Inhibition of Subjective and Physiological Sexual Arousal in Women by Clonidine

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Objective: The present investigation was designed to provide the first empirical examination of the effects of clonidine, a selective α_2-adrenergic agonist, on sexual arousal in women with and without prior sympathetic nervous system (SNS) stimulation by exercise. The purpose was to help elucidate the influence of adrenergic mechanisms on sexual function in women. **Methods:** Thirty sexually functional women participated in two experimental sessions in which subjective (self-report) and physiological (vaginal photoplethysmograph) sexual responses to erotic stimuli were measured after either clonidine (0.2 mg) or placebo administration in a randomized, double-blind, crossover protocol. Before viewing the experimental films, 15 subjects engaged in 20 minutes of intense exercise designed to elicit significant SNS activation. **Results:** Clonidine significantly decreased vaginal pulse amplitude, vaginal blood volume, and subjective sexual responses to the erotic films in subjects who were in a state of heightened (via exercise), but not baseline (no exercise) SNS arousal. **Conclusions:** Clonidine can significantly inhibit subjective and physiological sexual arousal in women. These findings have implications for deriving an etiological theory of sexual function in women and for understanding the effects of psychotherapeutic drugs on female sexual function.

Key words: α-adrenergic, clonidine, sexual arousal, photoplethysmography, exercise.

INTRODUCTION

An understanding of the adrenergic control of sexual function in women has lagged considerably behind that of men (1–4). In fact, assertions regarding adrenergic influences on female sexuality are based primarily on analogies to men, which have equated the male erectile response with the female vasocongestive response and the male ejaculatory response with female orgasm. With regard to animal research, one explanation for the relative paucity of studies conducted in females is that fewer parallels can be drawn between the sexual responses of female rats and women than between the sexual responses of male rats and men. In male rats, behavioral indices of initiation, maintenance, efficiency, ejaculatory threshold, and reinitiating mating after ejaculation may be generalized to interest, arousal, orgasm, and refractory stages of the human sexual response. In females, however, indices of proceptive (eg, ear wiggling, hopping) and rejection (eg, kicking, vocalization) behaviors all reflect sexual interest or motivation. Limited research suggests that sexual interest in the female rat is inhibited by α_2-adrenergic agonists clonidine and naphazoline and, to some extent, this effect seems to be peripherally mediated (5). Lordosis behavior, a spinal reflex in response to a male's attempt to mate, is the most frequently studied sexual behavior in female mammals but it is uncertain exactly what stage of sexual responding this corresponds to in human females. Moreover, interpretation of studies that have examined the influence of adrenergic influences on lordosis behavior are complicated by the fact that agonists such as clonidine have been shown to both increase and decrease lordosis behavior depending on which species (ie, guinea pig (6) vs rat (5)) of animal is being studied. Hence, in contrast to male sexual function, animal models tell us little about the influence of adrenergic mechanisms on the arousal and orgasm stages of female sexual responding.

Of the few studies that have examined the influence of adrenergic mechanisms on sexual function in human females, interpretation of results is complicated by the almost exclusive reliance on subjective measures of sexual function. Charny and Heninger (7) reported that single oral doses of the selective α_2-antagonist yohimbine (30 mg) had no apparent influence on subjective reports of sexual desire or vaginal lubrication, and Hodge et al. (8) found that the α_1-antagonist prazosin had no influence on subjective ratings of sexual desire or orgasm among 15 women with mild hypertension and normal sexual function. The α_1-adrenergic antagonist labetalol (100 mg) has been shown to decrease subjective reports of vaginal lubrication compared with

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placebo (9), but to have no effect on genital secretions when measured gravimetrically (10). Labetalol has also been reported to cause a dose-dependent delay in subjective reports of orgasm with masturbation (10). The only study to date that has examined the effects of adrenergic agonists on female sexual function (8) found that clonidine had no significant influence on subjective ratings of sexual desire or orgasm among hypertensive women.

The present investigation provides the first empirical examination of the effects of α-adrenergic activity, via clonidine administration, on self-report and vaginal photoplethysmograph indices of sexual arousal in women. Clonidine was chosen to assess adrenergic activity because of its selectivity to the α_2 receptor—an adrenergic receptor that has been long implicated in male sexual function (1–4). Clonidine was also chosen because of its common use in the treatment of hypertension, and because anecdotal reports have linked clonidine to impaired sexual function in women (11, 12). The study was conducted using a randomized, double-blind, placebo-controlled, crossover design in which subjective and physiological sexual arousal to erotic stimuli were measured in each individual after clonidine and placebo administration. Because Meston and Gorzalka (13) recently found that disturbances in sexual function may become apparent only under conditions of increased nervous system arousal, the effects of clonidine on sexual arousal were measured in half ($N = 15$) of the subjects after nervous system activation via acute exercise. The purpose of the present investigation was to help elucidate the influence of adrenergic mechanisms on sexual function in women, and to gain insight into the effects of antihypertensive medications on female sexual responding.

METHOD

Subjects

Thirty sexually functional women (mean age 25.0 years, range 18–42) participated in one of two experimental conditions, Increased sympathetic nervous system (SNS) or Baseline SNS arousal. The subjects were recruited via advertisements in the university and local municipal newspapers. Because of reported ethnic and racial differences in sexual activity (14), subject background information was recorded. Racial background of the subjects was: Caucasian (27), Southeast Asian (2), and African (1). All subjects were currently involved in sexual relationships; one subject was married. Initial telephone screening criteria were: between the ages of 18 and 45 years, no use of medications known to affect vascular or sexual functioning, no history of treatment for sexual dysfunction, no medical condition that may put the subject at risk when exercising, no history of high or low blood pressure, and current involvement in a heterosexual relationship. Additional inclusion criteria, based on subject information from the Derogatis Sexual Functioning Inventory (DSFI) (15), the Orgasmic Functioning Questionnaire (OFQ) (16), a brief medical history questionnaire, the Physical Readiness Exam for Fitness Test (developed by the British Columbia Ministry of Health), and a general cardiovascular examination included: absence of general psychopathology, absence of sexual dysfunction, absence of anorgasmia, within the normative range of sexual experience, no history of heart disease or cardiovascular dysfunction, no history of dizzy spells or "light-headedness," and no bone or joint problem that might be aggravated by 20 minutes of cycling.

Profile descriptions of all subjects were obtained via the DSFI and the OFQ. The DSFI is a standardized self-report inventory composed of 10 distinct subtests designed to measure current levels of sexual functioning. The Sexual Functioning Index (SFI), and the Drive subscale of the DSFI were used to screen for absence of sexual dysfunction. All subjects employed in the study scored at or above 30th percentile (ie, within 2 SDs of the normative mean) on the SFI (mean 51.36, range 30–74) and the Drive subscale (mean 55.26, range 36–72). In addition, the Brief Symptom Inventory (BSI)(17) subtest of the DSFI was used to screen for absence of general psychopathology. The BSI is a distinct psychometric diagnostic instrument, empirically validated as an independent measure of psychopathology. All subjects employed in the study scored at or above the 30th percentile on the BSI (mean 44.70, range 30–75). Data from the Experience subtest of the DSFI were used to ensure that all subjects were within the normative range of sexual experience. All subjects scored at or above the 30th percentile on the Experience subtest (mean 50.40, range 30–63). As in previous studies (18, 19), data from the OFQ were used to screen for absence of orgasmic dysfunction. The OFQ is a self-report inventory of one's ability to achieve orgasm in response to a wide variety of sexual activities. All subjects employed in the study were able to achieve orgasm by some means (eg, intercourse, oral sex, masturbation) on at least 50% of the attempted trials (mean per cent = 93).

Two subjects were eliminated from the study because they scored below the cutoff criterion for general psychopathology, one subject was eliminated because she scored below the cutoff criterion for sexual experience, and two subjects were eliminated because they did not pass the general cardiovascular examination. Data for two subjects were eliminated because of technical difficulties that may have influenced the results. Thirty subjects met all inclusion criteria and served as subjects in the study.

Design and Procedure

Fifteen subjects participated in the Increased SNS condition and 15 subjects participated in the Baseline SNS condition. The Increased SNS and Baseline SNS condition each consisted of three sessions: a 2-hour orientation screening and questionnaire session, a 2-hour clonidine experimental session, and a 2-hour placebo experimental session. Order of the experimental sessions, Clonidine and Placebo, was counterbalanced across subjects (in both conditions, seven subjects received the Placebo session before the Clonidine session). The experimental sessions were scheduled at approximately 1-week intervals and excluded times during which the subjects were menstruating. Phase of the menstrual cycle was not controlled for, given that sexual arousability to erotic stimuli is only minimally, if at all, influenced by the menstrual cycle (20). To control for daily circadian fluctuations, subjects were scheduled at approximately the same time during

both sessions (ie, either morning, afternoon, or evening). All subjects were asked to abstain from psychoactive drugs (including caffeine and alcohol) and to refrain from engaging in any strenuous physical activity for 24 hours before each experimental session. Because rate of drug absorption may be influenced by food in the stomach, subjects were also asked to refrain from eating for 4 hours before the experimental sessions.

During the orientation screening and questionnaire session, subjects were shown the laboratory facilities and equipment, were informed of the experimental procedures and the reported side effects of clonidine, and were encouraged to ask any questions relating to the experiment. Subjects who agreed to participate in the study signed a written consent form and completed a brief medical history questionnaire designed to screen for subjects with cardiovascular dysfunction, and the Physical Readiness Exam for Fitness Test (developed by the British Columbia Ministry of Health), which is designed to identify subjects who would be put at risk when exercising. Subjects whose medical histories indicated that they would not be put at risk either when exercising or taking clonidine were then given a cardiovascular examination by a fourth-year medical student from the Faculty of Medicine, University of British Columbia. This examination included supine and standing blood pressure, peripheral pulses, and cardiac and chest examination. Subjects who were not considered at risk either when exercising or taking clonidine completed the DSFI and OFQ in a private room and then began one of the two experimental sessions.

During the experimental sessions for both the Increased SNS and Baseline SNS conditions, subjects were given either a placebo (icing sugar) or clonidine (0.2 mg) (mixed with icing sugar) capsule. Both capsules were taken orally with 250 ml of water. Both the subject and the experimenter were blinded to the session in which the subject received the placebo or clonidine. Subjects' heart rates and blood pressure were monitored using an oscillometric electronic digital blood pressure and pulse monitor (Omron Healthcare Inc., Vernon Hill, IL) 10 minutes before drug administration and every 15 minutes for 60 minutes after the drug had been ingested. Both systolic and diastolic blood pressure measures were taken. The 1-hour waiting period after drug administration was used to ensure that clonidine had been absorbed into the circulation.

Baseline SNS Condition. After the 1-hour waiting period, during both the Clonidine and Placebo experimental sessions, subjects entered a private, internally locked room inside the Sexual Psychophysiology Laboratory at the University of British Columbia. They were told that, when the experimenter left the room, they were to sit in the chair and insert the photoplethysmograph so as to allow approximately a 2.5-cm distance between the end of the probe and the vaginal opening. They were also asked to remain as still as possible throughout the session to minimize potential movement artifacts. When subjects notified the experimenter, via an intercom system, that they were ready, a 10-minute adaptation recording was taken to allow the plethysmograph time to adapt to subjects' body temperatures. After the adaptation period, subjects viewed one of two 7-minute videotaped sequences that consisted of a 1-minute display of the word "relax" followed by a 3-minute neutral travelog film and then a 3-minute erotic film. The sequences differed only in the content of the neutral and erotic films. One neutral film depicted geographic scenes from the Antarctic, and the other depicted wildlife scenes from the Antarctic. In both sequences, the erotic films depicted a nude, heterosexual couple engaging in foreplay and intercourse. The erotic films were accompanied by fast-paced music and included explicit sexual communication by the couple. The two erotic films were matched on the number, order, type, and duration of sexual acts, and included the same actors and settings. The films were identical to those used by Meston and Gorzalka (13, 18, 19). Immediately after the erotic film, subjects were asked to complete the subjective rating scale.

Increased SNS Condition. During both the Clonidine and Placebo experimental sessions, after the 1-hour waiting period, subjects engaged in 20 minutes of stationary cycling. During the first session, subjects were asked to cycle at a constant 70% of their maximum heart rate (HR). Maximum heart rate was determined using the standardized formula: HR maximum = 220 −age in years (21). Exercise at this intensity and duration has been shown to elicit significant SNS activity (22). Subjects were given continual feedback on their heart rate levels, and were asked to cycle faster or slower if their heart rate indicated they were below or above the required exertion level. Because clonidine has, in some cases, been shown to decrease heart rate responses to acute exercise (23), subjects' workload and cycle speed (rpm) were recorded during the first session, and subjects were asked to cycle at the same speed and intensity during the second exercise session. This procedure was used to ensure that subjects were exercising at equivalent intensities during the Clonidine and Placebo sessions. Subjects' fitness levels were not assessed, given that Meston and Gorzalka (18) reported no correlation between fitness levels and physiological measures of sexual arousal when subjects exercised at equivalent levels (ie, 70%) of their maximum heart rate. After exercise, subjects viewed one of the two videotaped sequences and then completed the subjective rating scale. With the exception of 20 minutes of exercise, experimental procedures for the Increased SNS and Baseline SNS conditions were identical. At the end of the second experimental session, subjects in both conditions were thoroughly debriefed, informed about the additional purposes and goals of the study, and given an opportunity to view the records of their vaginal responses. All subjects were paid $40.00 for their participation. The study design and consent forms were approved by the Clinical Screening Committee for Research and Other Studies Involving Human Subjects at the University of British Columbia.

Data Sampling and Reduction

Physiological Measurements. Physiological sexual measures were obtained using a vaginal photoplethysmograph (24). The photoplethysmograph was washed with Hibitane and sterilized by soaking in Cidex, 2% glutaraldehyde, 98% inert ingredients (long-life activated dialdehyde solution; Surgikose Canada, Peterborough, Ontario) for 10 hours between uses.

Changes in vaginal pulse amplitude (VPA), vaginal blood volume (VBV), and heart rate were monitored simultaneously during all experimental sessions. Light and heating effects were minimized by allowing the photoplethysmograph a 45-minute warm-up period before insertion, and a 10-minute adaptation period after insertion. Vaginal pulse amplitude, the AC signal, reflects short-term changes in engorgement (25). Vaginal blood volume, the DC signal, reflects slow changes in the pooling of blood in the vaginal tissue (26). Several investigators have found VPA to be a more sensitive measure of sexual arousal than VBV (13, 18, 19), to be less influenced by temperature changes (27), and to be a superior measure in terms of both convergent and divergent validity (28). Vaginal pulse amplitude was recorded throughout the entire 180 seconds of neutral film and 180 seconds of erotic film. The data were hand scored from the polygraph recordings by a research assistant who was kept blind to the

experimental manipulations. For each experimental condition, an average peak-to-peak amplitude was computed for both the neutral and erotic films by summing the amplitudes of each peak during the middle 20 seconds of the neutral or erotic film stimulus and dividing by the number of peaks per interval. Difference scores were computed for each experimental condition by subtracting the average VPA score during the neutral film from the average VPA score during the erotic film. Vaginal blood volume was sampled during the last 80 seconds of neutral film, and during the entire 180 seconds of erotic stimuli. Because there is no absolute method of calibrating VBV and hence, no zero point, the data were scored as 0.0001 mV units of blood volume deviation from a baseline reference level defined as the mean of the last 80 seconds of the neutral stimulus. The data reduction procedures used for VPA and VBV were identical to those used by Meston and Gorzalka (13, 18, 19). Shapiro-Wilks' test for normality was conducted independently on VBV and VPA scores obtained for each of the experimental sessions and conditions using SPSS for Windows, version 6.0. Results indicated that the physiological data did not significantly deviate from normality.

Heart rate and systolic and diastolic blood pressure were monitored using an oscillometric electronic digital blood pressure and pulse monitor 10 minutes before drug administration and every 15 minutes for 60 minutes after clonidine or placebo ingestion. These scores each yielded five measures for each subject per experimental condition. Heart rate during film presentations was scored from the VPA polygraph records by counting the number of beats across the entire 180 seconds of neutral and 180 seconds of erotic film. The scores were averaged across time to yield two measures (bpm) for each subject per experimental condition (one measure during each of the neutral and erotic films).

Subjective Measurements. A self-report rating scale, adapted from Heiman and Rowland (29), was used to assess subjective measures of sexual arousal (five items), autonomic arousal (five items), anxiety (one item), positive affect (11 items), and negative affect (11 items). Subjects rated each of these items, depending on the degree to which they experienced the sensations, on a 7-point Likert Scale, from *not at all* = 1 to *intensely* =7. Subjective sexual arousal was defined by the following five items on the scale: Sexually aroused, warmth in genitals, genital wetness or lubrication, genital pulsing or throbbing, and any genital feelings.

For a detailed summary of the data reduction and sampling procedures used, see Meston and Gorzalka (18).

RESULTS

Analyses of Vaginal Pulse Amplitude

Increased SNS Condition. Nonparametric analyses were conducted using Wilcoxon's matched-pairs signed rank test. Results revealed a significant increase in VPA responses with exposure to an erotic film in both the Clonidine, $z = -3.41$, $p = .0007$, and Placebo, $z = -3.41$, $p = .0007$, session. Analyses conducted on VPA difference scores between the Clonidine and Placebo sessions revealed a significant inhibitory effect of clonidine on pulse amplitude scores, $z = -2.78$, $p = .005$. Interestingly, clonidine had no significant effect on VPA responses during the neutral films but significantly decreased VPA responses during the erotic films, $z = -2.29$, $p = .022$.

Baseline SNS Condition. Results from analyses conducted using Wilcoxon's matched-pairs signed rank test indicated a significant facilitatory effect of the erotic films on VPA responses during both the Clonidine, $z = -3.11$, $p = .002$, and Placebo, $z = -3.12$, $p = .002$, sessions. Together with the VPA results from the Increased SNS condition, these findings indicate that the experimental stimuli were effective in eliciting sexual arousal. Despite the fact that clonidine decreased VPA responses to erotic stimuli among nine of 15 subjects, the influence of clonidine on VPA scores did not reach statistical significance.

Analyses Between Increased SNS and Baseline SNS Conditions. To determine whether exercise increased VPA responses to erotic stimuli as in previous research of this nature (13, 18, 19), a Mann-Whitney *U*-test for independent samples was conducted on VPA difference scores between the Placebo session of the Increased SNS condition and the Placebo session of the Baseline SNS condition. Results indicated a significant increase in VPA responses with exposure to exercise, $z = -1.68$, $p = .045$, one-tailed. Mean VPA difference scores during the Clonidine and Placebo sessions of both the Increased and Baseline SNS conditions are presented in Figure 1.

Analyses of Vaginal Blood Volume

Increased SNS Condition. Wilcoxon's matched-pairs signed rank test conducted on VBV raw scores between neutral and erotic films revealed a significant increase in VBV with exposure to an erotic film in both the Clonidine, $z = -3.29$, $p = .001$, and Placebo, $z = -3.41$, $p = .0007$, sessions. Analyses conducted on VBV deviation scores revealed a significant decrease in VBV with clonidine administration, $z = -3.41$, $p = .0007$. All 15 subjects showed a decrease in VBV responses to erotic stimuli with clonidine administration.

Baseline SNS Condition. Results of Wilcoxon's matched-pairs signed rank tests conducted on VBV raw scores between neutral and erotic films indicated significant increases in blood volume responses with exposure to an erotic film in both the Clonidine, $z = -3.24$, $p = .001$, and Placebo, $z = -3.12$, $p = .002$, sessions. Together with the VBV findings from the Increased SNS condition, these results further indicate that the experimental films were effective in eliciting sexual arousal. Results of

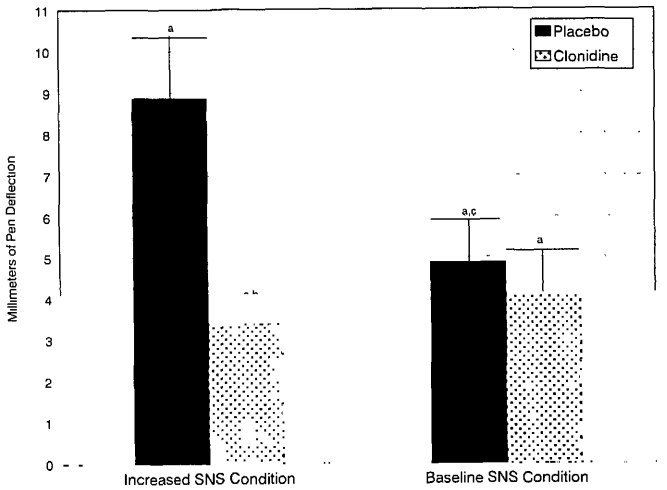

Fig. 1. Mean vaginal pulse amplitude (millimeters of pen deflection) ± SEM between neutral and erotic stimulus presentations during the Clonidine and Placebo sessions of the Increased SNS and Baseline SNS conditions. Statistically significant ($p<.05$) difference: *a*, between neutral and erotic films; *b*, between Placebo and Clonidine sessions; *c*, between Increased SNS and Baseline SNS Placebo sessions.

analyses conducted on VBV deviation scores between Clonidine and Placebo sessions revealed no significant effect of clonidine on VBV.

Analyses Between Increased SNS and Baseline SNS Conditions. To examine whether exercise facilitated VBV responses to erotic stimuli as in previous research of this nature (13, 18, 19), a Mann-Whitney *U*-test for independent samples was conducted on VBV deviation scores between the Placebo session of the Increased SNS condition and the Placebo session of the Baseline SNS condition. Results indicated a marginally significant increase in VBV responses with exposure to exercise, $z = -1.60$, $p = .055$, one-tailed. Mean VBV deviation scores during the Clonidine and Placebo sessions of the Increased and Baseline SNS conditions are presented in Figure 2.

Analyses of Heart Rate

Wilcoxon's matched-pairs signed rank tests conducted on heart rate levels revealed no significant differences between sessions before clonidine or placebo administration in either the Increased SNS or Baseline SNS condition. There were no significant effects of clonidine on heart rate levels measured every 15 minutes during the 1-hour waiting period after drug administration in either the Increased SNS or Baseline SNS condition.

Heart rate showed a marginally significant decrease with clonidine administration during both the neutral, $z = -1.90$, $p = .057$, and erotic, $z = -1.90$, $p = .057$, film presentations of the Increased SNS, but not Baseline SNS, condition. This finding is consistent with research that indicates that clonidine significantly inhibits SNS influences of exercise (30). There were no significant differences in heart rate between neutral and erotic films during either the Increased SNS or Baseline SNS condition. Mean heart rates during the Placebo neutral film, Placebo erotic film, Clonidine neutral film, and Clonidine erotic film were 82.6, 81.5, 73.8, 73.1, respectively, for the Increased SNS condition, and 64.2, 67.0, 62.3, 63.7, respectively, for the Baseline SNS condition.

To determine whether heart rate during the Increased SNS condition was influenced by exposure to exercise, Mann-Whitney *U*-tests for independent samples were conducted on heart rate between the

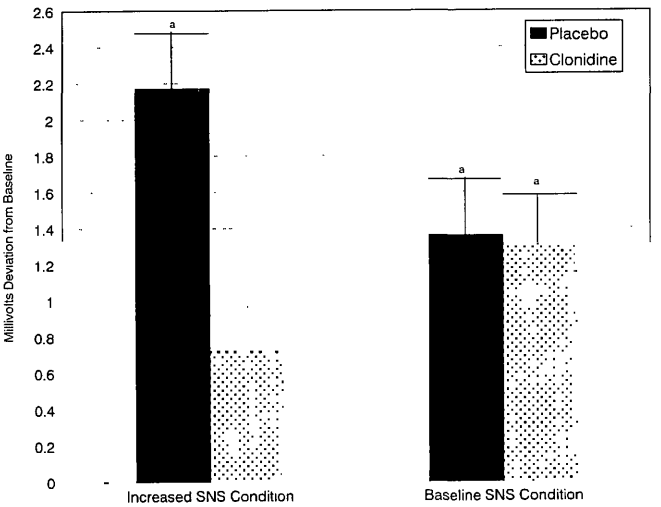

Fig. 2. Mean vaginal blood volume (millivolts deviation from baseline) ± SEM between neutral and erotic stimulus presentations during the Clonidine and Placebo sessions of the Increased SNS and Baseline SNS conditions. Statistically significant ($p<.05$) difference: *a*, between neutral and erotic films; *b*, between Placebo and Clonidine sessions.

Placebo session of the Increased SNS condition and the Placebo session of the Baseline SNS condition for each of the neutral and erotic films. Heart rate was significantly increased after exercise during both the neutral, $z = -3.38$, $p = .0007$, and erotic, $z = -2.80$, $p = .005$, film presentations. These findings provide indirect support for the effectiveness of using exercise to elicit SNS arousal.

Analyses of Blood Pressure

To examine whether blood pressure was influenced with clonidine administration during the 1-hour waiting period before film presentation, Wilcoxon's matched-pairs signed rank tests were conducted separately for systolic and diastolic measures 10 minutes before drug administration and every 15 minutes after drug ingestion. Results revealed a significant decrease in diastolic blood pressure, $z = -2.04$, $p = .041$, and a nonsignificant trend toward decreasing systolic blood pressure, $z = -1.78$, $p = .075$, at 45 minutes after clonidine administration during the Baseline SNS condition. This finding is consistent with previous research, which has noted that clonidine may decrease resting levels of systolic and diastolic blood pressure (31). There were no significant effects of clonidine on systolic or diastolic blood pressure levels during the Increased SNS condition.

Analyses of Subjective Measures

Wilcoxon's matched-pairs signed rank tests were conducted on subjective ratings of sexual arousal, positive affect, negative affect, autonomic arousal, and anxiety. Analyses indicated clonidine significantly decreased subjective ratings of sexual arousal during the Increased SNS condition, $z = -2.20$, $p = .028$, and showed a nonsignificant trend toward decreasing subjective sexual arousal in the Baseline SNS condition, $z = -1.67$, $p = .096$. There were no significant effects of clonidine on subjective ratings of positive affect, negative affect, or anxiety during either the Increased or Baseline SNS condition. Clonidine significantly decreased subjective ratings of autonomic arousal during the Baseline SNS condition only, $z = -2.17$, $p = .03$.

To examine whether exercise influenced subjective sexual arousal, a Mann-Whitney *U*-test for independent samples was conducted on subjective ratings of sexual arousal between the Placebo session during the Increased SNS condition and the Placebo session during the Baseline SNS condition. Exercise had no significant influence on subjective ratings of

sexual arousal. Mean subjective ratings are presented in Table 1.

DISCUSSION

The present investigation examined the effects of clonidine, an α_2-adrenergic agonist, on self-report and photoplethysmograph indices of sexual arousal in women. The results revealed clonidine inhibited sexual responding when subjects were in a state of heightened, but not baseline, nervous system arousal. These effects included significant decreases in VPA, VBV, and subjective self-reports. The inhibition of sexual arousal by clonidine is consistent with research conducted in males that indicates administration of α_2-adrenergic agonists impair the erectile response (1), and with animal research that indicates clonidine inhibits copulatory behavior in female rats (5). The finding that clonidine inhibited sexual responses only during the Increased SNS condition is consistent with Meston and Gorzalka's (13) recent finding that disturbances in physiological sexual arousal may become apparent only under conditions of enhanced nervous system activity. Clonidine had no significant influence on subjective measures of positive affect, negative affect, or anxiety during either experimental condition. This suggests that the decreases in sexual arousal noted during the Increased SNS condition are not likely attributable to changes in cognitive factors, such as mood, which potentially may have been altered with clonidine administration.

Because clonidine has both central and peripheral properties, it is unclear at which level clonidine acted to influence sexual responding. At a central level, clonidine may have suppressed sexual responses indirectly via changes in neurohypophyseal hormone release, or directly by activating central sites responsible for the inhibition of sexual reflexes (3). At a peripheral level, clonidine may have suppressed sexual arousal by the direct inhibition of sympathetic outflow. Support for this latter notion was provided by the finding that clonidine inhibited sexual responding only when subjects were in a state of heightened SNS activity. The fact that clonidine has been reported to significantly inhibit SNS responses to exercise (30) is consistent with the suggestion that clonidine acted to inhibit sexual responding via suppressed SNS activity.

Comparison of the sexual responses during the placebo sessions of the heightened and baseline nervous system arousal conditions allowed for examination of the effects of acute exercise on sexual responding in women. Exercise significantly increased VPA and marginally increased VBV responses to an erotic film. These findings corroborate those of Meston and Gorzalka (18, 19) where both VPA and VBV were increased by moderate levels of exercise using the same experimental protocol as that used in the present study. Previous research in women has shown that SNS activity, indexed by plasma noradrenaline and its synthetic enzyme dopamine-α-hydroxylase, increases during sexual arousal, reaches a peak during orgasm then, after orgasm, decreases rapidly to preexcitement levels (32). It is worth noting that the increase in noradrenaline levels during intercourse is in the same range as that which occurs during moderate levels of bicycle ergometric exercise (32). The finding that exercise increased vaginal indices of sexual arousal suggests that increased SNS activity may not only accompany sexual arousal in women, but may also serve to facilitate sexual responding. This assertion is, of course, highly speculative given that the present study measured SNS activity only indirectly using heart rate measures.

The finding that clonidine decreased sexual responses to erotic stimuli provides evidence of an inhibitory influence of antihypertensive drugs on physiological sexual function in women. Although drug-induced sexual dysfunction is well known to

TABLE 1. Mean[a] (± SEM) Subjective Ratings of Sexual Arousal, Autonomic Arousal, Positive Affect, Negative Affect, and Anxiety with Clonidine and Placebo Administration During the Increased SNS and Baseline SNS Conditions

Condition	Sexual	Autonomic	Positive Affect	Negative Affect	Anxiety
Increased SNS					
Clonidine	2.8 ± 0.5[b]	2.4 ± 0.4	2.4 ± 0.4	1.5 ± 0.1	1.4 ± 0.3
Placebo	3.6 ± 0.5	2.9 ± 0.4	2.7 ± 0.4	1.4 ± 0.1	1.3 ± 0.3
Baseline SNS					
Clonidine	3.1 ± 0.4	2.3 ± 0.3	2.4 ± 0.4	1.6 ± 0.1	1.3 ± 0.2
Placebo	4.1 ± 0.6	2.9 ± 0.4	3.2 ± 0.5	1.5 ± 0.1	1.7 ± 0.4

[a] Means are based on an item response format of low = 1 to intense = 7.
[b] Statistically significant difference between Clondine and Placebo sessions ($p < .05$).

occur with antihypertensive drugs in men, research on the effects of these drugs in women has been largely ignored. The paucity of research in this area is surprising given that hypertension is just as common in women as in men (33), and that reports of the incidence of sexual dysfunction among women with hypertension include estimates of up to 23% (34). The present findings have important implications for women taking antihypertensive medications, and may also help to explain the high reported incidence of inhibited sexual arousal and orgasm secondary to other psychotherapeutic drug use (35). For example, several antipsychotic medications, such as chlorpromazine, thioridazine, and trifluoperazine, have been reported to inhibit sexual arousal and orgasm in women (35), and also have been shown to have high affinities for α-adrenoreceptors (36). Given that the present study examined the effects of clonidine on sexual responding only among relatively young, healthy women, the present results may be limited in their generalizability to clinical cases of women with hypertension. Generally, females taking antihypertensive medications are of an older, postmenopausal age group than subjects in the present study. On one hand, the present findings are not confounded by the potential influences of either past medication use or hormonal changes that occur during menopause. On the other hand, however, it is uncertain whether women with abnormally high blood pressure levels would experience a similar decline in sexual responding with clonidine administration. It may be that antihypertensive drugs inhibit physiological sexual responses only when administered to persons whose blood pressure levels are not increased.

Several other limitations to the present study warrant consideration. First, because of clonidine's sedative properties, subjects in the present study were asked at the end of each session whether the drug made them feel tired or sleepy during the session. Two subjects in the Baseline SNS condition reported feeling somewhat tired after taking what was later revealed to be clonidine. Given that clonidine inhibited sexual responses only during the Increased SNS condition—the condition in which there were no reports of tiredness—it seems unlikely that sexual responses were suppressed simply due to sedation. Regardless, the potential sedative influences of clonidine on sexual responding cannot be ruled out in the present study. Future studies to examine the effects of antihypertensive drugs on sexual function would benefit from including a comprehensive checklist of sedative symptoms. Second, the present study relied exclusively on vaginal photoplethysmograph measures as indices of physiological sexual arousal. Vaginal blood volume and VPA reliably indicate enhanced blood flow into the vagina and, in this regard, reliably reflect changing levels of sexual arousal. As noted by Levin (37), however, it is unclear how the signals are to be interpreted in relation to the vessels of the vascular bed. That is, it is unknown whether vasodilation induced by sexual arousal occurs in the arteries, arterioles, capillaries, venules, or veins (38). Precise interpretation of what these measures reflect is further complicated in the present study by the fact that clonidine alters the peripheral vascular system. Future studies that use additional measures of physiological sexual arousal, such as vaginal temperature change, are needed to further understand the effects of peripherally acting drugs on sexual arousal in women.

In conclusion, the results of the present study provide the first empirical suggestion of an inhibitory influence of α_2-adrenergic activity on sexual arousal in women. Future research is needed to assess the effects of other selective adrenergic agonists and antagonists on sexual arousal and orgasm in women. An understanding of the adrenergic control of sexual function in women may help in the development of pharmacotherapeutic approaches to the management of sexual dysfunction, and aid in the development of pharmacological agents devoid of adverse sexual side effects.

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