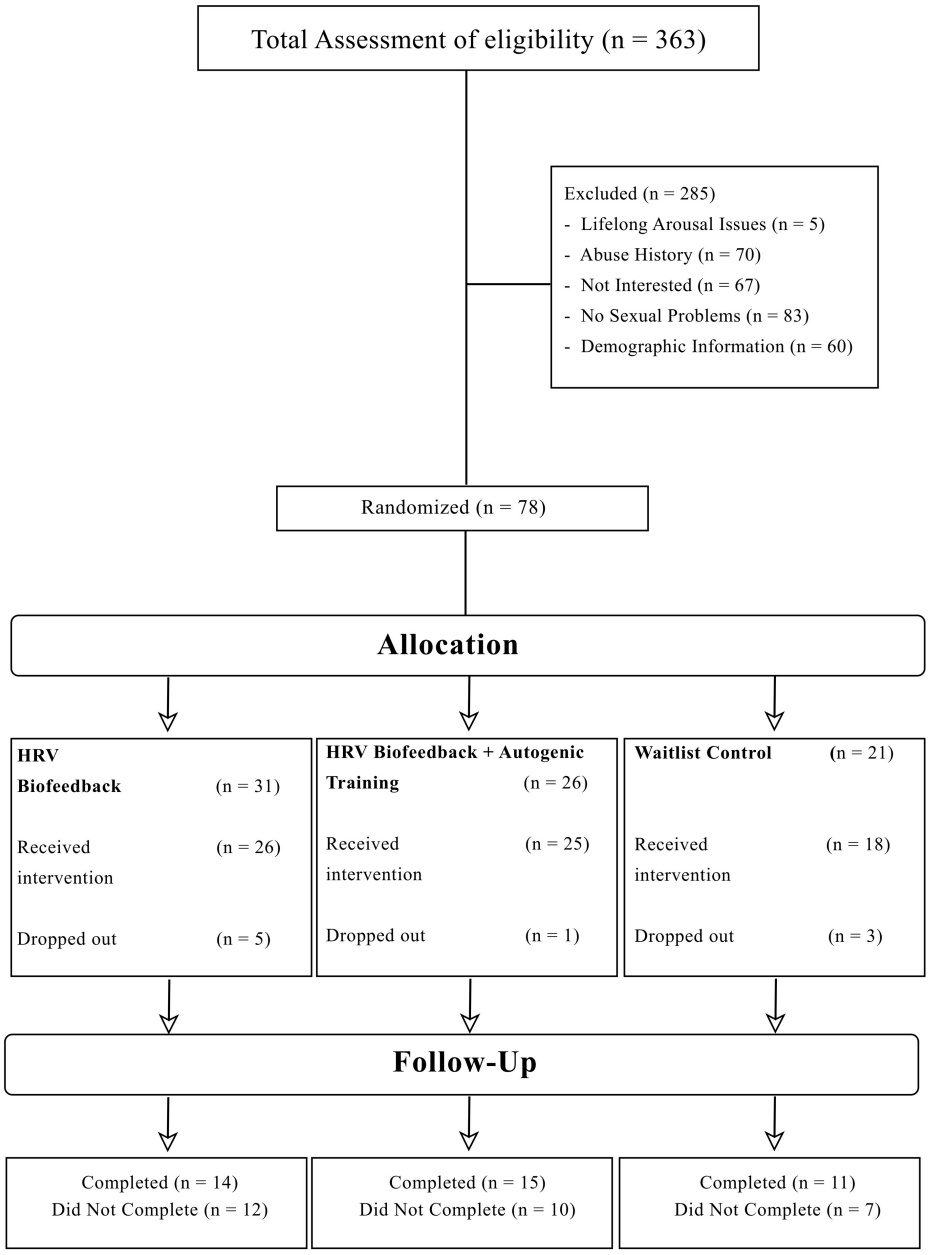


Figure 12. Consort diagram.

4.3. Analyses

4.3.1. Statistical power considerations and proposed sample size

According to sample size guidelines for multilevel modeling, 50 participants is a reasonable minimum for multilevel analyses (Maas & Hox, 2005). A sample size of less than 50 participants has been shown to lead to biased estimates of second-level standard errors (Maas & Hox, 2005). Based on this guideline, we determined that a sample size of 65 women was appropriate for this study. It is important to note that, even with a sample size of 65, we will likely be unable to achieve 80% power for detecting a medium effect size; it is more realistic that power will be around 60% (Bell et al., 2010).

4.3.2. Procedure for missing data

Following the intent to treat approach, all participants who were enrolled and randomly allocated to a treatment condition were included in the analyses and were analyzed in the groups to which they were randomized. For the analyses involving two of the primary outcome measures, genital sexual arousal and continuous subjective sexual arousal, participants with missing data were not excluded. In general, hierarchical linear modeling accommodates missing data well. For example, if a participant forgot to use the Arousometer to document her continuous subjective arousal during one of her laboratory visits, I could still include her VPA data from that visit as well as her Arousometer data from her other laboratory visits in the model.

The Qualtrics survey tool that was used to collect data for the other two primary outcome measures (discrete subjective arousal and perceived genital sensations) did not allow participants to proceed without selecting an answer choice. They were able to select an item ("I do not feel comfortable answering this question.") to indicate that they did not want to answer the question, but they were not able to leave an item blank. Only one participant indicated her discomfort

answering one Film Scale item at one of her laboratory visits. This participant was excluded from analyses involving the Film scale for that particular visit.

4.3.3. Analyses of primary outcome measures

First, both raw change and percent change in HRV were analyzed by condition via a one-way ANOVA. These analyses assessed differences in SDNN between laboratory visit one and laboratory visit two, as well as between laboratory visit one and laboratory visit three, among the three conditions.

Second, as in Study 3 and Study 4, HLM was used to assess changes in genital sexual arousal (VPA) and continuous subjective arousal due to the treatment. These analyses were conducted using the NLME package (Pinheiro et al., 2017) in the R Software environment (R Foundation, 2014). The effects of time, condition, and visit on genital sexual arousal were evaluated in a model that included a three-way interaction term and a random intercept term. Similarly, the effects of time, condition, and visit on continuous subjective sexual arousal were evaluated in a separate model that included a three-way interaction term and a random effect for subject ID. Consistent with standard practices in the analysis of VPA data, participants who had a negative VPA slope over the 10 minute neutral-erotic film at a given laboratory visit were excluded from the HLM analyses, as VPA may decrease over time due to poor or inconsistent placement of the vaginal photoplethysmograph. In total, 57 visits were dropped; 30 participants had at least one visit excluded; five participants had two visits excluded, and three participants had all three visits excluded.

The following two models assessed the relationship among time, condition, visit and either VPA or continuous subjective arousal during the film sequences:

$$Y(VPA)_{ij} = \beta_0 + \beta_1(time)_{ij} + \beta_2(condition)_{ij} + \beta_3(visit)_{ij} + \beta_4(time * condition)_{ij} + \beta_5(time * visit)_{ij} + \beta_6(condition * visit)_{ij} + \beta_7(time * condition * visit)_{ij} + r_{ij}$$

$$Y(Arousometer)_{ij} = \beta_0 + \beta_1(time)_{ij} + \beta_2(condition)_{ij} + \beta_3(visit)_{ij} + \beta_4(time * condition)_{ij} + \beta_5(time * visit)_{ij} + \beta_6(condition * visit)_{ij} + \beta_7(time * condition * visit)_{ij} + r_{ij}$$

$Y(VPA)_{ij}$ and $Y(Arousometer)_{ij}$ are the $_i$th participant's VPA and continuous subjective arousal, respectively, at the $_j$th time point. In these models, β_1 represents the main effect of time on either genital or subjective sexual arousal, β_2 represents the main effect of condition (where 1 = HRVBF, 2 = HRVBF + A, and 3 = WL), β_3 highlights the main effect of visit (where 1 = laboratory visit 1, 2 = laboratory visit 2, and 3 = laboratory visit 3), and $\beta_{5\text{-}7}$ represent the various two-way interactions effects and the three-way interaction effect among time, condition, and visit. The time variable refers to the course of each of the neutral-erotic film segments; all three neutral-erotic film segments were 10 minutes (600 seconds) in length. Finally, β_0 represents the participant-specific intercept and r_{ij} are the individual error terms.

Third, repeated measures ANOVAs were used to analyze differences in discrete subjective arousal and perceived genital sensations among the three conditions across the three visits. Repeated measures ANOVAs were also used to identify differences in FSFI total scores and FSFI arousal domain scores among the three conditions and across the visits at which that measure was administered.

4.3.4. Mediation analyses

Heart rate variability was analyzed as a mediator of treatment-related increases in all four arousal variables (genital arousal, continuous subjective arousal, discrete subjective arousal, and perceived genital sensations) using the mediation package (Tingley, Yamamoto, Hirose, Keele, & Imai, 2013) in R. These analyses were univariate, not multivariate; separate models were run

for each of the arousal outcome variables. All variables included in these analyses were standardized via z-scores. The mediation package allows for causal mediation analysis of multilevel data, where individual observations are clustered within groups (Tingley, Yamamoto, Hirose, Keele, & Imai, 2014). In this study, the treatment was assigned at the group level, whereas the mediator and outcome variables were measured at the individual level. The mediation package dissects total effect of a treatment into direct and indirect effects, and the indirect effect is transmitted via the mediator to the outcome (Zhang et al., 2016). The user specifies which variable should be treated as the predictor and which variable should be treated as the mediator. In this case, condition served as the predictor variable, and SDNN was the mediator. By design, the analyses compared (1) the HRVB condition against the WL condition and (2) the HRVB+A condition against the WL condition. The output produced by the package includes the average causal mediation effect (ACME), which is total effect minus the direct effect, and the average direct effect (ADE), or the direct effect of X on Y after taking the effect of M into account.

Because the mediation package does not provide output for the traditional "A" and "B" paths described by Baron and Kenny (1986), separate linear mixed effects models were run when the magnitude of the ACME was significant to estimate the relationships between the predictor and HRV (the "A" path) and between HRV and the arousal measure (the "B" path).

Importantly, the mediation analyses were only conducted on the data of participants who were compliant with the treatment. Participants in the HRVB condition were required to complete at least eight at-home biofeedback sessions, and participants in the HRVB+A condition were also required to couple autogenic training and HRV biofeedback at least eight times.

Therefore, participants (n = 9) who completed seven or fewer at-home biofeedback sessions were excluded.

4.3.5. Analyses of moderated mediation

The mediation package in R allows for analyses of moderated mediation. Often, in treatment-outcome research, the magnitude of the ACME depends on one or several pre-treatment covariates, which are referred to as moderators. Moderated mediation analyses were conducted if HRV significantly mediated increases in genital arousal, continuous subjective arousal, discrete subjective arousal, and perceived genital sensations. Four a priori moderators were selected: mindfulness, interoceptive awareness, depression, and anxiety.

Unfortunately, we were unable to conduct any moderation analyses. To run the moderation models, we needed to use observations that had data for (1) condition, (2) outcome measure, (3) mediator, and (4) moderator. Only 88 observations had all four of these data categories. When we excluded participants who did not comply with the treatment protocol and participants with atypical sexual arousal patterns, we reduced the amount of data available to run these analyses. The moderation analyses were further complicated by the fact that we only assessed the moderators at laboratory visit 1 and laboratory visit 3, not laboratory visit 2. The moderators were assessed in the one-month follow up survey, but almost half of the participants who went to all three laboratory visits failed to complete the survey (about 42%). Although the moderation analyses would have provided some important insight on the applicability of the treatment to certain populations, these analyses would also have inflated the rate of Type 1 error.

4.4. Results

4.4.1. Target engagement

A one-way ANOVA revealed that raw change in HRV (indexed by SDNN) from laboratory visit one to laboratory visit three significantly differed among the three conditions, $F(2, 66) = 5.49$, $p = .006$. Percent change in SDNN between these two laboratory visits also significantly different among the conditions, $F(2, 66) = 3.68$, $p = .031$. There were no statistically significant differences in SDNN raw change or SDNN percent change among the three groups from laboratory visit one to laboratory visit two. Between laboratory visits one and three, women randomized to the HRVB+A condition had the greatest average raw change and percent change, followed by women randomized to the HRVB condition. On average, women randomized to the WL condition experienced little change. Please see Table 14. These analyses indicate that the two active conditions effectively targeted HRV as intended.

Table 14

Mean raw change and percent change in HRV by condition

	Condition	M	SE	*F*
Percent change in SDNN, v1-v2				
	HRVB	8.35	5.81	1.37
	HRVB+A	15.99	7.29	
	WL	-.51	6.70	
Raw change in SDNN, v1-v2				
	HRVB	2.99	2.15	2.28
	HRVB+A	7.13	3.35	
	WL	-1.87	2.81	
Percent change in SDNN, v1-v3				
	HRVB	15.40	8.10	3.68*
	HRVB+A	39.26	11.24	
	WL	3.64	6.37	
Raw change in SDNN, v1-v3				
	HRVB	6.20	3.61	5.49*
	HRVB+A	17.14	3.91	
	WL	.57	1.91	

Note. HRV = heart rate variability; SDNN = standard deviation of the N-N intervals; v1 = laboratory visit one; v2 = laboratory visit two; v3 = laboratory visit three; HRVB = HRV biofeedback condition; HRVB+A = HRV biofeedback plus autogenic training condition; WL = wait list condition
*p < .05

4.4.2. Primary outcomes

4.4.2.1. Genital sexual arousal

The HLM analyses revealed that the interaction of cubic time, condition, and visit significantly predicted changes in genital arousal (measured by VPA), $\beta = .00$, $t(26067) = 2.14$, $p < .05$ (see Table 3, Figures 13-15). This model was compared to a model that included a linear

term for time, and the cubic model had a lower AIC (196,854.80 vs. 196,6917.10), so it was retained. Figures 13-15 highlight the VPA trajectories of the women in the HRVB, HRVB+A, and WL conditions over the three 10 minute film clips at each of the laboratory visits. It is evident in Figures 13-15, which represent the raw data, that women who were randomized to the waitlist control condition experienced the least positive change in VPA during the course of the neutral-erotic film across the three visits. Women in the HRVB condition had the greatest increases in VPA from the first laboratory visit to the third laboratory visit. Women in the WL condition experienced an increase in their VPA from their first laboratory visit to their third laboratory visit, but a decrease from their first visit to their second visit.

Table 15

Results from an HLM analysis examining centered time, condition, and visit as predictors of genital arousal (VPA)

Predictor	β	SE	df	*t*-ratio	*p*-value
(Intercept)	12.04	3.34	26057	3.60	0.0003
Time	0.006	0.006	26057	0.96	0.34
Condition	0.79	1.64	76	0.47	0.64
Visit	3.35	0.30	26057	11.09	0.000
$Time^2$	-.000001	0.00002	26057	-.08	0.93
$Time^3$	0.00	0.00	26057	-0.57	0.57
Time*Condition	0.01	0.003	26057	3.47	0.0005
Time*Visit	0.01	0.003	26057	4.99	0.000
Condition*Visit	-0.67	0.15	26057	-4.51	0.000
Condition*$Time^2$	0.00	0.00	26057	0.45	0.66
Visit*$Time^2$	0.00	0.00	26057	0.49	0.62
Condition*$Time^3$	0.00	0.00	26057	-1.78	0.07
Visit*$Time^3$	0.00	0.00	26057	-2.40	0.02
Time*Condition*Visit	-0.006	0.001	26057	-4.03	0.0001
$Time^2$*Condition*Visit	-0.000001	0.00	26057	-0.23	0.82
$Time^3$*Condition*Visit	0.00	0.00	26057	2.15	0.03

Time = -300-300 seconds, binned in 5 second intervals; Condition = HRVB (1), HRVB + A (2), and WL (3); Visit = laboratory visit 1, 2, or 3; SE = standard error; df = degrees of freedom.

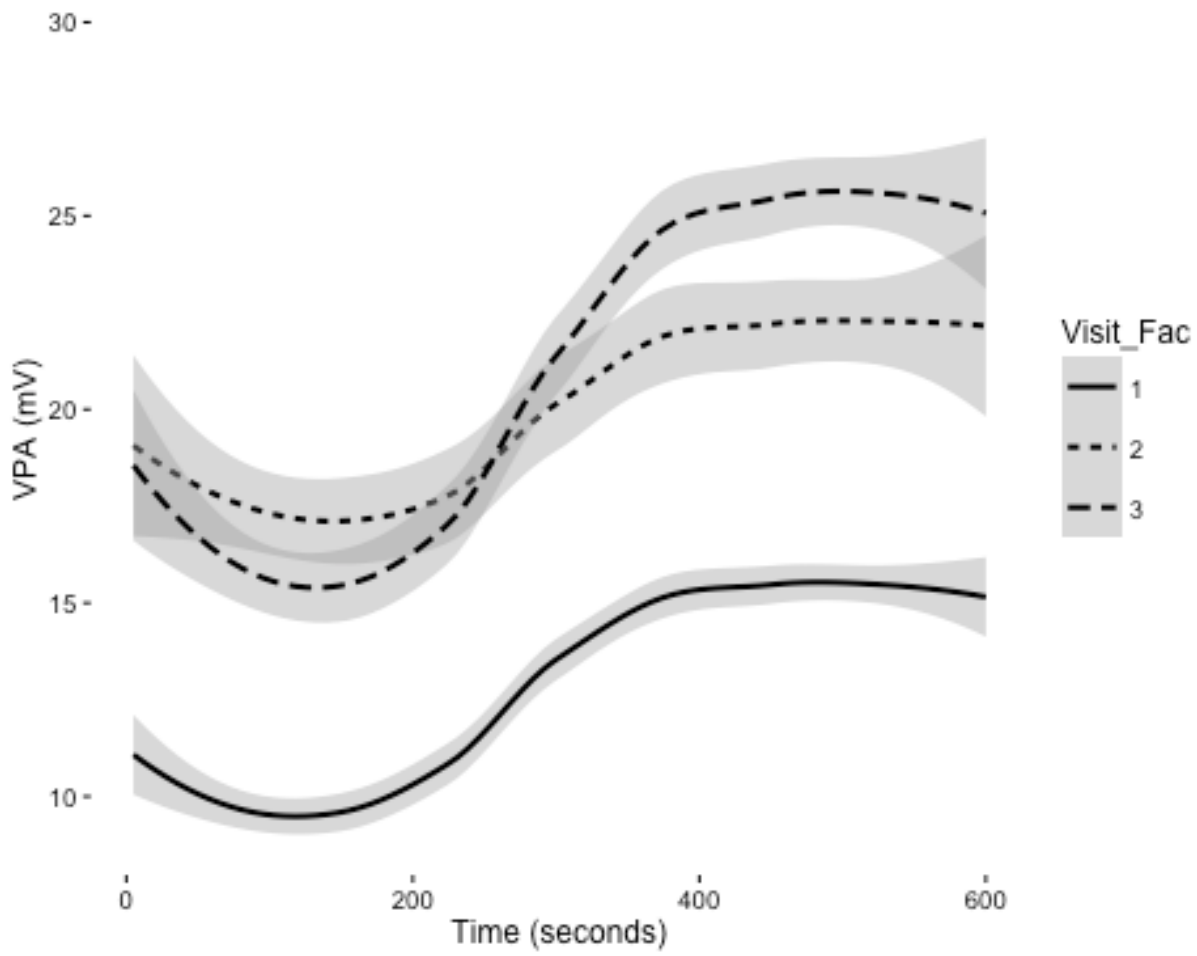


Figure 13: Smoothed representation of the raw VPA data for women in the HRV biofeedback (HRVB) condition across all laboratory visits. The solid line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 3.

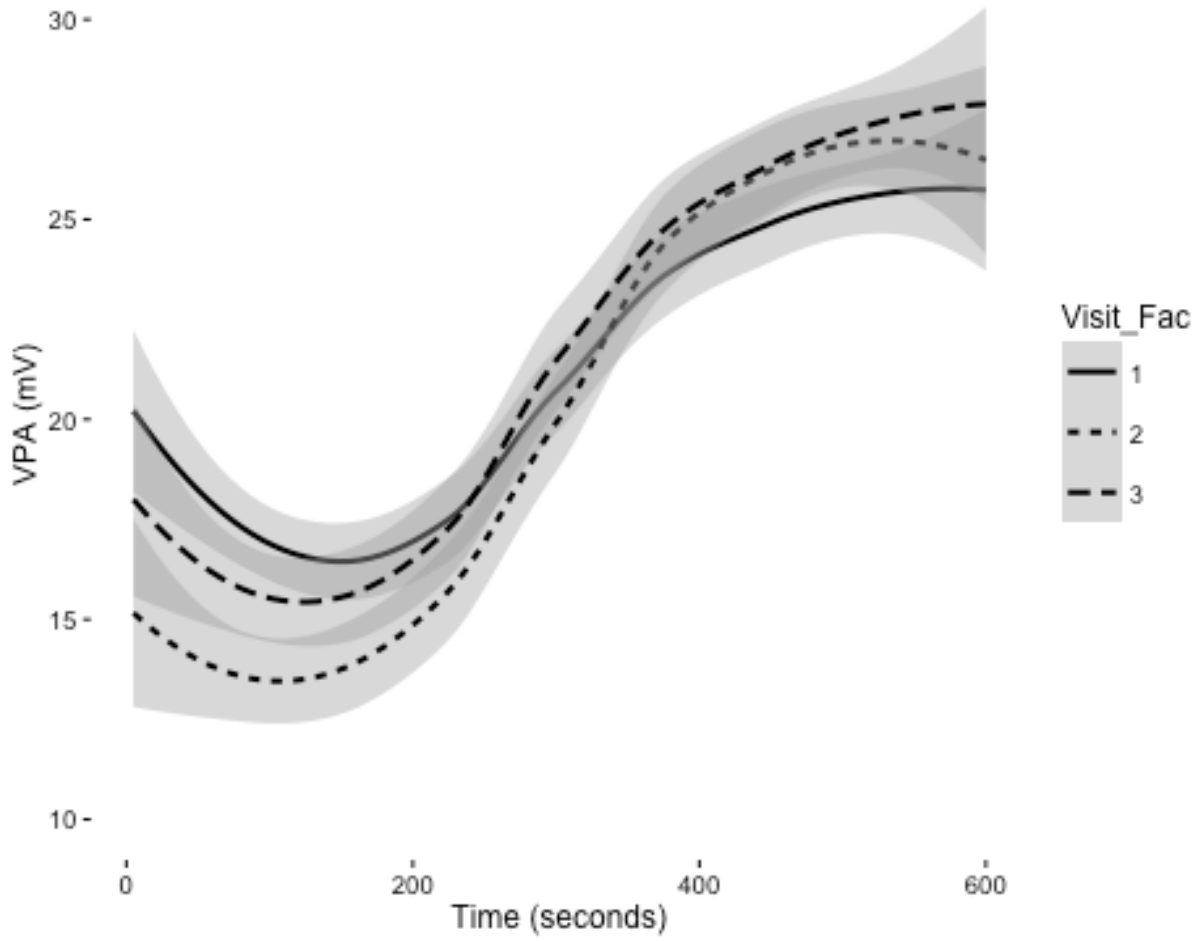


Figure 14: Smoothed representation of the raw VPA data for women in the HRV biofeedback plus autogenic training (HRVB+A) condition across all laboratory visits. The solid line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 3.

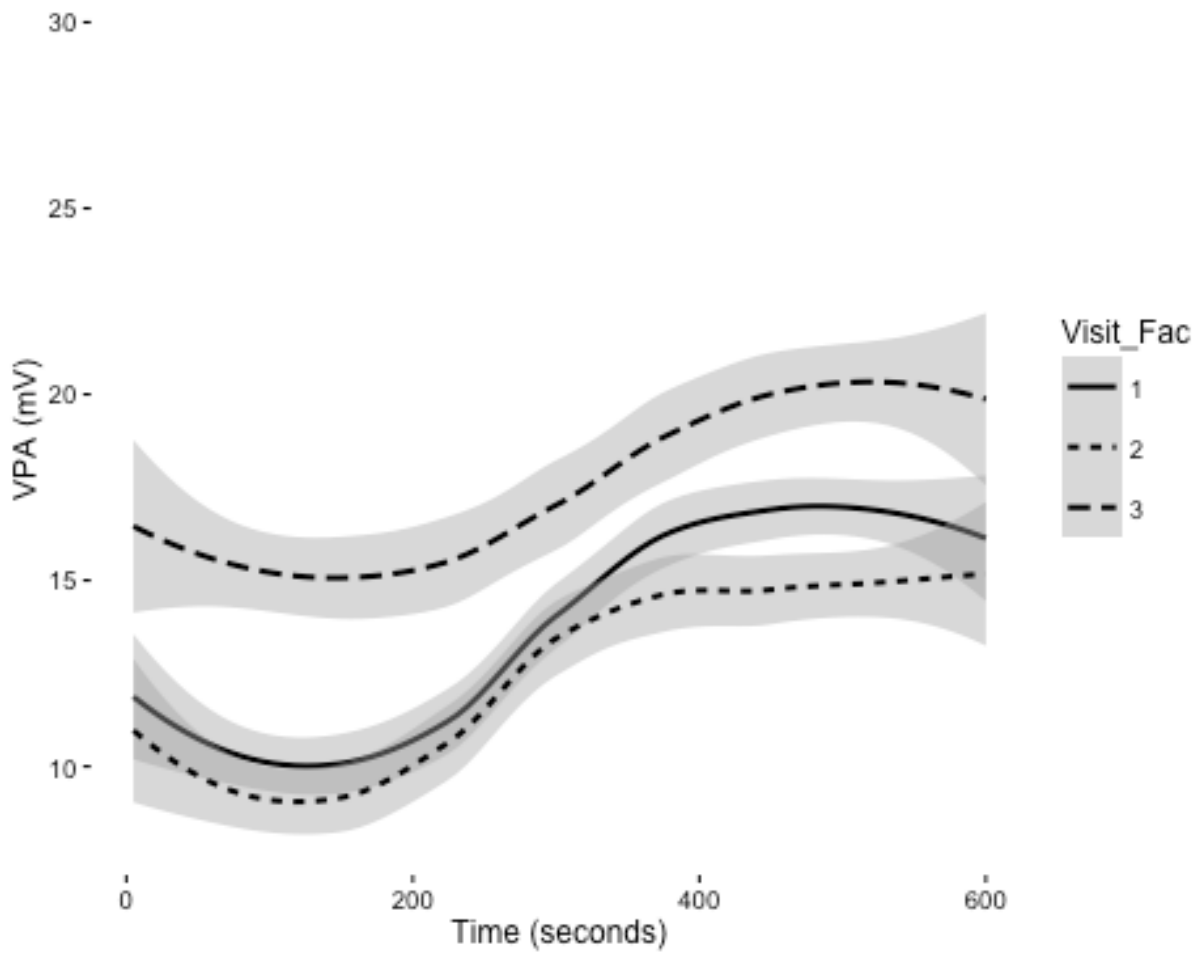


Figure 15: Smoothed representation of the raw VPA data for women in the wait list (WL) condition across all laboratory visits. The solid line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw VPA data during the 10-minute neutral-erotic film presented at visit 3.

4.4.2.2. Continuous subjective sexual arousal

The HLM analyses revealed that the interaction of cubic time, condition, and visit significantly predicted changes in continuous subjective arousal (measured by the Arousometer), $\beta = .000$, $t(25946) = -2.46$, $p < .005$ (see Table 15, Figures 16-18). This model was compared to a model that included a linear term for time, and the cubic model had a lower AIC (-11869.41vs. -9958.797), so it was retained. Figures 16-18 present the Arousometer trajectories of the women

in the HRVB, HRVB+A, and WL conditions over the three 10 minute film clips at each of the laboratory visits. Based on Figures 16-18, it is clear that women who were randomized to the WL experienced decreases in continuous subjective arousal during the course of the neutral-erotic film across the three visits. In contrast, women in the HRVB and HRVB+A conditions demonstrated increases in their subjective arousal from the first laboratory visit to the third laboratory visit.

Table 16

Results from an HLM analysis examining centered time, condition, and visit as predictors of continuous subjective arousal

Predictor	β	SE	df	*t*-ratio	*p*-value
(Intercept)	0.24	0.04	25946	5.92	0.000
Time	0.002	0.0001	25946	18.77	0.000
Condition	-0.001	0.02	76	-0.04	0.96
Visit	0.04	0.006	25946	7.15	0.000
$Time^2$	-0.000	0.000	25946	-0.64	0.52
$Time^3$	-0.000	0.000	25946	-10.60	0.000
Time*Condition	-0.000	0.000	25946	-0.64	0.52
Time*Visit	0.000	0.000	25946	0.23	0.82
Condition*Visit	-0.03	0.003	25946	-9.59	0.000
Condition*$Time^2$	0.000	0.000	25946	2.81	0.005
Visit*$Time^2$	0.000	0.000	25946	4.14	0.000
Condition*$Time^3$	0.000	0.000	25946	2.11	0.035
Visit*$Time^3$	0.000	0.000	25946	3.44	0.001
Time*Condition*Visit	-0.000	0.000	25946	-3.35	0.001
$Time^2$*Condition*Visit	-0.000	0.000	25946	-1.74	0.08
$Time^3$*Condition*Visit	0.000	0.000	25946	-2.46	0.004

Time = -300-300 seconds, binned in 5 second intervals; Condition = HRVB (1), HRVB + A (2), and WL (3); Visit = laboratory visit 1, 2, or 3; SE = standard error; df = degrees of freedom.

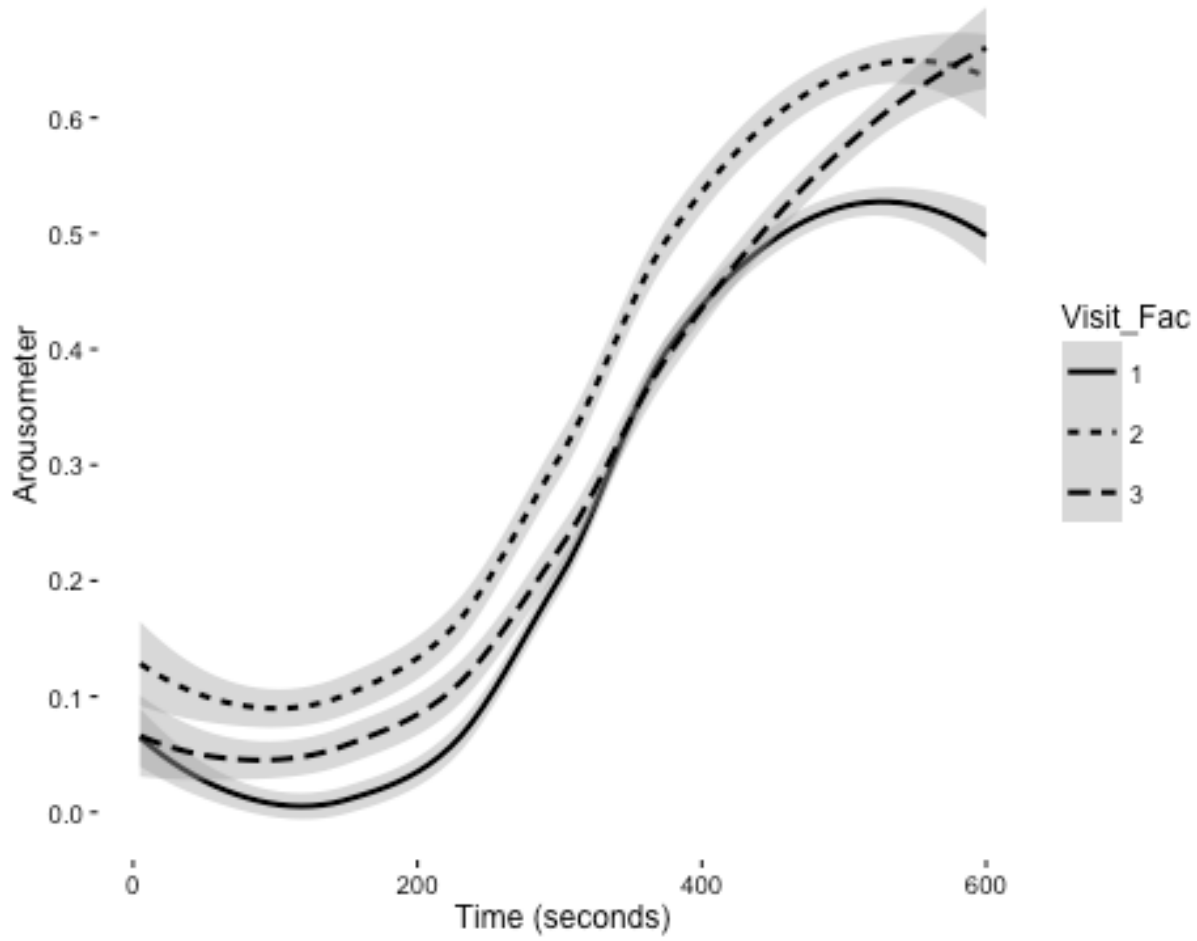


Figure 16: Smoothed representation of the raw Arousometer data for women in the HRV biofeedback (HRVB) condition across all laboratory visits. The solid line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 3.

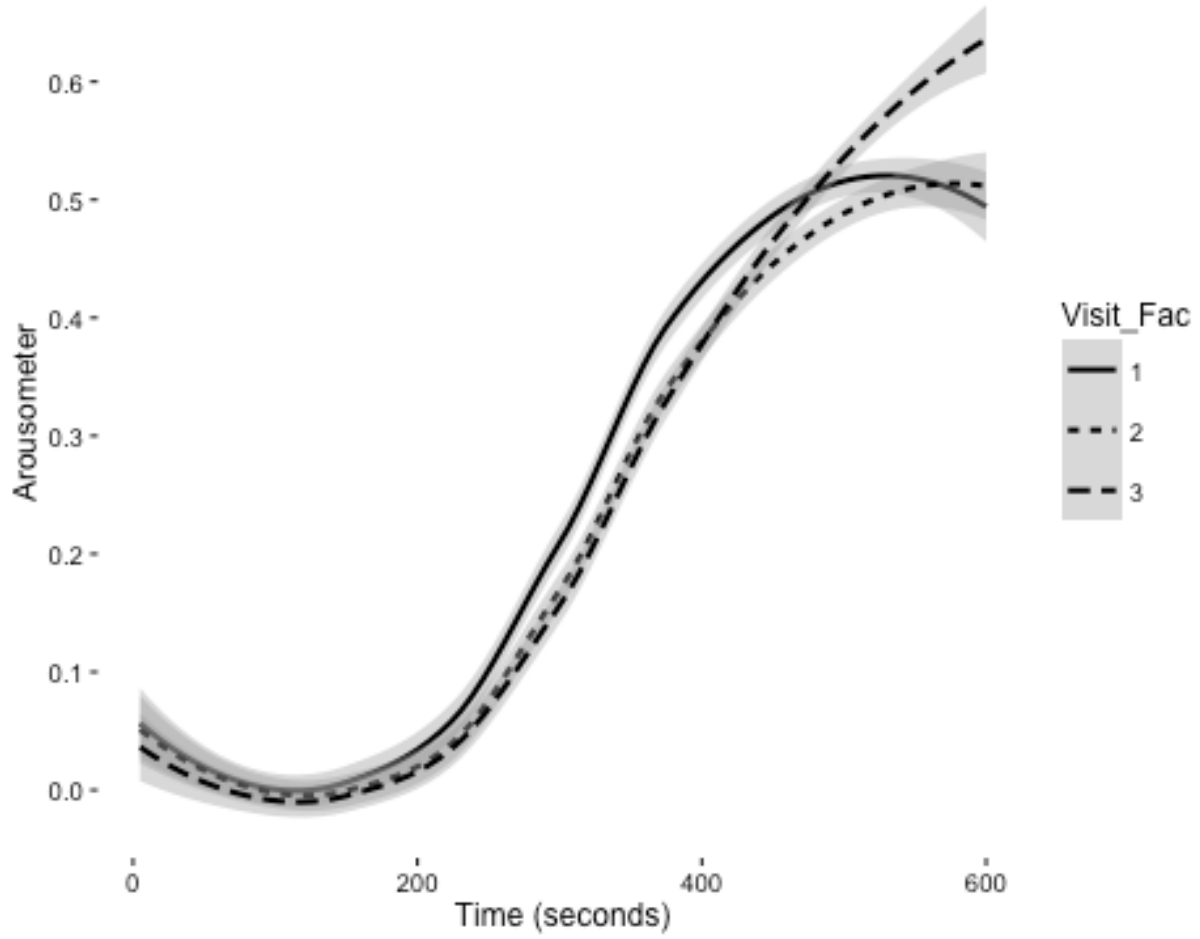


Figure 17: Smoothed representation of the raw Arousometer data for women in the HRV biofeedback plus autogenic training (HRVB+A) condition across all laboratory visits. The solid line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 3.

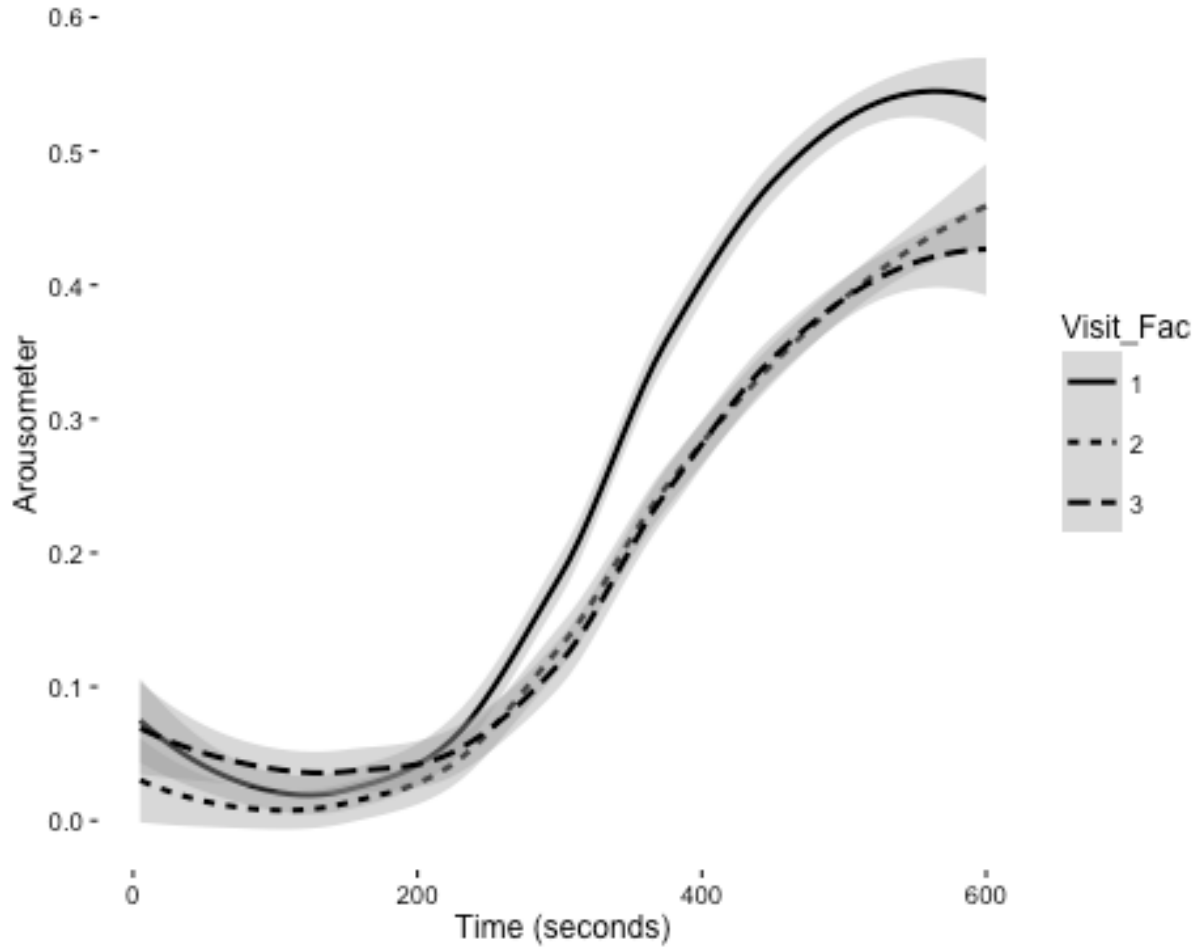


Figure 18: Smoothed representation of the raw Arousometer data for women in the wait list (WL) condition across all laboratory visits. The solid line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 1, the dotted line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 2, and the dashed line represents the raw Arousometer data during the 10-minute neutral-erotic film presented at visit 3.

4.4.2.3. Discrete subjective arousal

Changes in discrete subjective arousal were analyzed with a univariate repeated measures analyses of variance (ANOVA). There was a significant difference in mean discrete subjective arousal, measured by the Film Scale, among the three conditions and across the three visits, $F(4,132) = 2.48$, $p = .04$. This difference had a small to medium effect size ($\eta^2 = 0.07$). Post-hoc analyses did not indicate any significant differences in discrete subjective arousal among the

three conditions at specific laboratory visits. Given that HLM is more robust to variance constancy violations than repeated measures analyses of variance, a separate set of HLM analyses were conducted to validate these findings. These analyses indicated that the interaction of condition and visit significantly predicted changes in discrete subjective arousal (measured by the Film Scale), $\beta = -.82$, $t(25959) = -38.14$, $p < .0001$. Participants in the two active conditions experienced the greatest increases in subjective sexual arousal throughout the course of the intervention (see Figure 19).

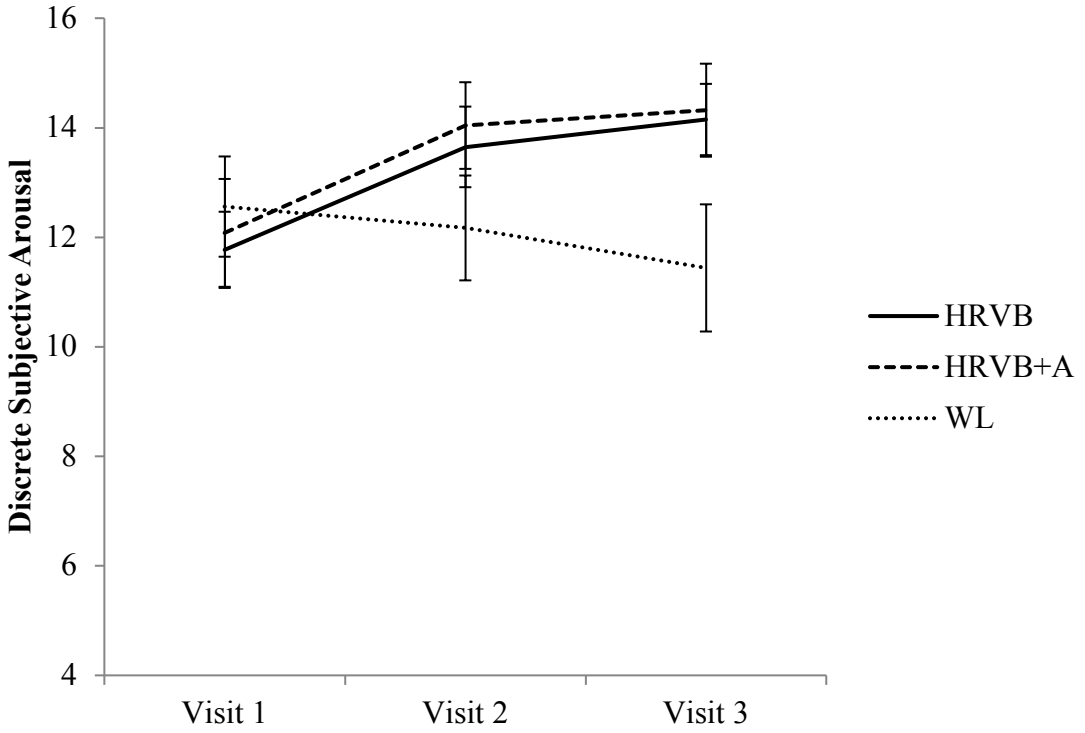


Figure 19. Changes in discrete subjective arousal, measured via the Film Scale, by condition.

4.4.2.4. Perceived genital sensations

Changes in perceived genital sensations were also analyzed with a univariate repeated measures analyses of variance (ANOVA). There was a significant difference in mean perceived genital sensations, measured by the Film Scale, among the three conditions and across the three

visits, F(4, 132) = 3.38, p = .01. This difference had a medium effect size (η^2 = 0.09). Mauchly's test, $\chi^2(2) = 6.53$, p = .04, indicated a violation of the sphericity assumption, so the Greenhouse-Geisser correction was applied. Post-hoc analyses did not indicate any significant differences in perceived genital sensations among the three conditions at specific laboratory visits. Again, because HLM is more robust to variance constancy violations than repeated measures ANOVAs, a separate set of HLM analyses were run to validate these findings. The HLM analyses revealed that the interaction of condition and visit significantly predicted changes in perceived genital sensations (measured by the Film Scale), β = -.90, $t(25959) = -25.98$, $p < .0001$. Collectively, these results indicate that participants in the two active conditions experienced the greatest increases in subjective sexual arousal throughout the course of the intervention (see Figure 20).

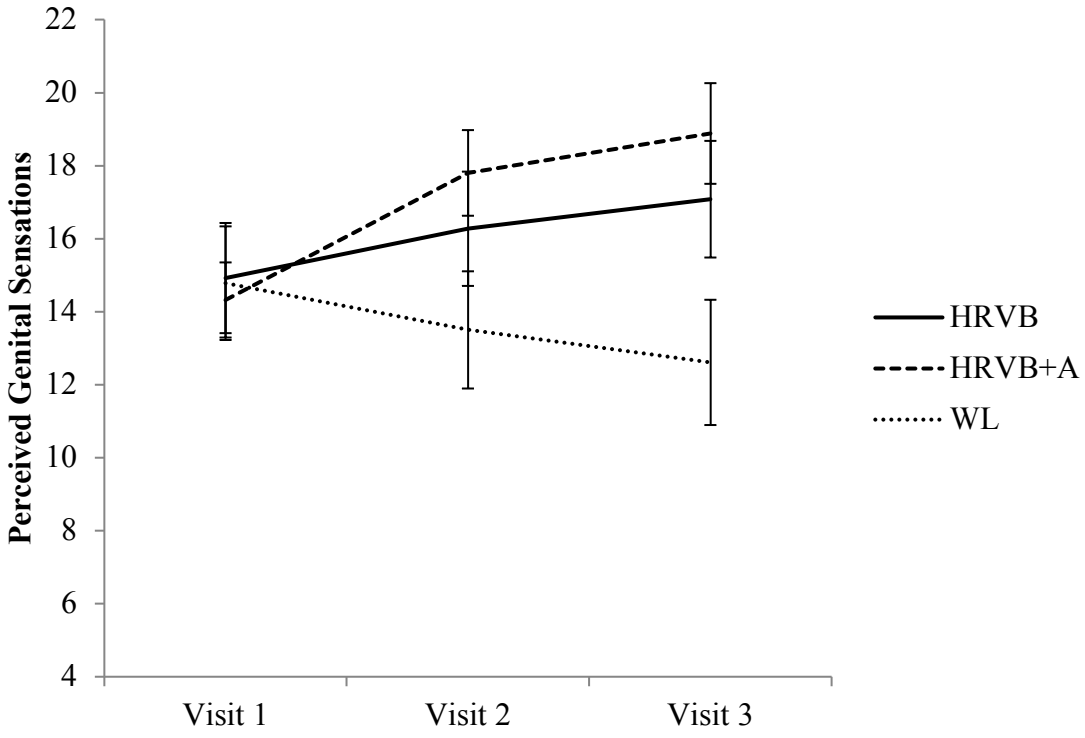


Figure 20. Changes in perceived genital sensations, measured via the Film Scale, by condition.

4.4.3. Mediation

HRV, indexed by SDNN, was assessed as a mediator of changes in the four arousal variables (genital arousal, continuous subjective arousal, discrete subjective arousal, and perceived genital sensations). Compared to women who were randomized to the WL condition, women in the HRVB condition demonstrated significant indirect effects of condition on perceived genital sensations that were mediated through SDNN, ACME = 0.17 [0.002, 0.42], p = .04. The direct path from the HRVB condition to perceived genital sensations was also significant, ADE = 0.54 [0.02, 1.05], p = .04. These results indicate that, compared to the WL condition, the HRVB condition facilitated an increase in SDNN, which then led to an increase in perceived genital sensations. Again, compared to women in the WL condition, women who were randomized to the HRVB condition experienced a trend toward significant indirect effects of condition on discrete subjective arousal that were mediated through SDNN, ACME = 0.15 [-.0009, 0.41], p = .06, and a trend toward significant direct effects from the HRVB condition to discrete subjective arousal, ADE = 0.42 [-.06, 0.87], p = .08. Though the magnitude of the ACME did not reach statistical significance, the HRVB condition led to increases in SDNN, when then caused increases in discrete subjective arousal over the course of the intervention.

Because the output provided by the mediation package does not include estimates for the magnitude of the relationship between the predictor variable and the mediator (Baron and Kenny's "A" path) or the magnitude of the relationship between the mediator and the outcome (Baron and Kenny's "B" path), we ran separate linear mixed effects models using the lme4 package (Bates, Maechler, Bolker, & Walker, 2014) and the nlme package (Pinheiro et al., 2017) to test these associations. For these analyses, we used standardized data. First, to assess the "A" path, SDNN was regressed on condition. The HRVB condition was significantly related to

SDNN in the positive direction, β = 0.56, $F(1, 41) = 4.68$, $p = .04$. These results confirm that the HRVB condition did have a significant positive effect on HRV. To estimate the relationship between SDNN and perceived genital sensations (the "B" path), we ran a model with SDNN predicting perceived genital sensations. For participants in the HRVB condition, SDNN was significantly associated with perceived genital sensations, β = 0.21, $F(1,55) = 4.12$, $p = .04$. We then ran a separate linear mixed effects model with SDNN as a predictor of discrete subjective arousal (also the "B" path), given the trend toward a statistically significant indirect effect of SDNN on the relationship between condition and subjective arousal. Although the effect of SDNN on discrete subjective arousal was in the expected direction, it did not reach statistical significance for women in the HRVB condition, β = 0.17, $F(1, 55) = 1.60$, $p = .21$.

We can use the separate "A" and "B" paths to approximate the magnitude of the ACME. For the genital sensations analyses, the product of the "A" and "B" paths is 0.12, which is relatively close to the ACME (0.17). The product of the "A" and "B" paths corresponding to the discrete subjective arousal analyses is 0.1, which again is relatively similar to the magnitude of the ACME (0.15). Although the separate "A" and "B" path analyses are useful in that they help us conceptualize the breakdown of the ACME, the mediation package provides a more sophisticated analysis of the total indirect path because the ACME estimates are the result of repeated simulations (Imai, Keele, & Tingley, 2010). The package's default simulation type, the quasi-Bayesian Monte Carlo approximation in which the posterior distribution of variables of interest is approximated by their sampling distribution (King, Tomz, & Wittenberg, 2000), was used in the mediation analyses.

Increased SDNN did not mediate the relationship between the HRVB condition and continuous genital arousal ($p > .10$), nor did it mediate the relationship between the HRVB

condition and genital arousal ($p > .10$). Finally, SDNN did not mediate the relationship between the HRVB+A condition and any of the arousal variables (all ps > .10).

4.5. Discussion

This randomized-controlled trial examined the effect of targeting and increasing heart rate variability on several indices of sexual arousal in women with FSAD. Building on previous research, which indicated that increasing heart rate variability via autogenic training in the laboratory facilitated increases in both genital arousal and subjective arousal, we designed a month-long, three-armed intervention for women with genital and/or subjective arousal concerns. Participants were randomized to one of three conditions: HRVB, HRVB + A, or WL. The two active conditions (HRVB, HRVB+A) required two to three 20-minute HRV biofeedback sessions per week. Participants in the HRVB+A condition listened to a 14-minute autogenic training recording prior to engaging in the biofeedback. The intervention led to increases in HRV as well as increases in genital arousal, continuous subjective arousal, discrete subjective arousal, and perceived genital sensations among women in the two active conditions; this was not the case for women in the WL condition. For women in the HRVB condition, increases in HRV significantly mediated the relationship between condition and perceived genital sensations. That is, randomization to this specific condition led to increases in SDNN, which then led to increases in perceived genital sensations. In addition, there was a trend toward statistically significant indirect effects of SDNN on the relationship between the HRVB condition and discrete subjective arousal. Again, only for women in HRVB condition, increases in HRV partially accounted for increases in subjective arousal. To our knowledge, this study was the first randomized controlled trial of HRV biofeedback, with and without autogenic training, in a population of women with sexual arousal problems.

It is particularly notable that the intervention facilitated increases in genital arousal *and* increases in perceived genital arousal. Not only did participants experience increased blood flow to the genitals, they improved in their ability to perceive this physiological change. To date, no published randomized-controlled trials of psychosocial interventions for FSAD have demonstrated significant increases in VPA alongside increases in perceived sensations. Mindfulness-based protocols have led to increases in perceived genital sensations and subjective arousal, but not in VPA (Brotto et al., 2008; Brotto, Chivers, Millman, & Albert, 2016). Some pharmacologic agents (e.g., L-arginine glutamine plus yohimbine, gingko biloba, tibolone, and sildenafil), have increased genital arousal relative to placebo (Laan, van Lunsen, et al., 2002; Laan et al., 2001; Meston et al., 2008; Meston & Worcel, 2002), but others have not (Chivers & Rosen, 2010; Foster et al., 2009). For the most part, the drugs that do increase vasocongestion do not increase women's self-reported genital sensations, nor do they lead to improvements in women's mental engagement during sexual activity. Unlike these existing treatments, the HRV-based intervention seems to have positive effects on both perceptions of arousal and objective indices of arousal. This is exciting, as the intervention may be appropriate for women who have compromised genital blood flow due to neurovascular or other organic factors *and* women who have appropriate levels of vaginal vasocongestion but may not be attending to their genital sensations.

Even though increases in the four arousal measures were observed in women randomized to the HRVB and HRVB+A conditions compared to women in the WL condition, the role that HRV played with respect to these increases is somewhat unclear. Indeed, the evidence for increased HRV as a mediator of change in arousal was relatively weak. Specifically, increasing SDNN facilitated improvements in only one index of arousal (perceived genital sensations) and

only among randomized to only one of the two active conditions (HRVB). Interestingly, women who randomized to the other active condition, HRVB+A, experienced the greatest gains in HRV, but these gains were not strongly related to any of the arousal indices. We can only speculate as to what accounts for these seemingly divergent findings. It is possible, for example, that the purported mechanism of action only emerges in training that exclusively focuses on attending to and manipulating the breath and that adding sensory activation (evident in the HRVB+A condition) may engage alternative mechanisms underlying increases in arousal.

As is true for all interventions, the two active conditions examined in this study engaged multiple mechanisms critical to sexual arousal. We focused on and measured HRV as a mediator. It is possible though that the combination of HRV biofeedback and autogenic training, while engaging this putative mediator, also activated an alternative or complementary (unmeasured) mechanism that overrode the hypothesized mediational effects of HRV. For example, autogenic training increases sensory acuity; HRV biofeedback does not direct participants to engage with the senses, nor does it direct participants to actively increase their sensations. When a practitioner listens to an autogenic training recording, she mentally repeats certain phrases that target specific sensations, such as muscular relaxation, feelings of warmth, and feelings of heaviness (Kanji, 1997). Although HRV is an excellent measure of autonomic nervous system function, it only indexes one aspect of autonomic function: the variation in the lengths of time between adjacent heartbeats. Autogenic training may have facilitated autonomic balance in a way that was not picked up by HRV. It is possible that attention to sensations of warmth may have manipulated blood flow, leading to changes in blood pressure, which would have impacted genital arousal and possibly emotion regulation (potentially affecting subjective arousal). Attention to sensations in general may have also increased attendance to erotic cues, which could

have led to increases in subjective arousal. The combination of HRV biofeedback and autogenic training clearly increases sexual arousal, but the mechanism or group of mechanisms driving that effect have yet to be determined.

The HRVB condition was the "purer" of the two active conditions in that it aimed to exclusively increase HRV by training women to attend to and adjust their autonomic arousal via their breath; it is perhaps unsurprising, then, that increases in HRV were associated with increased genital sensations, another component of autonomic arousal. Women in this condition slowed down the pace of their breath following Elite HRV's breathing guide and then used their breath to increase their HRV, which was graphically demonstrated for them on their mobile devices. Unlike the women in the HRVB+A condition, participants in the HRVB condition were not asked to activate sensations like warmth or heaviness in different areas of the body. This intense, exclusive focus on the breath was intended to regulate their autonomic arousal. It is well known that the amplitude of HRV is systematically related to breathing frequency; higher amplitudes are achieved with slower respiration (Lehrer & Gevirtz, 2014). During normal breathing, the phase relationship between breathing and heart rate is not synchronous (Vaschillo, Lehrer, Rishe, & Konstantinov, 2002). At rest, most people breathe at a rate between 0.15 and 0.4 Hz, or about 9 to 24 breaths per minute (Lehrer, 2007); heart rate increases tend to follow inhalation at the mid point of the breath, and heart rate decreases also occur in the middle of exhalation (Vaschillo et al., 2002). When paced breathing is facilitated by biofeedback, the relationship between heart rate and respiratory rate changes dramatically. The amplitude of heart rate oscillations increases, and heart rate oscillates in phase with respiration (Lehrer & Gevirtz, 2014). That is, heart rate and breathing are exactly in sync. After a month of training their breath (i.e., training their non-sexual, autonomic arousal) in a non-sexual context, women in the HRVB

condition were better able to perceive another aspect of their autonomic arousal, namely their genital arousal. Although perceived genital sensations may not be the most appropriate clinical outcome measure for all women with sexual arousal concerns (especially not for women who report a lack of mental arousal), it is the measure that is most relevant to the mechanism that was targeted in the HRVB condition.

This study had several limitations that warrant mention. First, baseline HRV was measured during the neutral segment of the neutral-erotic film at each laboratory visit, as in previous studies (Stanton et al., 2018; Stanton & Meston, 2016). It is arguable that measuring HRV during the film is not a true baseline measurement, as women had already inserted the vaginal photoplethysmograph and were therefore anticipating the start of the erotic segment of the film. To avoid additional participant burden, we did not ask women to come to the lab for a separate visit to measure their baseline HRV. Limiting our measurement of baseline HRV to three "snapshots" in the laboratory may also have missed the effect of increasing HRV on some of the arousal indices. Baseline HRV could have been measured more times throughout the trial (e.g., at home every morning or every couple of days), though that might have been challenging for participants given the length of the trial. Second, three neutral-erotic films were prepared for this study, and the order of their presentation was randomized. Though extreme efforts were taken to match the films for content, some women likely found certain films more arousing than others. It is possible, though unlikely, that preferences for certain settings or certain actors contributed to changes in genital or subjective arousal over time. Third, few participants completed the one-month follow up survey, which made it impossible to conduct the proposed moderated mediation analyses. The moderation analyses could only be run on observations that had date for condition, outcome measure, mediator, and moderator. Compounding the issue, the

proposed moderator variables were assessed at the first laboratory visit, the third laboratory visit, and in the follow up survey, *not* at the second laboratory visit.

In summary, our intervention had meaningful effects on genital arousal, subjective arousal, and perceived genital sensations. There is some evidence that the effects are indeed mediated by increased HRV, but it appears likely that there are multiple mechanisms at play. Future research aimed at shedding light on the mechanisms of action of HRVB and HRVB+A should include multiple mediators at multiple levels assessed frequently throughout the intervention, which would allow testing of specific and causal effects (Kazdin & Nock, 2003). In the meantime, clinicians should consider offering HRV biofeedback or the combination of HRV biofeedback and autogenic training to female patients with arousal concerns.

5. GENERAL DISCUSSION

Sexual arousal dysfunction affects one out of every four women in the United States (Shifren et al., 2008). Although the number of women distressed by their arousal concerns is considerably smaller than the number of women who report arousal problems, the age-stratified prevalence rates of arousal dysfunction with distress are not trivial; 3.3% of women between the ages of 18 and 44, 7.5% of women aged 45 to 64, and 6% of women above the age of 65 experience low arousal coupled with distress (Shifren et al., 2008). Given the scope of the condition, the availability of a new psychosocial intervention that effectively increases arousal among women with FSAD is clinically meaningful.

Few treatments explicitly target sexual arousal in women, and those that have done so have only led to marginal improvements in some arousal indices. Historically, sexual desire has received more attention in treatment development research than any other domain of female sexual function. Psychological treatment studies have focused primarily on testing CBT protocols and mindfulness-based protocols on women with low desire, though a few of the mindfulness-based studies have included women with low arousal. The results of the CBT-based studies have not been particularly promising; in the two experiments that have examined the efficacy of CBT for low desire, a sizeable portion of the samples did not benefit from the treatment (McCabe, 2001; Trudel et al., 2001). Mindfulness-based treatments, which train participants to focus on their thoughts, emotions, and sensations without judgment, have been comparatively more successful at mitigating symptoms of female sexual dysfunction. In one of the first mindfulness-based treatment studies, women with low desire and/or arousal experienced significant increases in desire and decreases in distress, but only marginally significant improvements in subjective arousal and perceived genital sensations (Brotto et al., 2008). The

one study that has compared a mindfulness-based treatment against a control group demonstrated that the intervention led to significant increases in desire, lubrication, sexual satisfaction, and overall sexual functioning (Brotto & Basson, 2014); subjective arousal and genital arousal are notably absent from this list.

Furthermore, all mindfulness protocols that have been adapted for women with sexual dysfunction have been group-based, which may not be feasible or accessible for all women who are distressed by their level of arousal. Brotto and Basson (2014) developed four, 90-minute group sessions that included mindfulness meditation, cognitive therapy, and psychoeducation; these four sessions were spaced two weeks apart, lasting eight weeks in total. Similarly, a separate study that adapted mindfulness-based cognitive therapy to treat the combination of low desire and arousal included eight weekly group sessions (Paterson, Handy, & Brotto, 2017). The group-based treatments not only require a significant time commitment from participants, they also require access to trained facilitators. Women who are unable to commit eight weeks to the treatment of their sexual concerns or who live in areas that lack skilled providers or specialty sexual medicine clinics will likely will not benefit from mindfulness-based interventions.

Mindfulness is not the only appropriate target for interventions that aim to increase sexual arousal in women. In my graduate work and in this dissertation, I have chosen to focus on HRV and to design studies that increase HRV and, subsequently, sexual arousal. I have done so for several reasons. First, the autonomic nervous system is highly relevant to the etiology of genital arousal, and HRV level is a marker of autonomic balance. Mental health disorders that are characterized by autonomic imbalance, such as depression and anxiety, have been associated with low HRV (Kemp et al., 2012; Licht et al., 2009), so it seemed logical to assess the relationship between HRV and female sexual arousal disorder, which is also characterized by

autonomic imbalance. Second, HRV has also been associated with emotional regulation, which depends on an individual's ability to adjust physiological arousal on a momentary basis (Gross, 1998). Higher HRV, which is indicative of a more flexible ANS, allows for rapid generation and/or modulation of both physiological and emotional states in order to meet situational demands. In contrast, autonomic rigidity compromises one's ability to adjust bodily responses in tandem with environmental changes. I hypothesized that HRV might be related to subjective sexual arousal due to its role in the regulation of physiological and emotional responses because subjective sexual arousal reflects positive engagement during sexual activity. Consider a woman who is not seeking to engage in sex when her partner approaches her and initiates sexual activity. If this woman is receptive to her partner's advances and has a relatively high degree of autonomic flexibility, her body will adapt physiologically to meet the demands of the sexual situation. This adaptive response will likely facilitate feelings of mental arousal or psychological excitement, which might then contribute to a positive feedback loop. A woman with a lower level of autonomic flexibility may not as readily able to quickly adjust her body in accordance with the sexual situation, leaving her physiologically and, subsequently, emotionally unprepared, and perhaps ultimately compromising her subjective arousal.

Finally, I chose to focus on HRV because it is fairly easy to manipulate through targeted, *home-based* interventions. After identifying low HRV as a marker of sexual arousal dysfunction in women and formulating hypotheses about the ways in which HRV relates to both genital and subjective arousal, I learned that specific interventions have been shown to increase HRV over time (e.g., Miu et al., 2009; Zucker et al., 2009). These interventions include autogenic training and HRV biofeedback, both of which were examined in this dissertation. Unlike the mindfulness-based protocols that have been tested by Brotto and colleagues over the past decade,

HRV biofeedback and autogenic training are geared toward the individual, not the group. Although the mindfulness groups did assign homework and directed participants to practice their new skills at home, the protocols were not primarily home-based. The flexibility of an at-home intervention enables women who are uncomfortable talking about their sexual arousal in a group format and women who do not have access to these groups to receive the care that they need.

Given (1) the hypothesized relationships between HRV and the two components of female sexual arousal and (2) the accessibility and flexibility of existing, home-based HRV-targeted interventions, I developed a trajectory of research—five distinct studies—with the ultimate goal of increasing HRV to improve sexual arousal among women with FSAD. Brief synopses of the results of these studies are described here.

In Study 1, I examined the associations among HRV, sexual arousal, and overall sexual function in a sample of pre-menopausal women. Participants were recruited from The University of Texas at Austin's subject pool and from the local community. They were asked to complete self-report measures to assess their sexual function, and their resting state HRV was determined via electrocardiogram as they watched a three-minute neutral film. Women with below average resting HRV were significantly more likely to report sexual arousal dysfunction and overall sexual dysfunction than both women with average resting HRV and above average resting HRV. Based on these findings, I concluded that low HRV might be a marker of sexual arousal problems in women.

Study 2 attempted to explain the findings of Study 1 by assessing the possibility that differences in vagal activity between sexually function and sexually dysfunctional women may be driving the association between low HRV and female sexual dysfunction. Fluctuation in HRV that occurs in the high frequency range is the result of respiratory sinus arrhythmia (RSA), the

increase and decrease in heart rate that occurs with respiration (Porges et al., 1994) and is thought to be mediated by the vagus nerve (Berntson et al., 1993). The quantification of RSA in response to a stressor provides valuable insight on the body's ability to respond to demanding tasks or environmental challenges. Rapid decreases in RSA in response to a stressful situation are healthy and adaptive, as is rapid RSA rebound following the stressful event. In this study, the RSA of sexually functional and dysfunctional women was tested at baseline, during an erotic film, and following the erotic film. Sexually functional women experienced RSA withdrawal in response to the erotic film, whereas sexually dysfunctional women demonstrated vagal activation. Importantly, among sexually dysfunctional women, there was no RSA withdrawal and therefore no vagal break. It is possible, then, that the lack of vagal withdrawal during sexual arousal may contribute to female sexual arousal dysfunction.

With the understanding that vagal pathways, RSA, and HRV may be important potential targets for future intervention, Study 3 assessed the effects of increasing HRV on sexual arousal in women without sexual arousal concerns. It was critical to establish an association between increased HRV and increased arousal in sexually functional women before directing resources toward the recruitment of women with FSAD. Participants were recruited from The University of Texas at Austin's subject pool and asked to watch an erotic film while their genital sexual arousal and subjective sexual arousal were measured. Following the erotic film, they were directed to listen to an autogenic training recording, the purpose of which was to increase their HRV. Participants then watched a second erotic film, and their genital arousal and subjective sexual arousal were measured again. During the film that followed the autogenic training recording, women experienced significant increases in both genital and subjective arousal. The women who had the greatest changes in HRV from pre to post-autogenic training had the

greatest increases in subjective sexual arousal. These findings provided sufficient support for the hypothesized link between increased HRV and increased sexual arousal to test the same HRV-targeted manipulation among women with FSAD. Study 4 did just that; women with FSAD were recruited from the Austin community to complete the same protocol as Study 3. Participants in Study 4 experienced marginally significant increases in discrete subjective arousal and significant increases in perceived genital sensations during the film that followed the autogenic training recording compared to the film the preceded the recording. Again, the women who experienced the greatest increases in HRV had the greatest gains in subjective sexual arousal. However, unlike women in Study 3, women in Study 4 did not experience significant increases in genital arousal following the manipulation.

In Study 5, I conducted a more rigorous examination of the relationship between HRV and female sexual arousal among women with FSAD. Using an additive design, I compared the effects of HRV biofeedback alone and the combination of HRV biofeedback with autogenic training against a waitlist condition. Instead of one laboratory visit, women in this study had three laboratory assessments during which their genital arousal, subjective arousal, and perceived genital sensations were documented. In between these visits, they completed at least eight 20-minute biofeedback sessions using their mobile devices from the privacy of their own homes. Women randomized to the HRB biofeedback plus autogenic training condition listened to a 15-minute autogenic training recording before completing their biofeedback. At the end of the month-long study, there were significant differences in genital arousal, continuous subjective arousal, discrete subjective arousal, and perceived genital sensations among the three conditions. Visualizations of the data revealed that women in the two active conditions outpaced women in the control condition on all four arousal metrics. Although HRV was successfully targeted in

both of the active conditions, increased HRV was significantly associated with only one measure of arousal (perceived genital sensations) in only one of the conditions (the HRV biofeedback condition). Given that women in the HRV biofeedback condition were trained to manipulate and perceive changes in their autonomic arousal using their breath, it is perhaps not surprising that their ability to perceive changes in their genital sensations improved over the course of the intervention. However, for women in the HRV biofeedback plus autogenic training condition, increases in HRV did not mediate increases in any of the arousal variables, suggesting that autogenic training introduced a different mechanism that may be driving those changes.

Although focusing on a single mechanism can provide valuable insight on the role of that mechanism in the etiology and maintenance of a specific disorder, it can also be detrimental in that it may overemphasize the role of that mechanism to the exclusion of other important variables. When I began studying the relationship between HRV and female sexual arousal, I became interested in experimentally increasing HRV as a means of increasing sexual arousal. I sought interventions that targeted HRV, and in doing so, I did not address and measure other mechanisms that may have contributed to improvements in arousal. This is particularly true for the studies that used autogenic training as the experimental manipulation. Though autogenic training does indeed lead to increases in HRV, it also may affect other important physiological and psychological variables that are connected to sexual arousal, such as blood pressure, sensory perception, and concentration.

This series of studies had several other limitations that warrant mention. Sexual psychophysiological testing may be considered a rather invasive form of measurement in that it requires a woman to insert a vaginal photoplethysmograph into her vagina. As such, there may be a natural selection bias in the women who volunteer for sexual psychophysiology studies.

Women who are willing to use a vaginal probe while viewing erotic material may be categorically different than women who are not, with respect to their sexual histories, their comfort with sexuality, and the content of their sex education. Selection biases would be more likely to impact subjective reports than physiological measures. Measurement and design challenges across the five studies, but particularly with respect to Study 5, also limit the generalizability of these findings. In Studies 2-5, baseline HRV was measured after participants learned about the details of the experiment; their readings may have been affected by anticipatory anxiety or excitement prior to the start of the sexual film. In Study 5, although I tried to measure baseline HRV as often as possible without increasing participant burden (i.e., during the three laboratory visits), it would have been ideal if participants had taken baseline readings more often—to document day-to-day changes—and *at home*, so that the measurements could reflect baseline levels in a familiar environment rather than in the laboratory. Though at-home measurements would have likely decreased the sensitivity and the accuracy of the HRV assessments (i.e., ECG in the laboratory vs. app-based assessments at home), they would have facilitated a greater number of available data points. Finally, only one of the five studies included a follow up survey; the number of participants who completed that survey was so low that I could not conduct any moderation analyses, which would have helped me identify certain characteristics or demographic variables that make specific groups of women more likely to benefit from the intervention than others. The follow up survey was sent via email, and participants were not paid to complete it. In the future, dedicating additional monetary resources to the follow up protocol would help ensure that more data is collected.

The results of these five studies suggest several targets for future experiments that examine the relationship among female sexual arousal, HRV, and autonomic balance. First, it

will be crucial to establish the ways in which increased HRV influences female sexual arousal in the positive direction. It is clear that increased HRV facilitates increases in perceived genital sensations and that larger increases in HRV drive greater changes in subjective sexual arousal, but it is not yet evident *how* increased HRV catalyzes these effects. A more nuanced examination of the mechanisms underlying the relationship between HRV and sexual arousal may reveal the importance of additional variables to isolate during treatment for arousal concerns, such as sensory acuity, interoceptive awareness, and other physiological indices of autonomic regulation that may be related to but are distinct from HRV. These examinations will be particularly important with respect to genital arousal, which increased as a result of the intervention in Study 5, but these increases were unrelated to changes in HRV.

Second, after the underlying relationship between HRV and the two components of female sexual arousal is elucidated, researchers can begin to focus on treatment matching. It is unlikely that an intervention will be a good match for *all* women with arousal dysfunction, so care must be paid to identify the women who would most benefit from HRV biofeedback, autogenic training, or a combination of the two. Given that women who present with low arousal may not identify their concerns as primarily subjective or primarily genital, it is important that researchers ask participants to describe the nature of their arousal problem via direct, standardized questions that inquire about the presence of genital sensations as well as the level of mental engagement during sexual activity. If assessments of *both* genital arousal and subjective arousal are not conducted, women with primarily subjective complaints might receive treatments that aim to increase vasocongestion, which likely will not lead to substantive improvements. Likewise, women whose primary complaint is a lack of genital response might not be directed toward interventions that address the underlying causes of decreased vasocongestion. The results

of Study 5 suggest that increasing HRV via HRV biofeedback may be particularly appropriate for women with decreased genital sensations, but it does not appear that increased HRV facilitates increased subjective or genital arousal. If both researchers and clinicians address the two components of sexual arousal in their work and acknowledge that some interventions may be more applicable to women with certain concerns, we will ultimately increase the number of treatment options and adequately meet the needs of these women.

6. APPENDICES

6.1. Appendix A

Modified Film Scale
Heiman & Rowland, 1983

Please use the following scale to evaluate how you felt during your film session. Please answer honestly and carefully. On the scale, circle the number which best describes how you felt during the film from 1 (not at all) to 7 (intensely).

During the film, I felt:

	Not at all						Intensely
1. Warmth in genitals_____	1	2	3	4	5	6	7
2. Genital wetness or lubrication_	1	2	3	4	5	6	7
3. Genital pulsing or throbbing__	1	2	3	4	5	6	7
4. Genital tenseness or tightness_	1	2	3	4	5	6	7
5. Any genital feeling_____	1	2	3	4	5	6	7
6. ***IF*** you experienced the above sensations, to what extent were they:							
..……..***neutral*** for you?	1	2	3	4	5	6	7
…….....***guilty*** for you?	1	2	3	4	5	6	7
…….....***positive*** for you?	1	2	3	4	5	6	7
…….... ***worried*** for you?	1	2	3	4	5	6	7
…….....***angry*** for you?	1	2	3	4	5	6	7
……...***shameful*** for you?	1	2	3	4	5	6	7
……..... ***sexy*** for you?	1	2	3	4	5	6	7
…… ***exciting*** for you?	1	2	3	4	5	6	7

…….. ***negative*** for you?	1	2	3	4	5	6	7
……..... ***disgusting*** for you?	1	2	3	4	5	6	7
…….. ***pleasurable*** for you?	1	2	3	4	5	6	7
…… ***anxious*** for you?	1	2	3	4	5	6	7

During the film, I felt:

	Not at all						Intensely
7. Faster breathing_____	1	2	3	4	5	6	7
8. Faster heart beat_____	1	2	3	4	5	6	7
9. Perspiration_____	1	2	3	4	5	6	7
10. Feelings of warmth_____	1	2	3	4	5	6	7
11. Any physical reaction at all_____	1	2	3	4	5	6	7

12. **IF** you experienced the above sensations, to what extent were they:

……....***neutral*** for you?	1	2	3	4	5	6	7
…….....***guilty*** for you?	1	2	3	4	5	6	7
…….....***positive*** for you?	1	2	3	4	5	6	7
…….. ***worried*** for you?	1	2	3	4	5	6	7
…….....***angry*** for you?	1	2	3	4	5	6	7
……...***shameful*** for you?	1	2	3	4	5	6	7
…….... ***sexy*** for you?	1	2	3	4	5	6	7
…… ***exciting*** for you?	1	2	3	4	5	6	7
…….. ***negative*** for you?	1	2	3	4	5	6	7
……..... ***disgusting*** for you?	1	2	3	4	5	6	7

…….. ***pleasurable*** for you? 1 2 3 4 5 6 7

…… ***anxious*** for you? 1 2 3 4 5 6 7

During the film, I felt:

	Not at all						Intensely
13. Sexually aroused_____	1	2	3	4	5	6	7
14. Mental sexual arousal_____	1	2	3	4	5	6	7
15. Sexually turned off_____	1	2	3	4	5	6	7

6.2. Appendix B

Female Sexual Function Index (FSFI)

Rosen, Brown, Heiman, Leiblum, Meston, Shabsigh, Ferguson, & D'Agostino, 2000

INSTRUCTIONS: These questions ask about your sexual feelings and responses during the past 4 weeks. Please answer the following questions as honestly and clearly as possible. In answering these questions the following definitions apply:

Sexual activity includes intercourse, caressing, foreplay, and masturbation.

Sexual intercourse is defined as penile penetration (entry) of the vagina.

Sexual stimulation includes situations like foreplay with a partner, self-stimulation (masturbation), or sexual fantasy.

CIRCLE ONLY ONE CHOICE PER QUESTION:

Sexual desire or interest is a feeling that included wanting to have a sexual experience, feeling receptive to a partner's sexual initiation, and thinking or fantasizing about having sex.

If you have ***not* engaged in sexual activity in the past 4 weeks please check here ____, and then complete the questions below in reference to the ***most recent*** one month period in which you engaged in sexual activity. **

1. Over the past 4 weeks, how often did you feel sexual desire or interest?

   5 = Almost always or always
   4 = Most times (more than half the time)
   3 = Sometimes (about half the time)
   2 = A few times (less than half the time)
   1 = Almost never or never

2. Over the past 4 weeks, how would you rate your level (degree) of sexual desire or interest?	5 = Very high 4 = High 3 = Moderate 2 = Low 1 = Very low or none at all
3. Over the past 4 weeks, how often did you feel sexually aroused ("turned on") during sexual activity or intercourse?	5 = Almost always or always 4 = Most times (more than half the time) 3 = Sometimes (about half the time) 2 = A few times (less than half the time) 1 = Almost never or never N/A = No sexual activity
4. Over the past 4 weeks, how would you rate your level of sexual arousal ("turn on") during sexual activity or intercourse?	5 = Very high 4 = High 3 = Moderate 2 = Low 1 = Very low or none at all N/A = No sexual activity
5. Over the past 4 weeks, how confident were you about becoming sexually aroused during sexual activity or intercourse?	5 = Very high confidence 4 = High confidence 3 = Moderate confidence 2 = Low confidence 1 = Very low or no confidence N/A = No sexual activity
6. Over the past 4 weeks, how often have you been satisfied with your arousal (excitement) during sexual activity or intercourse?	5 = Almost always or always 4 = Most times (more than half the time) 3 = Sometimes (about half the time) 2 = A few times (less than half the time) 1 = Almost never or never
7. Over the past 4 weeks, how often did you become sexually aroused (females–lubricated or "wet"; males–attained an erection) during sexual activity or intercourse?	5 = Almost always or always 4 = Most times (more than half the time) 3 = Sometimes (about half the time) 2 = A few times (less than half the time) 1 = Almost never or never N/A = No sexual activity

8. Over the past 4 weeks, how difficult was it to become aroused (females–lubricated or “wet"; males–erection) during sexual activity or intercourse?	1 = Extremely difficult or impossible 2 = Very difficult 3 = Difficult 4 = Slightly difficult 5 = Not difficult N/A = No sexual activity
9. Over the past 4 weeks, how often did you maintain your arousal (females–lubrication or "wetness"; males–erection) until completion of sexual activity or intercourse?	5 = Almost always or always 4 = Most times (more than half the time) 3 = Sometimes (about half the time) 2 = A few times (less than half the time) 1 = Almost never or never N/A = No sexual activity
10. Over the past 4 weeks, how difficult was it to maintain your arousal (females–lubrication or "wetness"; males–erection) until completion of sexual activity or intercourse?	1 = Extremely difficult or impossible 2 = Very difficult 3 = Difficult 4 = Slightly difficult 5 = Not difficult N/A = No sexual activity
11. Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you reach orgasm (climax)?	5 = Almost always or always 4 = Most times (more than half the time) 3 = Sometimes (about half the time) 2 = A few times (less than half the time) 1 = Almost never or never N/A = No sexual activity
12. Over the past 4 weeks, when you had sexual stimulation or intercourse, how difficult was it for you to reach orgasm (climax)?	1 = Extremely difficult or impossible 2 = Very difficult 3 = Difficult 4 = Slightly difficult 5 = Not difficult N/A = No sexual activity

13. Over the past 4 weeks, how satisfied were you with your ability to reach orgasm (climax) during sexual activity or intercourse?	5 = Very satisfied 4 = Moderately satisfied 3 = About equally satisfied and dissatisfied 2 = Moderately dissatisfied 1 = Very dissatisfied N/A = No sexual activity
14. Over the past 4 weeks, how satisfied have you been with the amount of emotional closeness during sexual activity between you and your partner?	5 = Very satisfied 4 = Moderately satisfied 3 = About equally satisfied and dissatisfied 2 = Moderately dissatisfied 1 = Very dissatisfied N/A = No sexual activity
15. Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?	5 = Very satisfied 4 = Moderately satisfied 3 = About equally satisfied and dissatisfied 2 = Moderately dissatisfied 1 = Very dissatisfied
16. Over the past 4 weeks, how satisfied have you been with your overall sexual life?	5 = Very satisfied 4 = Moderately satisfied 3 = About equally satisfied and dissatisfied 2 = Moderately dissatisfied 1 = Very dissatisfied
17. Over the past 4 weeks, how often did you experience discomfort or pain during vaginal penetration?	1 = Almost always or always 2 = Most times (more than half the time) 3 = Sometimes (about half the time) 4 = A few times (less than half the time) 5 = Almost never or never N/A = No vaginal penetration

18. Over the past 4 weeks, how often did you experience discomfort or pain <u>following</u> vaginal penetration?	1 = Almost always or always 2 = Most times (more than half the time) 3 = Sometimes (about half the time) 4 = A few times (less than half the time) 5 = Almost never or never N/A = No vaginal penetration
19. Over the past 4 weeks, how would you rate your level (degree) of discomfort or pain during or following vaginal penetration?	N/A = No sexual activity 1 = Very high 2 = High 3 = Moderate 4 = Low 5 = Very low or none at all N/A = No vaginal penetration

6.3. Appendix C

Positive and Negative Affect Schedule (PANAS)
Watson, Clark, & Tellegen, 1988

This scale consists of a number of words that describe different feelings and emotions. Read each item and then mark the appropriate answer in the space next to that word. Indicate to what extent you feel this way right now, at the present moment. Use the following scale to record your answers.

1	2	3	4	5
very slightly	a little	moderately	quite a bit	extremely

___ interested	___ irritable
___ distressed	___ alert
___ excited	___ ashamed
___ upset	___ inspired
___ strong	___ nervous
___ guilty	___ determined
___ scared	___ attentive
___ hostile	___ jittery
___ enthusiastic	___ active
___ proud	___ afraid

6.4. Appendix D

Beck Depression Inventory-II (BDI-II)

Beck, Brown, & Steer, 1996

After reading each group of statements carefully, place a mark next to the number (0, 1, 2, 3) and statement in each group which best describes the way you have been feeling the past two weeks, including today. If several statements within a group seem to apply equally well, place a mark next to each one. Be sure to read all the statements in each group before making your choice.

1. _____ (0) I do not feel sad.
   _____ (1) I feel sad much of the time.
   _____ (2) I am sad all the time.
   _____ (3) I am so sad or unhappy that I can't stand it.

2. _____ (0) I am not discouraged about the future.
   _____ (1) I feel more discouraged about the future than I used to be.
   _____ (2) I do not expect things to work out for me.
   _____ (3) I feel my future is hopeless and will only get worse.

3. _____ (0) I do not feel like a failure.
   _____ (1) I have failed more than I should have.
   _____ (2) As I look back, I see a lot of failures.
   _____ (3) I feel I am a total failure as a person.

4. _____ (0) I get as much pleasure as I ever did from the things I enjoy.
   _____ (1) I don't enjoy things as much as I used to.
   _____ (2) I get very little pleasure from the things I used to enjoy.
   _____ (3) I can't get any pleasure from the things I used to enjoy.

5. _____ (0) I don't feel particularly guilty.
   _____ (1) I feel guilty over many things I have done or should have done.
   _____ (2) I feel quite guilty most of the time.
   _____ (3) I feel guilty all the time.

6. _____ (0) I don't feel I am being punished.
   _____ (1) I feel I may be punished.
   _____ (2) I expect to be punished.
   _____ (3) I feel I am being punished.

7. _____ (0) I feel the same about myself as ever.
   _____ (1) I have lost confidence in myself.
   _____ (2) I am disappointed in myself
   _____ (3) I dislike myself.

8. _____ (0) I don't criticize or blame myself more than usual.
   _____ (1) I am more critical of myself than I used to be.
   _____ (2) I criticize myself for all of my faults.
   _____ (3) I blame myself for everything bad that happens.

9. _____ (0) I don't have any thoughts of killing myself.
   _____ (1) I have thoughts of killing myself, but I would not carry them out.
   _____ (2) I would like to kill myself.
   _____ (3) I would kill myself if I had the chance.

10. _____ (0) I don't cry anymore than I used to.
    _____ (1) I cry more than I used to.
    _____ (2) I cry over every little thing.
    _____ (3) I feel like crying, but I can't.

11. _____ (0) I am no more restless or wound up than usual.
    _____ (1) I feel more restless or wound up than usual.
    _____ (2) I am so restless or agitated that it's hard to stay still.
    _____ (3) I am so restless or agitated that I have to keep moving or doing something.

12. _____ (0) I have not lost interest in other people or activities.
    _____ (1) I am less interested in other people or things than before.
    _____ (2) I have lost most of my interest in other people or things.
    _____ (3) It's hard to get interested in anything.

13. _____ (0) I make decisions about as well as ever.
_____ (1) I find it more difficult to make decisions than usual.
_____ (2) I have much greater difficulty in making decisions than I used to.
_____ (3) I have trouble making any decisions.

14. _____ (0) I do not feel I am worthless.
_____ (1) I don't consider myself as worthwhile and useful as I used to.
_____ (2) I feel more worthless as compared to other people.
_____ (3) I feel utterly worthless.

15. _____ (0) I have as much energy as ever.
_____ (1) I have less energy than I used to have.
_____ (2) I don't have enough energy to do very much.
_____ (3) I don't have enough energy to do anything.

16. _____ (0) I have not experienced any change in my sleeping pattern.
_____
_____ (1) I sleep somewhat more than usual
_____ (1) I sleep somewhat less than usual.
_____
_____ (2) I sleep a lot more than usual.
_____ (2) I sleep a lot less than usual.
_____
_____ (3) I sleep most of the day.
_____ (3) I wake up 1-2 hours early and can't get back to sleep.

17. _____ (0) I am no more irritable than usual.
_____ (1) I am more irritable than usual.
_____ (2) I am much more irritable than usual.
_____ (3) I am irritable all the time.

18. _____ (0) I have not experienced any change in my appetite.
_____
_____ (1) My appetite is somewhat less than usual.
_____ (1) My appetite is somewhat greater than usual.
_____
_____ (2) My appetite is much less than before.
_____ (2) My appetite is much greater than usual.
_____
_____ (3) I have no appetite at all.
_____ (3) I crave food all the time.

19. _____ (0) I can concentrate as well as ever.
_____ (1) I can't concentrate as well as usual.
_____ (2) It's hard to keep my mind on anything for very long.
_____ (3) I find I can't concentrate on anything.

20. _____ (0) I am no more tired or fatigued than usual.
_____ (1) I get more tired or fatigued more easily than usual.
_____ (2) I am too tired or fatigued to do a lot of the things I used to do.
_____ (3) I am too tired or fatigued to do most of the things I used to do.

21. _____ (0) I have not noticed any recent change in my interest in sex.
_____ (1) I am less interested in sex than I used to be.
_____ (2) I am much less interested in sex now.
_____ (3) I have lost interest in sex completely.

6.5. Appendix E

Beck Anxiety Inventory (BAI)
Beck et al., 1988

Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by each symptom during the PAST WEEK, INCLUDING TODAY, by placing an X in the corresponding space in the column next to each symptom.

	NOT AT ALL	**MILDLY** It did not bother me much.	**MODERATELY** It was very unpleasant, but I could stand it.	**SEVERELY** I could barely stand it.
1. Numbness or tingling.				
2. Feeling hot.				
3. Wobbliness in legs.				
4. Unable to relax.				
5. Fear of the worst happening.				
6. Dizzy or lightheaded.				
7. Heart pounding or racing.				
8. Unsteady.				
9. Terrified.				
10. Nervous.				
11. Feelings of choking.				
12. Hands trembling.				
13. Shaky.				
14. Fear of losing control.				
15. Difficulty breathing.				
16. Fear of dying.				
17. Scared.				
18. Indigestion or discomfort in abdomen.				

19. Faint.				
20. Face flushed.				
21. Sweating (not due to heat).				

6.6. Appendix F

Multidimensional Assessment of Interoceptive Awareness (MAIA)
Mehling et al., 2012

Below you will find a list of statements. Please indicate how often each statement applies to you generally in daily life.

	Never					**Always**
1. When I am tense I notice where the tension is located in my body.	0	1	2	3	4	5
2. I notice when I am uncomfortable in my body.	0	1	2	3	4	5
3. I notice where in my body I am comfortable.	0	1	2	3	4	5
4. I notice changes in my breathing, such as whether it slows down or speeds up.	0	1	2	3	4	5
5. I do not notice (I ignore) physical tension or discomfort until they become more severe.	0	1	2	3	4	5
6. I distract myself from sensations of discomfort.	0	1	2	3	4	5
7. When I feel pain or discomfort, I try to power through it.	0	1	2	3	4	5
8. When I feel physical pain, I become upset.	0	1	2	3	4	5
9. I start to worry that something is wrong if I feel any discomfort.	0	1	2	3	4	5
10. I can notice an unpleasant body sensation without worrying about it.	0	1	2	3	4	5
11. I can pay attention to my breath without being distracted by things happening around me.	0	1	2	3	4	5

12. I can maintain awareness of my inner bodily sensations even when there is a lot going on around me.	0	1	2	3	4	5
13. When I am in conversation with someone, I can pay attention to my posture.	0	1	2	3	4	5
14. I can return awareness to my body if I am distracted.	0	1	2	3	4	5
15. I can refocus my attention from thinking to sensing my body.	0	1	2	3	4	5
16. I can maintain awareness of my whole body even when a part of me is in pain or discomfort.	0	1	2	3	4	5
17. I am able to consciously focus on my body as a whole.	0	1	2	3	4	5
18. I notice how my body changes when I am angry.	0	1	2	3	4	5
19. When something is wrong in my life I can feel it in my body.	0	1	2	3	4	5
20. I notice that my body feels different after a peaceful experience.	0	1	2	3	4	5
21. I notice that my breathing comes free and easy when I feel comfortable.	0	1	2	3	4	5
22. I notice how my body changes when I feel happy/joyful.	0	1	2	3	4	5
23. When I feel overwhelmed I can find a calm place inside.	0	1	2	3	4	5
24. When I bring awareness to my body I feel a sense of calm.	0	1	2	3	4	5
25. I can use my breath to reduce tension.	0	1	2	3	4	5

26. When I am caught up in my thoughts, I can calm my mind by focusing on my body/breathing.	0	1	2	3	4	5
27. I listen for information from my body about my emotional state.	0	1	2	3	4	5
28. When I am upset, I take time to explore how my body feels.	0	1	2	3	4	5
29. I listen to my body to inform me about what to do.	0	1	2	3	4	5
30. I am at home in my body.	0	1	2	3	4	5
31. I feel my body is a safe place.	0	1	2	3	4	5
32. I trust my body sensations.	0	1	2	3	4	5

6.7. Appendix G

Five Facet Mindfulness Questionnaire (FFMQ)
Baer et al., 2006

Please rate each of the following statements using the scale provided. Circle the number that best describes your own opinion of what is generally true for you.

	Never or very rarely true	Rarely true	Sometimes true	Often true	Very often or always true
1. When I'm walking, I deliberately notice the sensations of my body moving.	1	2	3	4	5
2. I'm good at finding words to describe my feelings.	1	2	3	4	5
3. I criticize myself for having irrational or inappropriate emotions.	1	2	3	4	5
4. I perceive my feelings and emotions without having to react to them.	1	2	3	4	5
5. When I do things, my mind wanders off and I'm easily distracted.	1	2	3	4	5
6. When I take a shower or bath, I stay alert to the sensations of water on my body.	1	2	3	4	5
7. I can easily put my beliefs, opinions, and expectations into words.	1	2	3	4	5
8. I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted.	1	2	3	4	5
9. I watch my feelings without getting lost in them.	1	2	3	4	5

10. I tell myself I shouldn't be feeling the way I'm feeling.	1	2	3	4	5
11. I notice how foods and drinks affect my thoughts, bodily sensations, and emotions.	1	2	3	4	5
12. It's hard for me to find the words to describe what I am feeling.	1	2	3	4	5
13. I am easily distracted.	1	2	3	4	5
14. I believe some of my thoughts are abnormal or bad and I shouldn't think that way.	1	2	3	4	5
15. I pay attention to sensations, such as the wind in my hair or sun on my face.	1	2	3	4	5
16. I have trouble thinking of the right words to express how I feel about things.	1	2	3	4	5
17. I make judgments about whether my thoughts are good or bad.	1	2	3	4	5
18. I find it difficult to stay focused on what's happening in the present.	1	2	3	4	5
19. When I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it.	1	2	3	4	5
20. I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing.	1	2	3	4	5
21. In difficult situations, I can pause without immediately reacting.	1	2	3	4	5
22. When I have a sensation in my body, it's difficult for me to describe it because I can't find the right words.	1	2	3	4	5

23. It seems I am "running on automatic" without much awareness of what I am doing.	1	2	3	4	5
24. When I have distressing thoughts or images, I feel calm soon after.	1	2	3	4	5
25. I tell myself that I shouldn't be thinking the way I'm thinking.	1	2	3	4	5
26. I notice the smell and aroma of things.	1	2	3	4	5
27. Even when I am feeling terribly upset, I can find a way to put it into words.	1	2	3	4	5
28. I rush through activities without beign really attentive to them.	1	2	3	4	5
29. When I have distressing thoughts or images I am able just to notice them without reacting.	1	2	3	4	5
30. I think some of my emotions are bad or inappropriate and I shouldn't feel them.	1	2	3	4	5
31. I notice visual elements in art or nature, such as colors, shapes, textures, or patterns of light and shadow.	1	2	3	4	5
32. My natural tendency is to put my experiences into words.	1	2	3	4	5
33. When I have distressing thoughts or images, I just notice them and let them go.	1	2	3	4	5
34. I do jobs or tasks automatically without being aware of what I am doing.	1	2	3	4	5
35. When I have distressing thoughts or images, I judge myself as good	1	2	3	4	5

or bad, depending what the thought/image is about.					
36. I pay attention to how my emotions affect my thoughts and behaviors.	1	2	3	4	5
37. I can usually describe how I feel at the moment in considerable detail.	1	2	3	4	5
38. I find myself doing things without paying attention.	1	2	3	4	5
39. I disapprove of myself when I have irrational ideas.	1	2	3	4	5

6.8. Appendix H

Female Sexual Distress Scale Revised (FSDS-R)
Derogatis, Rosen, Leiblum, Burnett, & Heiman, 2002

Below is a list of feelings and problems that women sometimes have concerning their sexuality. Please read each item carefully, and circle the number that best describes HOW OFTEN THAT PROBLEM HAS BOTHERED YOU OR CAUSED YOU DISTRESS DURING THE PAST 30 DAYS INCLUDING TODAY. Circle only one number for each item, and take care not to skip any items. If you change your mind, erase your first circle carefully. Read the example before beginning, and if you have any questions, please ask about them.

Example: How often did you feel: **Personal responsibility for sexual problems**.

Never	Rarely	Occasionally	Frequently	Always
0	1	2	3	4

How often did you feel					
1. Distressed about your sex life	0	1	2	3	4
2. Unhappy about your sexual relationship	0	1	2	3	4
3. Guilty about sexual difficulties	0	1	2	3	4
4. Frustrated by your sexual problems	0	1	2	3	4
5. Stressed about sex	0	1	2	3	4
6. Inferior because of sexual problems	0	1	2	3	4
7. Worried about sex	0	1	2	3	4
8. Sexually inadequate	0	1	2	3	4
9. Regrets about your sexuality	0	1	2	3	4
10. Embarrassed about your sexual problems	0	1	2	3	4
11. Dissatisfied with your sex life	0	1	2	3	4

12. Angry about your sex life	0	1	2	3	4
13. Bothered by low sexual desire	0	1	2	3	4

6.9. Appendix I

Daily Diary of Sexual Activity

Date of sexual activity:

Time of sexual activity:

Type of sexual activity (circle all that apply to this sexual activity or encounter):

Self-stimulation (masturbation)	Vaginal penetration	Manual stimulation of your genitals by your partner	Oral stimulation of your genitals by your partner

Please circle only one choice for each question:

1. How easy was it for you to experience physical/sexual *arousal* from this sexual activity?	1. Extremely easy 2. Very easy 3. Somewhat easy 4. Somewhat difficult 5. Very difficult 6. Did not get aroused
2. How easy was it for you to feel *mentally "turned on"* during this sexual activity?	1. Extremely easy 2. Very easy 3. Somewhat easy 4. Somewhat difficult 5. Very difficult 6. Did not get aroused
3. How easy was it for you to become *lubricated ("wet")* during this sexual activity?	1. Extremely easy 2. Very easy 3. Somewhat easy 4. Somewhat difficult 5. Very difficult 6. Did not get lubricated at all or use a lubricant

4. How easy was it for you to reach an *orgasm (climax)* during this sexual activity?	1. Extremely easy 2. Very easy 3. Somewhat easy 4. Somewhat difficult 5. Very difficult 6. Did not reach orgasm
5. How much *desire or motivation* did you feel about engaging in this sexual activity?	1. Very much 2. Much 3. A moderate amount 4. A little 5. Very little 6. None (Engaged for other reasons; e.g., to please partner)
6. How *satisfied* were you with your sexual *arousal* during this sexual activity?	1. Very satisfied 2. Moderately satisfied 3. About equally satisfied and dissatisfied 4. Moderately dissatisfied 5. Very dissatisfied
7. Did you experience *sexual pleasure* during this sexual activity?	Yes No
8. How strongly did you experience a *tingling* feeling in your genitals?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
9. How strongly did you experience *warmth* in your genitals?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent

10. How strongly did you experience *pulsing and throbbing* in your genitals?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
11. How strongly did you experience a feeling of *fullness* in your genitals?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
12. How strongly did you experience *tightening* of your muscles in the pelvic area?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
13. How strongly did you experience *heart acceleration*?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
14. How strongly did you experience an increase in *perspiration*?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent
15. How strongly did you experience an increase in *breathing rate*?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent

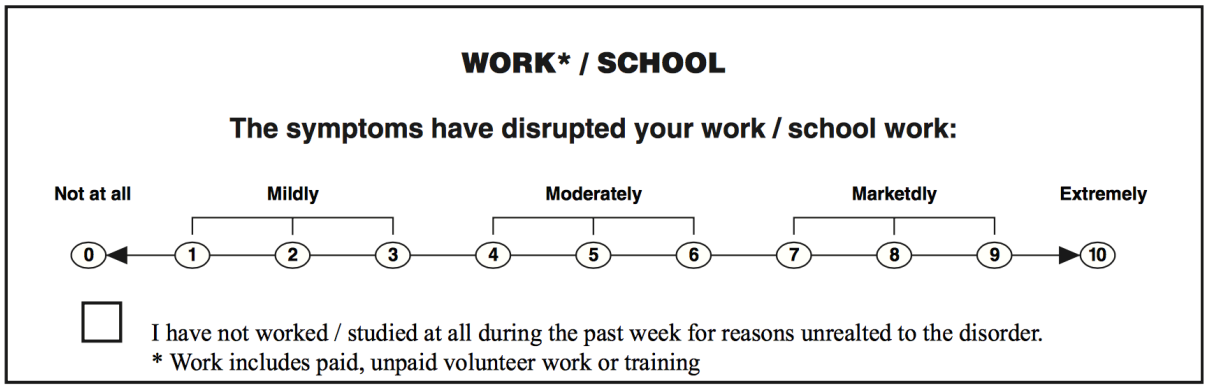
16. How strongly did you experience a feeling of *mental sexual arousal*?	1. Strong 2. Moderate 3. Weak 4. Barely detectable 5. Absent

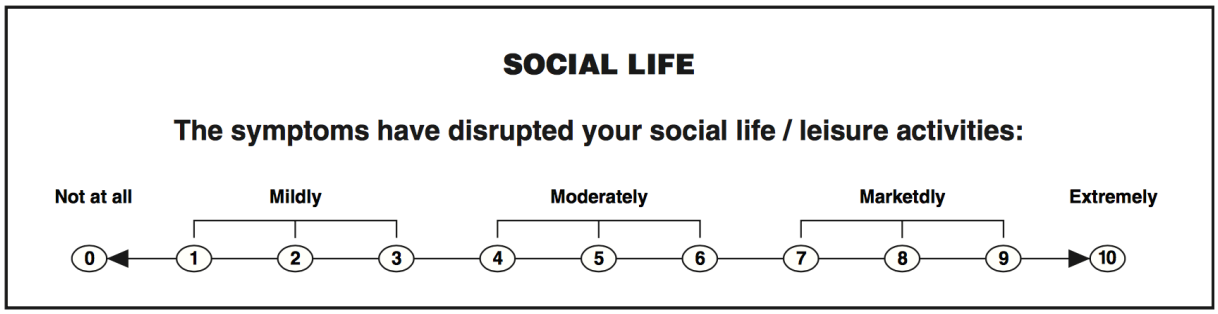
6.10. Appendix J

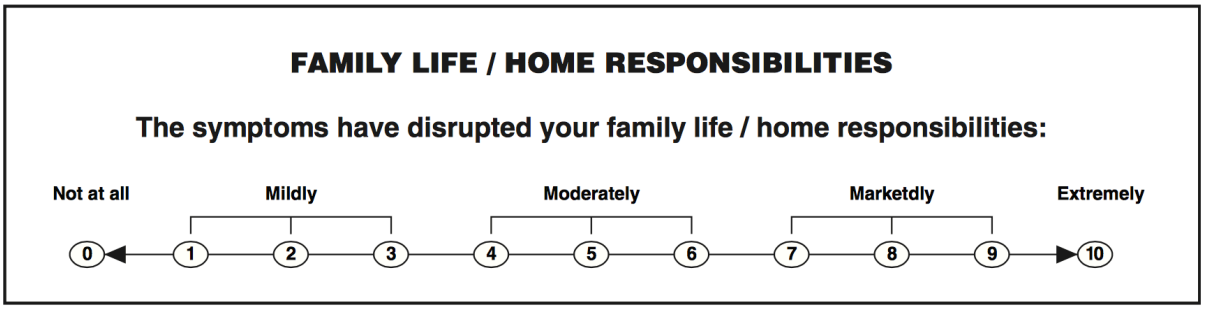
Sheehan Disability Scale
Sheehan, 1983

A brief, patient rated, measure of disability and impairment.

Please mark ONE circle for each scale.







Days Lost

On how many days in the last week did your symptoms cause you to miss school or work or leave you unable to carry out your normal daily responsibilities? _____

Days Unproductive

On how many days in the last week did you feel so impaired by your symptoms, that even though you went to school or work, your productivity was reduced? _____

6.11. Appendix K

Credibility/Expectancy Questionnaire
Devilly & Borkovec, 2000

Please slide the scale to answer the question.

At this point, how logical does the therapy offered to you seem?	Not at all successful Very successful 0 10 20 30 40 50 60 70 80 90 100

Please slide the scale to answer the question.

At this point, how successful do you think the treatment will be in increasing your sexual arousal?	Not at all successful Very successful 0 10 20 30 40 50 60 70 80 90 100

Please slide the scale to answer the question.

How confident would you be in recommending this treatment to a friend who experiences similar problems?	Not at all confident Very confident 0 10 20 30 40 50 60 70 80 90 100

Please slide the scale to answer the question.

By the end of the therapy period, how much improvement in your sexual arousal do you think will occur?	Not at all improved Very improved 0 10 20 30 40 50 60 70 80 90 100

Try to identify what you really *feel* about the therapy and its likely success. Please slide the scale to answer the question.

At this point, how much do you really feel that the therapy will help improve your sexual arousal?	0 10 20 30 40 50 60 70 80 90 100

Try to identify what you really *feel* about the therapy and its likely success. Please slide the scale to answer the question.

By the end of the therapy, how much improvement in your sexual arousal do you really feel will occur?	0 10 20 30 40 50 60 70 80 90 100

7. GLOSSARY

Autonomic nervous system – division of the peripheral nervous system that controls unconscious processes, such as heartbeat, breathing, and aspects of sexual arousal; includes the parasympathetic and sympathetic branches

Female sexual arousal disorder – defined by *DSM-IV-TR* as a persistent or recurrent inability to attain or maintain an adequate lubrication-swelling response until completion of sexual activity, must cause persistent or marked distress or interpersonal difficulty

Heart rate variability – the degree of variability in lengths of time between consecutive heartbeats; an index of the relative balance of the two branches of the autonomic nervous system

High frequency heart rate variability – the band of the heart rate variability power spectrum that includes oscillations between 0.15 Hz and 0.4 Hz; these oscillations are synchronous with respiration (see *respiratory sinus arrhythmia*)

Low frequency heart rate variability – the band of the heart rate variability power spectrum that includes oscillations between 0.04 Hz and 0.15 Hz; this band appears to be mediated by both the parasympathetic and the sympathetic nervous systems

Parasympathetic nervous system – a branch of the autonomic nervous system that conserves energy by slowing the heart rate when the body is at rest; sometimes referred to as the "rest and digest" system

Respiratory sinus arrhythmia – the high frequency band of heart rate variability; occurs as heart rate increases during inhalation and decreases during exhalation

Standard deviation of normal-to-normal inter-beat intervals – the most common measure of heart rate variability; reflects the general ebb and flow of factors contributing to heart rate variability

Sympathetic nervous system – a branch of the autonomic nervous system that triggers norepinephrine release, leading to bodily reactions such as pupil dilation, increased blood pressure, and increased heart rate; sometimes referred to as the "fight or flight" system

Ultra low frequency – the band of the heart rate variability power spectrum that includes all oscillations below 0.0033 Hz; these oscillations are associated with the circadian rhythm, core body temperature, and other slow acting systems

Vaginal pulse amplitude – a psychophysiological index that reflects short-term changes in the engorgement of blood in the vaginal tissue; an index of women's physiological, or genital, arousal

Very low frequency – the band of the heart rate variability power spectrum that includes oscillations between 0.0033 Hz and 0.04 Hz, which are associated with thermoregulation and other long-term regulatory mechanisms

8. LIST OF ABBREVIATIONS

ACME – average causal mediation effect
ADE – average direct effect
ANS – autonomic nervous system
BAI – Beck Anxiety Inventory
BDI – Beck Depression Inventory
CBT – cognitive behavioral therapy
CSA – childhood sexual abuse
CVD – cardiovascular disease
DHEA – dehydroepiandrosterone
ECG – electrocardiogram
ED – erectile dysfunction
FDA – Food and Drug Administration
FFMQ – Five Facet Mindfulness Questionnaire
FMRI – functional magnetic resonance imaging
FSAD – female sexual arousal disorder
FSDD – Female Sexual Dysfunction Diagnosis
FSDS-R – Female Sexual Distress Scale Revised
FSFI – Female Sexual Function Index
FSIAD – female sexual interest/arousal disorder
GAD – generalized anxiety disorder
HF – high frequency
HLM – hierarchical linear modeling
HPA – hypothalamic-pituitary-adrenal (axis)
HRV – heart rate variability
HRVB – heart rate variability biofeedback condition
HRVB+A – heart rate variability biofeedback plus autogenic training condition
HSDD – hypoactive sexual desire disorder
IBI – inter-beat interval
LF – low frequency
MAIA – Multidimensional Assessment of Interoceptive Awareness
MDD – major depressive disorder
NDRI – norepinephrine dopamine reuptake inhibitor
NN – beat-to-beat interval
PANAS – Positive and Negative Affect Schedule
PDEi – phosphodiesterase inhibitor
PNS – parasympathetic nervous system
PTSD – posttraumatic stress disorder
RSA – respiratory sinus arrhythmia
SDNN – standard deviation of normal-to-normal inter-beat intervals
SDS – Sheehan Disability Scale
SNS – sympathetic nervous system
ULF – ultra low frequency
V1 – laboratory visit one

V2 – laboratory visit two
V3 – laboratory visit three
VBV – vaginal blood volume
VLF – very low frequency
VPA – vaginal pulse amplitude
WL – Waitlist condition

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