

Since entering the field of women's sexuality 25 years ago, my research has focused primarily on understanding women's sexual arousal. To the extent that desire and arousal mechanisms are closely related in women, my research also has implications for understanding women's sexual desire. According to the Laumann et al. (1994) random probability sample of over 1,600 women in the US, approximately 33% report problems with desire and 19% report problems with arousal. Despite these high prevalence rates, to date there are no FDA-approved drug treatments for women's sexual dysfunction and no empirically validated treatments for desire or arousal dysfunction in women. Below is a summary of some of the studies I have conducted in this area. They may be broadly categorized as studies aimed at understanding the mechanisms underlying women's physiological sexual arousal, studies aimed at understanding some of myriad factors contributing to women's psychological sexual arousal (i.e., subjective or cognitive experience of feeling "turned on"), studies aimed at understanding the link between physiological and psychological arousal in women, and studies aimed at developing new treatments for sexually dysfunctional women. In the following studies, physiological sexual arousal is measured using a vaginal photoplethysmograph to detect changes in vaginal pulse amplitude. Psychological arousal is measured using self-report questionnaires and, in recent studies, using a device developed in my lab termed the "arousometer" that allows for the continuous measurement of subjective sexual arousal during stimulus presentation. Laboratory measures of sexual arousal are conducted in response to erotic videos that have been selected and piloted specifically for enhancing sexual responses in women. Measures are reported as change scores between a woman's response during a non sexual film (e.g., travel film) and her response during a sexual film.

I. PHYSIOLOGICAL STUDIES ON WOMEN'S SEXUAL FUNCTION

The Sympathetic Nervous System and Women's Sexual Arousal

For over 30 years, clinicians, researchers, and theorists in the field of human sexuality have worked largely under the assumption that the SNS plays an inhibitory role, and the parasympathetic nervous system (PNS) plays a facilitatory role in initiating and maintaining the early stages of sexual arousal. In women, this assumption has been based primarily on analogies that have been drawn between the erectile response in men and the vasocongestive response in women. Together with colleagues, I have conducted a series of human and animal studies that were designed to help understand autonomic nervous system influences on female sexual arousal. The effects of SNS activation on sexual arousal were assessed in five studies using intense acute exercise (Meston & Gorzalka 1995; 1996a; 1996b; Rellini & Meston, 2006; Hamilton, Fogle, & Meston, 2009), and in two studies using ephedrine (Meston & Heiman, 1998; Meston, 2004), to activate the SNS. I have also examined the effects of SNS inhibition on sexual responses in both animals (Meston, Moe, & Gorzalka, 1996), and humans (Meston, Gorzalka, & Wright, 1997) using various agents known to suppress SNS activation. The findings from these studies suggest that, contrary to assumptions held for over three decades, SNS activation does not simply impair sexual arousal in women. Rather, it appears that a certain level of SNS activation may in fact be necessary for women's physiological sexual arousal (for reviews, see Meston, 2000; Meston & Frohlich, 2000; Meston & Bradford, 2007; Bradford & Meston, 2007). These findings have led me to explore physiological arousal responses in women with potential impairments in mechanisms linked to autonomic nervous system function, including women with high levels of anxiety, women who have undergone hysterectomy and women with a history of childhood sexual abuse.

Anxiety. The mechanisms by which anxiety impacts sexual arousal in women are not firmly established. Sex-related anxiety can make it difficult to psychologically engage in sexual activity, as the woman may be too preoccupied with her sex-related fears to fully attend to sexual stimuli.

Because both acute anxiety and sexual arousal are mediated by changes in autonomic arousal, there may also be a physiological basis to impaired sexual responding secondary to anxiety. We (Bradford & Meston, 2006) examined the impact of state and trait anxiety on physiological and subjective sexual arousal. Results suggested a curvilinear relationship between state anxiety and physiological sexual arousal. Trait anxiety was correlated with self-reported sexual arousal outside the laboratory. The findings are consistent with the earlier studies I conducted on exercise and physiological sexual arousal which suggested a moderate level of SNS activation (in this case state anxiety) may facilitate, and high levels inhibit, physiological sexual responding.

Hysterectomy and Sexual Arousal. Approximately 25-50 percent of women experience adverse sexual symptoms following hysterectomy surgery. Hysterectomy could feasibly affect the pelvic autonomic nerves through excision of the cervix and separation of the uterus from the cardinal and uterosacral ligaments. If sexual arousal processes are negatively impacted by hysterectomy surgery, and this is associated with impaired autonomic innervation, differences between women who have and have not undergone hysterectomy would be expected to emerge under conditions of heightened autonomic arousal. To examine this hypothesis, I conducted a study (Meston, 2004) that compared sexual arousal responses between women who had undergone hysterectomy for the treatment of benign uterine fibroids with non-hysterectomized women with a history of benign uterine fibroids under conditions of baseline and heightened SNS activation. The study was the first to document significant differences in physiological sexual arousal responses between women who had and had not undergone hysterectomy. In addition to this study, I have published two reviews on the impact of hysterectomy on sexual function (Meston & Bradford, 2004; Bradford & Meston, 2006), and recently published a study (Bradford & Meston, 2007) that examined the impact of pre-surgery education about the sexual consequences of hysterectomy on post-surgery satisfaction with hysterectomy.

Childhood Sexual Abuse and Sexual Arousal. Literature suggests that childhood sexual abuse (CSA) survivors with post traumatic stress disorder (PTSD) have higher baseline SNS activity than healthy controls. During a stressful experience, the SNS becomes activated and releases catecholamines which increase glucose availability, heart rate and blood pressure. After a non-traumatic stressor, the body returns to its original state but after a trauma, such as CSA, the homeostasis of the individual is often altered. Theoretically, this could help explain the high incidence of sexual arousal difficulties noted in women with CSA. In two studies comparing various components of the sexual arousal response between women with and without a history of CSA, we demonstrated that women with CSA and PTSD have a blunted physiological sexual response to SNS activation (via acute, intense exercise) compared to controls (Rellini & Meston, 2006), and a diminished cortisol response to sexual arousal compared to controls (Rellini, Hamilton, Delville, & Meston, in press). These findings are the first to suggest a biological difference in the physiological sexual arousal of women with and without CSA.

Nicotine and Sexual Arousal

Evidence that long-term cigarette smoking is an independent risk factor for vasculogenic impotence is robust. Cigarette smoking also causes a variety of acute changes such as impairment in endothelium dependent venodilation; however, few studies have investigated these acute changes with respect to sexual arousal in humans, and none have looked at the effects of nicotine on physiological sexual arousal in women. Recently, we (Harte & Meston, 2008a; Harte & Meston, 2008b) conducted two studies that examined the effects of 6 mg of nicotine gum versus placebo on sexual arousal in men and women nonsmokers. Male genital arousal was assessed via penile circumferential change using a mercury-in-rubber strain gauge while female genital arousal was measured using vaginal photoplethysmography. Nicotine significantly reduced physiological sexual responses in both males and females. These data are in line with other research delineating nicotine's vasoconstrictive

properties and may support the hypothesis that nicotine deleteriously affects nitric oxide synthesis mechanisms that are integral to the sexual response in both men and women.

Serotonin and Sexual Function

In addition to impacting central systems, SSRIs may affect sexual functioning by acting on the peripheral vascular system (Frohlich & Meston, 2000). Evidence suggests that serotonin produces vasoconstriction and increased blood pressure by acting primarily on the 5-HT₂ and vasodilation by acting primarily on the 5-HT₁. Since SSRIs alter CNS 5-HT₁ and 5-HT₂ receptor activity it is feasible that SSRIs also alter peripheral 5-HT₁ and 5-HT₂ receptor activity. If so, sexual functioning could be impaired directly by affecting vasocongestion to the genital tissue or indirectly by altering sensory functions, such as tactile sensation, that have been found to be affected by hypertension. To examine this hypothesis, we (Frohlich & Meston, 2005a) conducted the first empirical examination of tactile sensitivity in women with and without female sexual arousal disorder. Tactile sensitivity was examined on the distal portion of the dominant hand index finger and on the lower lip. Finger threshold was significantly associated with severity of arousal dysfunction. Logistic regression showed that 76.5% of participants were correctly classified as functional or dysfunctional and 23.5% were incorrectly classified using tactile sensation as a predictor variable.

In a second study (Frohlich & Meston, 2005b), we examined whether SSRI-induced sexual difficulties arise in part from an over-sensitivity or under-sensitivity of tactile sensation. Tactile sensitivity was examined in clinically depressed women at baseline (pre-medication), week 1, week 4, and week 8 of fluoxetine treatment. Fluoxetine treatment resulted in decreased orgasm functioning that was not mediated by tactile sensation. An independent association was found between sexual arousal functioning and finger sensation, such that as sexual desire decreased, finger threshold increased.

Dopamine, Norepinephrine, and Sexual Arousal

A growing literature suggests a prosexual role of dopamine (DA) and norepinephrine (NE) in female sexuality. Disruptions in these systems could feasibly lead to impaired sexual function in women. Given dopamine's well established role in the anticipation of reward, one would expect disruptions in central DA systems to most likely impact desire mechanisms. Women with clinically low levels of sexual desire may simply find sexual activity, or the anticipation of sexual activity, less rewarding and this may, in part, be linked to a blunted DA response in sexual situations. To begin testing this hypothesis, we examined whether DA and NE changes with sexual stimuli differ between women with and without desire dysfunction. We assayed blood levels of NE and homovanillic acid (HVA; the major metabolite of DA) taken during exposure to nonsexual and sexual films, while recording subjective and physiological sexual arousal responses (Meston & McCall, 2005). HVA levels significantly decreased during the erotic versus neutral film in both sexually functional and dysfunctional women. Sexually dysfunctional women had significantly higher levels of NE during both the neutral and erotic films compared with functional women.

Testosterone and Sexual Arousal

A growing literature has linked low sexual desire to low androgen levels in women. In recent years, exogenous testosterone, or the adrenal hormone dehydroepiandrosterone (DHEA) which serves as a precursor for testosterone, has been prescribed for women with low sexual desire. These treatments have been effective in some women with abnormally low testosterone levels, but not among women with normal testosterone (e.g., Meston & Heiman, 2002) and there are often unwanted side effects of testosterone administration (e.g., facial hair, acne). Very few studies have looked at the effects sexual activity may have on endogenous androgens in women. We (Hamilton & Meston, 2009) recently examined whether testosterone levels are influenced by either sexual activity or the anticipation of

sexual activity in women. Women in long distance relationships provided five saliva samples: at least one week before seeing their partner (and at least 2 weeks since their last sexual contact), the day before seeing their partner, when they were with their partner but prior to engaging in sexual activity, the day after their first sexual activity, and three days after their last sexual activity. As expected, salivary testosterone was found to be lowest when participants had abstained from sex for at least two weeks, highest in anticipation of sexual activity and the day after sexual activity, but declined in the presence of their partner (first seeing each other – before any sexual activity). Testosterone levels returned to baseline once the partner left. The present findings have important clinical implications in that they reveal a natural, non-invasive way of increasing androgens endogenously.

Oxytocin and Monogamy

A ubiquitous model for monogamy and promiscuity is the vole model that compares the closely related montane voles, which do not form pair bonds and mate freely with many partners, and prairie voles which are innately monogamous. Research comparing the montane and prairie voles has identified both oxytocin (OT) and vasopressin (AVP) as playing a key role in these behaviors with prairie voles having more OT and AVP as well as increased receptor density for these hormones (Insel & Shapiro, 1992). Vasopressin seems to play more of a role for male pair-bonding, while oxytocin is critical for female pair bonding (Carter et al., 1995). Specific brain areas, such as the ventral pallidum, nucleus accumbens, medial amygdala, medial preoptic area (MPOA) and the bed nucleus of the stria terminalis (BNST) have been identified as critical areas that are differentiated between montane and prairie voles. The most robust difference is seen in the large number of V1aR receptors in the ventral pallidum in prairie voles, while montane voles do not have these receptors. Researchers have also found that prairie voles have a much higher density of D2 dopamine receptors in the nucleus accumbens and other areas in the dopamine reward pathway (Edwards & Self, 2006). Many of the areas identified as key dopamine receptor areas involved in bonding are also key areas for vasopressin receptor areas involved in bonding. Thus, in male prairie voles, there seems to be great overlap between reward and bonding.

We (Hamilton & Meston) are currently examining whether it is possible that similar neural substrates underlie monogamy and non-monogamy in human males. Monogamous and nonmonogamous men are shown six alternating blocks of erotic photos, bonding/romantic photos, and neutral photos. Each stimulus block (erotic, bonding/romantic, and neutral) includes 10 photos presented for 5 seconds each separated by a 15 second rest period. Our hypothesis is that monogamous men will show similar brain activation, as measured by fMRI, for both the erotic and romantic stimuli, and that nonmonogamous men will show more activation in reward and emotion-related areas of the brain for erotic stimuli, as opposed to romantic stimuli.

II. PSYCHOLOGICAL STUDIES ON WOMEN'S SEXUAL FUNCTION

Self-Focused Attention on Sexual Arousal

The construct of self-focused attention has been discussed as relating to sexual function since Masters and Johnson's (1970) introduction of the constructs "spectatoring" and "sensate focus." Spectatoring refers to focusing on and evaluating oneself from a third person perspective during sexual activity. This focus of attention outward on sexual performance rather than inward on the sensory aspects of a sexual experience (i.e., sensate focus) is believed to have deleterious effects on sexual performance (see Trapnell & Meston, 1997). To begin empirically testing these constructs, I conducted a study (Meston, 2006) that examined state self-focused attention and trait self-consciousness on sexual arousal and function in sexually functional and dysfunctional women. Self-focused attention was induced using a 50% reflectant television screen in one of two counterbalanced

sessions during which sexual responses were measured. In a second study (Seal & Meston, 2007), self-focused attention was induced by placing a full-length mirror in front of the participants throughout testing and instructing them to use the mirror to place ten electrodes evenly on each side of their bodies in preparation for a possible electrocardiogram. The findings from these two studies provided empirical evidence for a role of both state and trait self-focused attention in female sexual function.

Expectancies and Sexual Arousal

Numerous laboratory studies have shown that men without sexual dysfunction respond to erotic cues with positive affect, positive expectancies, and perceived control of erectile response whereas men with a history of sexual dysfunction respond to erotic cues with negative affect, negative expectancies, and perceived lack of control of erectile response. These findings have been explained in terms of a feedback loop whereby expectancies are shaped by an individual's recollections of past sexual experiences (Barlow, 1986). To begin examining the role of expectancies on women's sexual response, we (McCall & Meston, 2007) investigated the impact of both false positive and false negative feedback (vaginal photoplethysmograph response print-out) on subsequent sexual responding in sexually healthy women and women with female sexual arousal disorder (FSAD). False positive feedback increased subjective arousal in both groups of women whereas false negative feedback decreased subjective levels of arousal in both groups of women. Sexually healthy women had overall higher expectancies for sexual arousal than women with FSAD. Unexpectedly, false positive feedback did not significantly impact physiological arousal in sexually healthy women but decreased physiological arousal in women with FSAD. False negative feedback had no significant effect on physiological sexual response in sexually healthy women or women with FSAD.

Social Desirability Influences on Self-Reported Sexuality.

Socially desirable responding, the tendency to tailor responses for the purpose of looking good, has been a topic of concern in self-report assessment for over five decades. The influence of socially desirable responding on self-report measures of sexual behavior has been of particular concern given the private nature of sexual activity, and the fact that people often feel embarrassed or threatened when asked to provide information on their sexual encounters. Together with colleagues, I have published two studies (Meston, Heiman, Trapnell, & Paulhus, 1998; Meston, Heiman Trapnell, & Carlin, 1999) and am in the process of writing a third manuscript that address the question of which relationships exist between self-reported sexuality and measures of socially desirable responding when the data is collected under well controlled, anonymous testing conditions. Examining these relationships provides insight into whether response biases play a role in self-report sex data and, if so, whether they differ as a function of ethnicity and/or gender.

Depression and Sexual Functioning

It has long been assumed that depression impairs sexual functioning. To date, studies have focused on global aspects of sexual functioning and the interpretation of findings is often confounded by antidepressant use among respondents. Results from a study comparing women with depressive symptoms with non depressed women (Frohlich & Meston, 2002) indicated, as expected, depressed women reported more impaired arousal, orgasm and sexual pain, and less sexual satisfaction and pleasure than did non depressed women. Novel to this study, depressed women reported greater desire for sexual activity alone (i.e., masturbation) than non depressed women reflecting, perhaps, a desire to engage in self-soothing behavior.

Excitation Transfer and Sexual Attraction

Excitation transfer theory posits that residual excitement from a previous arousing stimulus or situation may serve to intensify a later emotional state. For over three decades, excitation transfer theory has been empirically applied to the domain of sexual arousal and attraction. We (Meston & Frohlich, 2003) conducted the first study to investigate this phenomenon in both men and women with and without a salient dating partner using a real life situation to increase autonomic arousal (riding a roller coaster). We approached participants at amusement parks as they were either waiting to begin a roller coaster ride, or as they had just gotten off of a roller coaster ride. They were shown a photograph of an average attractive, opposite-gendered individual and asked to rate the individual on attractiveness and dating desirability. They were also asked to rate their seatmates' level of attractiveness. The findings were consistent with predictions of excitation transfer theory among persons who did not have a romantic partner present.

Ethnic Influences on Sexuality

Ethnicity and culture undoubtedly have a substantial impact on the expression of sexuality. Examination of potential differences in sexual behaviors, attitudes, and values between ethnic groups has important implications for designing culturally-appropriate treatments for sexual dysfunction. Together with colleagues, I have published three manuscripts (Meston, Heiman, Trapnell, & Carlin, 1999; Meston, Trapnell, & Gorzalka, 1996;1998) examining differences in sexual behaviors and attitudes between SE Asian and Caucasian individuals and two manuscripts that describes differences in such relations between individuals of European, Asian, and Hispanic ancestry (Meston & Ahrold, 2009; Ahrold & Meston, 2009).

Religion and Sexuality

Among the diverse functions of religion—the provision of certainty, meaning, social support, self-actualization, health, and emotional strength—the regulation of sexuality has been a historical priority for the Judeo-Christian tradition. Previous literature on religion and sexual behavior has focused on narrow and often atheoretical definitions of religiosity, including religious affiliation, religious participation, or well-established forms of religiousness (e.g., intrinsic religiosity). We (Farmer, Trapnell, & Meston, 2009; Ahrold, Meston, Trapnell, & Farmer, under review) examined relationships between five distinct measures of religiosity (religious denomination, intrinsic religiosity, paranormal religiosity, spirituality, fundamentalism) and measures of sexual behavior and attitudes in a college sample of over 1500 men and women. Findings indicated that religiosity measures were more associated with the sexuality of women than men. Among women, paranormal religiosity was positively correlated with sexual behavior, whereas spirituality, intrinsic religiosity, and fundamentalism were negatively correlated with sexual behavior. Significant negative correlations between intrinsic religiosity and sexual behaviors were reduced or diminished when the contribution of fundamentalism was partialled out.

Questionnaire Development

The Female Sexual Function Index (FSFI). This is currently the most widely used assessment tool for women's sexual dysfunction. I was a co-author on the original validation study in women with and without FSAD (Rosen, Brown, Heiman, Leiblum, Meston, Shabsigh, Ferguson, & D'agostino, 2000), the sole author on a revalidation study in women with and without hypoactive sexual desire disorder and/or female orgasmic disorder (Meston, 2003), and a co-author on the cross-validation study and development of clinical cut-off scores (Wiegel, Meston, & Rosen, 2005).

The Sexual Satisfaction Scale for Women (SSS-W; Meston & Trapnell, 2005). The SSS-W was developed based on the responses of over 800 women. It is a brief, 30-item measure of sexual satisfaction and sexual distress, comprised of five domains confirmed by factor analyses: contentment, communication, compatibility, concern: relational, personal. It exhibits sound psychometric properties and has a demonstrated ability to discriminate between clinical and nonclinical samples.

The Cues for Sexual Desire Scale (CSDS; McCall & Meston, 2006). The CSDS is a multidimensional assessment scale of cues associated with sexual desire in women. It consists of 4 factor analytic derived subscales: 1) Emotional Bonding Cues, 2) Erotic/Explicit Cues, 3) Visual/Proximity Cues, and 4) Implicit/Romantic Cues. The CSDS demonstrates good reliability and validity and is able to detect significant differences between women with and without hypoactive sexual desire disorder.

The Why Have Sex Questionnaire (YSEX?; Meston & Buss, 2007). Phase I of the development of the YSEX? used a nomination procedure to identify 237 expressed reasons for having sex. Phase II asked participants (N = 1,549) to evaluate the degree to which each of the 237 reasons had led them to have sexual intercourse. Factor analyses yielded four large factors and 13 meaningful subfactors, producing a hierarchical taxonomy. The Physical reasons subfactors included Stress Reduction, Pleasure, Physical Desirability, and Experience Seeking. The Goal Attainment subfactors included Resources, Social Status, Revenge, and Utilitarian. The Emotional subfactors included Love and Commitment and Expression. The three Insecurity subfactors included Self-Esteem Boost, Duty/Pressure, and Mate Guarding. Significant gender differences supported several previously advanced theories.

Validation of the McCoy Female Sexuality Questionnaire (MFSQ) in an Italian Sample (Rellini, Nappi, Vaccaro, Ferdeghini, Abbiati, & Meston, 2005). This study translated into Italian and validated the MFSQ on an Italian sample. The translated version of the MFSQ is a reliable and valid measure of sexual dysfunction among Italian women.

Childhood Sexual Abuse (CSA) and Sexuality (Cognitive Studies)

Among the long-term symptoms found to exist decades following CSA is a broad spectrum of sexual difficulties in adulthood. Several researchers have documented the existence of these relations but little research has aimed specifically at understanding the psychological mechanisms and processes by which sexual abuse experiences in childhood might precipitate, magnify, or sustain sexual problems in adulthood. Together with colleagues I have conducted a number of studies aimed specifically at trying to better understand these relations.

Sexual Self-Schema Studies. The role of sexual scripts has gained increasing attention in the diagnosis and treatment of sexual disorders. Sexual scripts may be defined as plans for overt sexual activity, as intermittent guides or cues used during sexual performance, and/or as storage devices for organizing memories of past sexual experiences into coherent narratives. We (Meston, Rellini, & Heiman, 2006) examined whether differences exist between women with and without a history of CSA in the way they view themselves as a sexual person and if so, whether such differences mediate the link between early unwanted sexual experiences and later adult sexuality. CSA survivors viewed themselves as less romantic and passionate than non-abused women and showed an inverse relationship between romantic/passionate sexual self-schemas and negative sexual affect during sexual arousal. This relationship was independent from symptoms of depression and anxiety, and suggests that the impact of CSA on sexual self-schemas may be independent from the impact that the abuse may have in other areas of the survivor's life.

Using more implicit methodologies, we (Meston & Heiman, 2000) compared responses between CSA survivors and controls on similarity ratings of word pairs using the computer program PATHFINDER. This program uses similarity scores to mathematically compute networks that are believed to represent the way in which information is stored or represented in memory. We found that CSA survivors differed from non-abused women in the meanings they attributed to a number of sexuality-relevant concepts.

Recently, we (Rellini & Meston, 2007) used the Linguistic Inquiry Word Count (LIWC) software program to examine potential language use differences between abused and non-abused women. Women were asked to write on sexual and non sexual topics and LIWC was used to compute the percentage of words that fell into positive emotions, negative emotions, body and sex categories. CSA survivors used more negative emotion words when writing about sexual topics compared to non abused women, and also used more sex words when writing the non-sexual topics compared to non abused women. Frequency of body and sex words used in the sexual texts was positively linked to levels of sexual desire. A history of CSA remained an independent predictor of levels of sexual desire dysfunction even when taking into consideration the language used in the sexual texts, indicating there may be unexplored aspects of the sexual desire experienced by CSA survivors that differ from non-abused women.

Identification as an Abuse Survivor. One of the major criticisms in the literature on sexual abuse is an overwhelming lack of agreement on how to operationalize CSA. Individual differences in the interpretations of the same type of unwanted sexual event may be an aspect of sexual abuse that carries important meaning and warrants consideration. We (Rellini & Meston, 2009) conducted a study examining potential differences in abuse experiences and sexual outcomes between CSA survivors who do and do not identify as an abuse survivor. Women with a history of CSA who self-identified as a sexual abuse survivor were more likely to have experienced penetration of the genitals during the abuse, had a familial relationship with the perpetrator, experienced fear at the time of the abuse, and experienced the abuse more frequently than CSA survivors who did not identify as an abuse survivor.

III. STUDIES ON THE RELATIONSHIP BETWEEN PHYSIOLOGICAL AND PSYCHOLOGICAL SEXUAL AROUSAL IN WOMEN

The results from my studies on physiological sexual arousal in women strongly suggest there are ways to enhance genital engorgement in pre-menopausal (e.g., exercise, ephedrine, ginkgo biloba) and post-menopausal (e.g., L-arginine glutamate plus yohimbine) women. More often than not, however, these increases in physiological sexual arousal are not accompanied by corresponding increases in subjective reports of arousal. The low correlation between subjective and physiological measures of sexual arousal in women contrasts findings in the male sexual psychophysiology literature that generally indicate a high concordance between erectile responding and self-reported arousal. This has many implications for the treatment of Female Sexual Arousal Disorder (FSAD) and also draws into question the wisdom of the current DSM-IV-TR definition of FSAD which focuses exclusively on a physiological, or lack thereof, genital response.

Explanations to account for the high variability in concordance rates in women include: an inability for women to detect subtle changes in vaginal blood flow, negative affect induced by erotic films, and demand characteristics associated with women's reluctance to report being aroused. Findings from research conducted in my lab and others that have tested these hypotheses indicate these explanations can only partially account for the desynchrony between responses in women (for review, see Meston, 2000). Much of my current research interest deals with understanding what accounts for this desynchrony, and what role, if any, it plays in sexual disorders.

We (Rellini, McCall, Randall, & Meston, 2005) tested the hypothesis that the lack of concordance between measures of women's sexual arousal relates, at least in part, to the data handling and statistical analyses used in past studies to assess the association between physiological and subjective sexual arousal. Past studies of this nature, including those conducted in my laboratory, have sampled numerous VPA data points and correlated an average of these points with a single Likert-scale subjective arousal data point or a mean composite of several Likert-scale questions. In doing so, the richness of the data is reduced, and how changes in one measure may be associated with changes in the other measure cannot be assessed. Also, the majority of previous studies of this nature have computed correlations based on within-participants repeated measures which provide meaningful information on individual participants but do not allow for assessment of the overall group or between group differences. With regard to analyses based on ANOVA techniques, the large between-subjects variance that characterizes VPA data violates the repeated measures ANOVA assumption of equal variance and covariance of the data at different points in time.

I proposed that a more appropriate way to analyze these relationships is to continuously and simultaneously measure the two variables throughout exposure to the films and to use hierarchical linear modeling (HLM) for the statistical analysis. To this end I, with the assistance of graduate students, developed a device termed the "arousometer" which allows for the continuous sampling of subjective arousal during stimulus presentation. Using the arousometer and HLM to assess the relation between genital and continuous measures of sexual arousal, we reported significant relations between genital and subjective sexual arousal in sexually healthy women. In a second study (Meston, Rellini, & McCall, in press) we used this methodology to examine these relations in women with and without sexual dysfunction. Relations between subjective and physiological measures of sexual arousal were significantly weaker among women with FSAD than sexually healthy women.

I intend to follow-up these findings with studies that examine whether concordance (or lack of concordance) between psychological and physiological arousal in women is mediated by factors such as the level of genital engorgement a woman experiences during sexual arousal, the degree to which a woman attends to genital cues during arousal, and the significance a woman attributes to genital cues in her overall experience of feeling sexually aroused. I am currently analyzing data from one of my large treatment outcome studies to help reveal whether enhancing the correspondence between genital and subjective sexual arousal can impact a woman's overall sexual well-being.

IV. CLINICAL TREATMENT OUTCOME STUDIES FOR FEMALE SEXUAL DYSFUNCTION

In addition to being a key investigator in several industry-sponsored FDA Phase III clinical trials for the pharmacological treatment of FSAD, over the past several years I have completed three large, independent treatment outcome studies for female sexual dysfunction, and am currently in the process of conducting two additional studies. They are as follows:

L-arginine Glutamate Plus Yohimbine for Female Sexual Arousal Disorder in Post-menopausal women

Nitric oxide plays an essential role in male erection. A role for nitric oxide as a vasodilator in clitoral and vaginal smooth muscle relaxation has been suggested. To examine the potential influence of exogenously administered nitric oxide on women's sexual arousal, we (Meston & Worcel, 2002) conducted a double-blind, placebo-controlled study which examined the effects of oral administration of the nitric oxide-precursor L-arginine, in combination with the alpha₂ blocker yohimbine, on subjective and physiological responses to erotic stimuli in postmenopausal women with Female Sexual Arousal Disorder. The combined oral administration of L-arginine glutamate and yohimbine induced a rapid and significant increase in vaginal pulse amplitude (VPA) response to the erotic film

at 60 min post drug administration compared with placebo. This finding has implications for deriving new pharmacological approaches to the management of FSAD in post-menopausal women.

Ephedrine for SSRI-induced Sexual Dysfunction

Several reviews have documented a high incidence of sexual side effects secondary to antidepressant treatment (e.g., Meston & Gorzalka, 1992). Although the precise mechanism of action by which antidepressants influence sexual function is unknown, central and/or peripheral serotonergic and adrenergic systems have been implicated most frequently. To date, there are no effective treatments for counteracting SSRI-induced sexual dysfunction. Clinicians have occasionally prescribed centrally acting antiserotonergic drugs that have been somewhat successful in reversing the SSRI-induced side effects but have also negatively impacted the therapeutic gains of the SSRIs. This casts doubt on the clinical utility of using centrally acting antiserotonergic drugs as antidotes for antidepressant-induced sexual dysfunction. In an effort to examine whether targeting peripheral mechanisms may be a more viable approach, I (Meston, 2004) conducted an 8 week, randomized, double-blind, placebo-controlled, cross-over study examining the effects of ephedrine, an alpha- and beta-adrenergic agonist that increases peripheral SNS activity, on sexual outcome measures in women who were receiving fluoxetine, sertraline, or paroxetine treatment and experiencing SSRI-induced sexual dysfunction. This study was based on an earlier study I conducted showing ephedrine significantly enhanced physiological sexual arousal in sexually functional women (Meston & Heiman, 1998). There were significant improvements relative to baseline in sexual desire and orgasm intensity/pleasure on 50mg ephedrine one hour prior to sexual activity. However, significant improvements in these measures, as well as in sexual arousal and orgasmic ability, were also noted with placebo.

Gingko Biloba Extract for Female Sexual Arousal Disorder

Gingko biloba extract (GBE), a naturally occurring substance from the Chinese Gingko tree, facilitates blood flow, influences nitric oxide systems and has a relaxant effect on smooth muscle tissue. These processes are integral to the female sexual response and, hence, it is feasible that GBE may enhance women's sexual response. To examine this hypothesis, I was funded by the *National Center for Complementary and Alternative Medicine* to provide a five-year, comprehensive examination of the potential effectiveness of using GBE to treat sexual desire, arousal, and orgasm difficulties in women. The acute effects of GBE on subjective and physiological sexual arousal were examined in 99 women with DSM-IV-TR diagnosed sexual dysfunction using a double-blind protocol in which the women received either 300mg GBE or placebo 90 min prior to viewing neutral and erotic film stimuli. A single dose of GBE significantly increased physiological, but not subjective levels of sexual arousal to erotic videos compared to placebo. The chronic effects of GBE on sexual function were assessed by randomly assigning participants to 8 weeks of either GBE, Placebo, Sex Therapy, or Sex Therapy plus GBE, and comparing sexual outcome measures at 4 weeks (Mid-Treatment), and 8 weeks (Post-Treatment). When combined with sex therapy, but not alone, 8 weeks daily treatment with 300mg GBE significantly increased sexual desire and contentment beyond placebo. Sex therapy alone significantly enhanced orgasm function versus placebo. Chronic GBE did not significantly enhance arousal beyond placebo (Meston, Rellini, & Telch, 2007).

A Treatment-Outcome Study for Sexually Dysfunctional Women with a History of Childhood Sexual Abuse (CSA)

Findings from numerous studies indicate that a history of CSA is associated with the tendency to engage in high-risk sexual behaviors and to experience a number of psychological disturbances known to adversely impact intimate relationships and sexual function. Despite these well-substantiated findings, little research has examined the mechanisms by which these detrimental

effects occur and/or are maintained in adulthood. I was funded by *The National Institute of Child Health and Human Development* to conduct a five-year investigation to help elucidate these processes. The study had two primary goals. The first goal was to explore the mediational role of schemas in the relation between CSA and adverse relational and sexual consequences in adulthood. Women with (n = 150) and without (n = 150) a history of CSA wrote a neutral essay as a control for writing style and an essay that serves as a proxy for intimacy schemas. Information on schemas was derived from conducting human-aided content analyses and computer-aided language analyses of the essays. The degree to which psychological variables, abuse variables (e.g., age at abuse, time since abuse), and physiological reactivity (heart rate variability, cortisol) serve as risk factors in the relation between CSA and outcome measures was being examined.

The second goal of this investigation was to examine whether a writing intervention that focuses specifically on intimacy themes would impact relational and sexual adjustment among women with a history of CSA. Pennebaker and associates have found that writing about emotionally relevant themes causes beneficial changes in numerous psychological, behavioral and physiological indices. To date, no studies have examined the impact of a writing intervention on relationship-relevant variables in women with a history of CSA. To accomplish this goal, 160 women with a history of CSA and sexual dysfunction were randomly assigned to one of three conditions, 1) writing about time management (control), 2) writing about a past traumatic experience, and 3) writing about relational-relevant schemas. Assessments were conducted at 1-month, 3- months, and 6-months following the writing intervention to examine the impact of the three writing interventions on relational and sexuality variables. The findings from this investigation have important implications for understanding the mechanisms that link CSA with detrimental intimacy/sexual factors in adulthood and may help develop effective and cost-efficient treatments for sexually dysfunctional women with a history of CSA.

The Role of Placebo in the Treatment of Female Sexual Dysfunction

Based on prior findings in the literature and on an analysis of the raw data from two previous clinical trials, in a recent manuscript we (Bradford & Meston, 2007) concluded that placebo responses in the treatment of women's sexual concerns are robust and may be related to participant-level variables such as age and length of relationship. There is also preliminary evidence to suggest that relationship changes might mediate or moderate improvements in sexual function during placebo treatment. Given placebo treatment elicited significant clinical responses among a large number of treatment-seeking women, examining placebo responses in the treatment of women's sexual problems may hold promise for understanding mechanisms of clinical change. Although from a conventional clinical trial perspective placebo responses are considered "noise" to be minimized or controlled, this outlook assumes – with little justification – that changes attributable to placebo and changes attributable to active treatment represent distinct underlying processes. There is likely some degree of overlap in the processes of change between active treatment and placebo groups in most pharmacological trials, as the study procedures responsible for placebo effects are necessarily imbedded in the active treatment. For example, enrolling and participating in a clinical trial is not a uniform experience for all persons but rather an event shaped by experience, expectancies, motives for treatment, and interpersonal dynamics between the participant and the investigator. Clinical trial procedures that are not components of the "active" treatment may implicitly facilitate the process of change (e.g., by offering hope, by giving meaning to the participant's symptoms, by asking the participant to attend more closely to changes in symptoms). Moreover, clinical trials focusing on sexual function are likely to affect not only the treatment-seeking person but also the sexual partner. The reactions of the partner and of the couple system to clinical trial procedures have received little study in clinical research on individual treatments for sexual problems in women. We (Bradford & Meston) have

examined the influence of some of these contextual factors in the absence of the active treatment itself in an effort to provide a more complete picture of the true “ingredients” of an efficacious treatment.