Sympathetic Nervous System Activity and Female Sexual Arousal

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The results of a series of human and animal studies that were conducted in an effort to better understand autonomic nervous system influences on female sexual arousal are presented. The effects of sympathetic nervous system (SNS) activation on self-report and vaginal photoplethysmographic measures of sexual arousal were examined in 4 studies using intense acute exercise, and in 1 study using ephedrine, to activate the SNS. The effects of SNS inhibition on sexual responses in the female rat were examined in 3 studies using clonidine, an α_2-adrenergic agonist; guanethidine, a postganglionic noradrenergic blocker; and naphazoline, an α_2-adrenoreceptor agonist, to inhibit sympathetic outflow. In humans, the effects of SNS inhibition on subjective and physiologic sexual arousal were also examined using clonidine to suppress SNS activity. Together, the findings from these studies suggest that SNS activation may facilitate, and SNS inhibition inhibit, the early stages of sexual arousal in sexually functional women and in women with low sexual desire. ©2000 by Excerpta Medica, Inc.

"It was often said: 'The great spectacle at the circus is not the game but the spectators.' During a race the crowd literally went mad. Women collapsed or had sexual orgasms. . . . (They) stood up in the stands drumming with their fists on the back of people in the seats before them and screaming hysterically: 'Kill!, Kill!, Kill!'. Even before the games started, smart young men could spot women who would give way to this madness and make a point of sitting next to them."

—Writings about the Roman circus, 169 B.C.[1]

Little research has focused directly on understanding the neural pathways involved in the initiation and maintenance of sexual arousal in women. In men, we know that erection is primarily a parasympathetic event, and the sympathetic nervous system (SNS) mediates detumescence by inhibiting blood flow to the erectile sinus tissue. For many years it was assumed that analogous neural processes took place in women. That is, sexual arousal, characterized by increased genital blood flow, clitoral erection, and increased lubrication were thought to be parasympathetically mediated. Inconsistent with this assumption, in 1977, Hoon, Wincze, and Hoon[2] reported that vaginal blood volume (VBV) was increased when women viewed an anxiety-evoking film before an erotic film versus a neutral travel film before an erotic film. One interpretation of this finding is that SNS activity, induced by the anxiety film, facilitated rather than inhibited sexual arousal in women. Other, more direct evidence for a facilitatory influence of SNS activation on female sexual arousal comes from biochemical and physiologic research that indicates diffuse SNS discharge occurring during the later stages of sexual arousal[3] with marked increases in heart rate and blood pressure occurring during orgasm.[4] Increases in plasma noradrenaline, a sensitive index of SNS activity, have also been shown to accompany increases in sexual arousal during intercourse, and to decrease rapidly after orgasm.[5] The following studies were designed to provide the first direct examination of the effects of SNS activation and inhibition on the early stages of the female sexual response.

In the first series of studies, the effects of SNS activation on sexual arousal were examined using intense, acute exercise as a means of eliciting SNS activity. Exercise was chosen based on a large number of pharmacologic and physiologic studies that indicate that moderate-to-high intensities of exercise are accompanied by significant SNS activity.[6] A total of 35 sexually functional women, 18–34 years of age, participated in 2 counterbalanced sessions where they viewed a neutral film followed immediately by an erotic film. In one of the sessions, subjects engaged in 20 minutes of intense stationary cycling before viewing the films. Before engaging in the 2 experimental sessions, all subjects received a submaximal bicycle ergometer fitness test to estimate their maximum volume of oxygen uptake. This allowed us to set the workload and cycle speed so that all subjects exercised at a constant 70% of their maximum volume of oxygen uptake. By exercising subjects at relative versus absolute workloads, research indicates that differences in physiologic response resulting from variations in fitness levels are minimized.[7] Sexual arousal was measured subjectively using a self-report questionnaire, and physiologically by means of a vaginal photoplethysmograph.[8] Both vaginal pulse amplitude (VPA) and VBV were used as indices of sexual arousal. VPA amplitude is an immediate measure of sexual responding in women, which represents moment-to-moment changes in vasocongestion. VBV is thought to represent a more gradual pooling of blood in the vaginal tissue. Heart rate was used as an indirect indicator of SNS activation. The results showed a significant increase in both VPA and VBV responses

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to the erotic films with exercise. Heart rate was significantly increased with exercise (70 beats per minute vs 90 beats per minute); there were no significant changes in heart rate between the neutral and erotic films. There were no significant differences in sexual arousal, positive affect, or negative affect with exercise alone, which suggests that the increases in physiologic sexual arousal are not likely attributable solely to a direct feedback system between cognitive and physiologic components of the sexual response.

Because the effects of exercise on plethysmographic measures of sexual arousal had not previously been investigated, it was important to examine whether the increases in plethysmographic responses to erotic stimuli may have been the result of other potential "nonsexual" consequences of exercise or, alternatively, to the passage of time after exercise, given that the presentation of the erotic films consistently followed that of the neutral films. To examine this possibility, 10 sexually functional women, 19–34 years of age, participated in a repeated-measures design study in which they engaged in 2 counterbalanced sessions where they viewed either a neutral film followed by an erotic film, or 2 consecutive neutral films.[9] In both sessions subjects engaged in 20 minutes of stationary cycling at 70% of their maximum volume of oxygen uptake. Both VPA and VBV were significantly increased with the presentation of an erotic film, but showed no change with the presentation of a second neutral film. There were no significant differences in heart rate between the neutral–erotic or neutral–neutral films. Subjective ratings of sexual arousal and positive affect were significantly increased with exposure to the erotic versus neutral film; no differences in negative affect between films were found. The results of this experiment are important in the sense that they suggest that (1) the findings from the original study are not simply due to the passage of time after exercise; (2) the vaginal photoplethysmograph did in fact measure only the sexual consequences of exercise; and most importantly, they illustrate that (3) exercise per se does not simply increase VBV and VPA responses but, rather, exercise in the presence of an erotic stimulus somehow prepares the body for sexual arousal.

In the previous 2 studies, from the cessation of exercise to the onset of the erotic stimulus, approximately 15 minutes had passed. Although research indicates that SNS influences remain significantly elevated for approximately 30–40 minutes after intense exercise, at 15 minutes after-exercise heart rate had decreased considerably from levels during and immediately after exercise. This leads one to question whether exercise would have an even greater facilitatory influence on physiologic sexual responses if measured immediately after exercise, and whether the level of SNS activation is in some way related to the level of physiologic sexual arousal.

A total of 36 sexually functional women, 18–45 years of age, participated in a study designed identically to the original exercise study with the following exception: sexual arousal was measured at either 5 minutes, 15 minutes, or 30 minutes after exercise in an effort to examine the approximate influences of high, moderate, and low levels of SNS activation on sexual responding.[10] VPA responses were significantly decreased at 5 minutes, significantly increased at 15 minutes (a direct replication of the original study), and marginally increased at 30 minutes after exercise. VBV findings showed a similar pattern to the VPA results, but did not reach statistical significance.

When scores were standardized within conditions (due to the fact there was significantly more variability at 30 minutes after exercise), there was a curvilinear relation such that responses were decreased at 5 minutes, significantly increased at 15 minutes, and then decreased somewhere between 15–30 minutes after exercise. Heart rate was significantly increased with exercise in each of the conditions (97, 87, 80 beats per minute at 5, 15, and 30 minutes after exercise, respectively), and there were no significant effects of exercise on subjective ratings of sexual arousal or on positive or negative affect. Together, these findings suggest that there may be an optimal level of SNS activation for physiologic sexual arousal below and above which SNS activation may have less of a facilitatory influence or even an inhibitory influence on sexual responses.

In addition to creating SNS dominance, exercise at the intensity used in the above studies has been shown to cause a number of changes in hormones such as testosterone, cortisol, and prolactin. Although short-term changes in these hormones have not been shown to influence sexual arousal in women, the potential role of these hormones in the interpretation of the study findings cannot be ruled out.

In an effort to provide a more direct examination of the effects of increased peripheral adrenergic activity on sexual arousal in women, we[11] examined the effects of ephedrine, an α- and β-adrenergic agonist, on VPA responses. Twenty sexually functional women participated in 2 counterbalanced conditions in which they received either placebo or ephedrine (50 mg) using a double-blind protocol. Ephedrine significantly increased VPA responses to an erotic, but not neutral, film, and had no significant effect on subjective ratings of sexual arousal or on measures of positive or negative affect. The finding that when subjects viewed a nonsexual, travel film, there were no significant differences in VPA responses between the ephedrine and placebo conditions, suggests that ephedrine did not simply facilitate physiologic responses through a general increase in peripheral resistance but, rather, acted in some way that selectively "prepared" the body for genital response (Figure 1).

If moderate levels of SNS activation increase sexual arousal, as the previous studies suggest, one would expect drugs that decrease SNS activity might also decrease sexual arousal. To examine this possibility, we[12] conducted a series of studies that examined the influence of various drugs that decrease SNS activity on sexual responding in the female rat. The first study examined the influence of clonidine, an antihypertensive medication, on sexual responding. Clonidine acts centrally as an α_2 adrenergic agonist, and peripherally

to block sympathetic outflow. In the second and third studies, the effects of guanethidine and naphazoline on sexual responding were examined. These drugs were chosen because their mechanism of action is similar to clonidine but they do not cross the blood–brain barrier, hence their action is strictly at peripheral sites (naphazoline acts selectively at the α_2 receptor). Each study involved 15 ovariectomized female rats treated with estrogen and progesterone to induce heat, and used a repeated measures design in which the animals received either saline solution or moderate or high doses of the drug. The following 3 independent measures of sexual responding were assessed: (1) receptivity (lordosis quotient), which is the ratio of the number of spinal reflexes in response to male attempts to mate; (2) proceptivity, which is measured as the number of ear wiggles per minute; and (3) rejection behaviors, which are measured as the number of kicking, boxing, running away, and squealing behaviors in response to a male's attempt to mate.

Clonidine, guanethidine, and naphazoline all significantly suppressed lordosis responses at both moderate and high doses. Clonidine and guanethidine significantly decreased proceptive behavior at both moderate and high doses, and naphazoline significantly decreased proceptivity at moderate doses. Clonidine significantly increased the number of rejection behaviors at both moderate and high doses; guanethidine and naphazoline also increased rejection behaviors but the results did not reach significance. The fact that rejection behaviors were increased, not decreased, with these drugs is important in that it suggests that the suppression of sexual responding is not likely attributable to the potential sedative effects of these drugs given that rejection behaviors are active behavioral responses. Because guanethidine and naphazoline act to selectively inhibit peripheral sympathetic outflow without influencing adrenergic mechanisms at a central level, the results of this study suggest that inhibition of the SNS may inhibit sexual behavior in the female rat.

To examine whether SNS inhibition, via clonidine, has a similar inhibitory influence on sexual responding in human females, 2 studies were conducted that examined the effects of moderate doses of clonidine on subjective and plethysmographic indices of sexual arousal.[13] In the first study, 15 sexually functional women, ages 18–42, participated in 2 sessions in which they viewed a neutral film followed immediately by an erotic film. In one session, subjects received a placebo, and in one session they received 0.2 mg clonidine 1 hour before viewing the films. The study was conducted using a double-blind, placebo-controlled, repeated-measures protocol. The second study was conducted identically to the first except that, in both sessions, subjects engaged in 20 minutes of intense stationary cycling 1 hour after either placebo or clonidine administration, but before viewing the films.

In the first study, 9/15 and 7/15 subjects showed a decrease in VPA and VBV, respectively, with clonidine, although the results did not reach statistical significance. In the second study, however, during heightened SNS activation, there was a significant decrease in both VPA and VBV with clonidine administration during the erotic films. Heart rate was significantly decreased with clonidine during the second (heightened SNS) study only. Subjective ratings of sexual arousal were marginally decreased in the first study and significantly decreased in the second (heightened SNS) study. Because clonidine has both central and peripheral properties, it is unclear at which level clonidine acted to influence sexual responding. Centrally, 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.[14] Peripherally, clonidine may have suppressed sexual arousal by the direct inhibition of sympathetic outflow. Support for this latter notion is 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, but not hormonal, responses to exercise[15] is consistent with the suggestion that clonidine acted to inhibit sexual responding via suppressed SNS activity. The findings from this study have important implications for cardiac patients who are taking antihypertensive or other medications that have high affinities for α adrenoreceptors (Figure 2).

The following study represents the first empirical examination of the influence of SNS activation on sexual arousal in sexually dysfunctional women.[16] A total of 36 women, ages 18–45 participated in this study, which was conducted identically to the original exercise study described above. Twelve women were sexually functional, 12 experienced low sexual desire, and 12 were anorgasmic. This is the first study to examine potential differences in sexual responding between subgroups of women with sexual difficulties; previous research combined women with a variety of sexual difficulties into 1 heterogeneous experimental group. There were no significant differences in VPA or VBV responses between the subject groups during the no-exercise condition. With exercise, however, there were significant increases in VPA and VBV among sexually functional women (a further replication of the original study findings), a significant increase in VPA and VBV responses among women with low sexual desire, and a significant decrease in VPA and a nonsignificant decrease in VBV with exercise among anorgasmic subjects. Heart rate was significantly increased with exercise among all subject groups. There were no significant effects of exercise on subjective ratings of sexual arousal, positive effect, negative effect, or anxiety among any of the subject groups, and no significant differences between groups on these measures (Figure 3).

These results have both clinical and research implications. First, from a clinical standpoint, the findings are interesting in that they provide the first empirical suggestion of a difference between orgasmic and anorgasmic women in physiologic sexual responses to increased SNS activation. Anorgasmia in women has generally been attributed to either lack of sexual education, insufficient stimulation, or a variety of cognitive factors such as fear of loss of control, fear of pregnancy, religious concerns, or relationship fac-
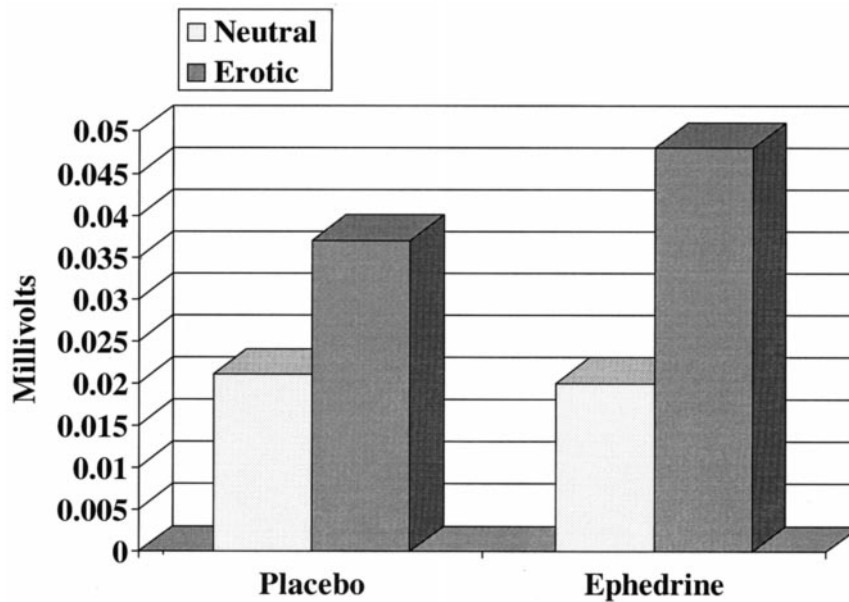
FIGURE 1. Mean vaginal pulse amplitude (millivolts) between neutral and erotic stimulus presentations during the ephedrine and placebo conditions.
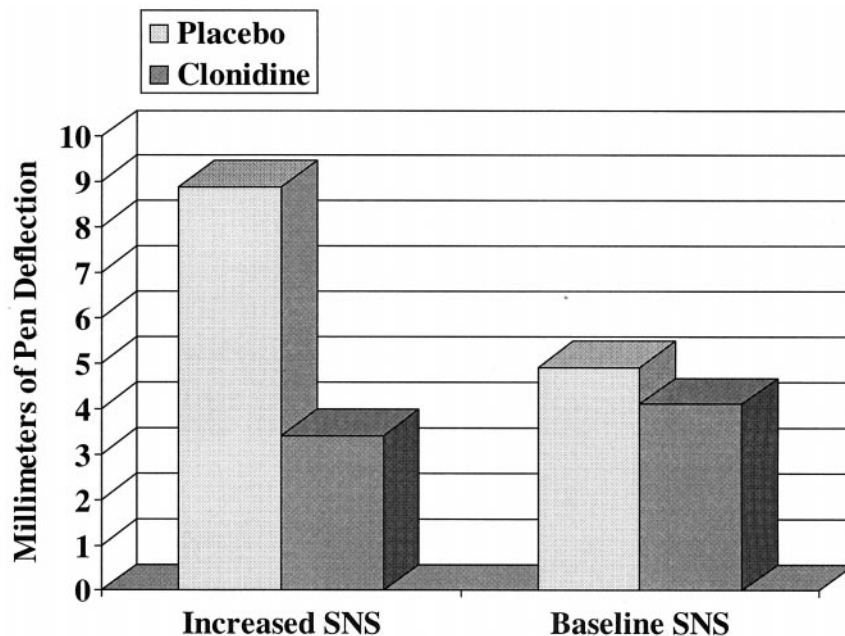

FIGURE 2. Mean vaginal pulse amplitude (millimeters of pen deflection) between neutral and erotic stimulus presentations during the clonidine and placebo sessions of the heightened sympathetic nervous system (SNS) and baseline SNS studies.

tors. This is the first study to suggest that, in addition, there may be a purely physiologic component. Second, the finding that moderate levels of SNS activation facilitated sexual arousal in women with low sexual desire has potential treatment implications. Since Wolpe's[17] introduction of systematic desensitization, anxiety-reduction techniques have been widely adopted in the treatment of sexual dysfunction. These techniques are thought to facilitate sexual responding by decreasing negative cognitions that disrupt the processing of erotic cues, and by inducing a state of relaxation that increases parasympathetic and decreases the presumably inhibitory SNS influences. With respect to the cognitive aspect of these treatments, numerous outcome studies have shown anxiety-reduction techniques to be highly successful in altering negative performance cognitions. From a purely physiologic viewpoint, however, the present results suggest that treatments that decrease SNS activity by inducing a state of relaxation may, in fact, be counterproductive to the sexual response.

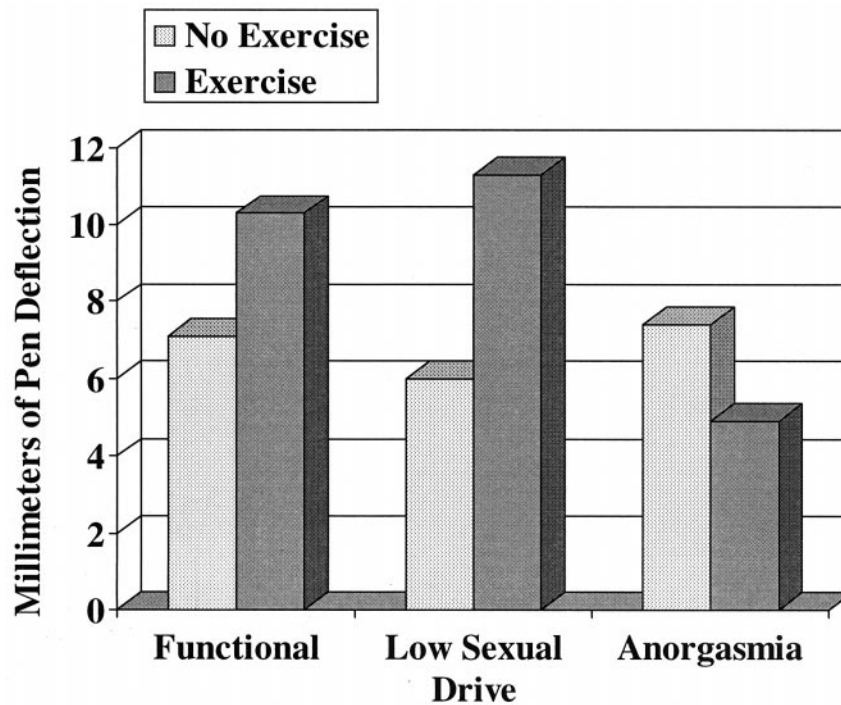The fact that differences in physiologic sexual re-

FIGURE 3. Mean vaginal pulse amplitude (millimeters of pen deflection between neutral and erotic films) responses for sexually functional, low sexual desire, and anorgasmic women during the no-exercise and exercise conditions.

sponses between orgasmic and anorgasmic women were apparent only under conditions of heightened, and not baseline, nervous system arousal, may help to explain why past research had failed to consistently note differences in VBV and VPA responses between sexually functional and dysfunctional women. Given that significant changes in autonomic arousal are believed to accompany real-life sexual activity, it is possible that differences in physiologic sexual responding between sexually functional and dysfunctional women have been disguised in laboratory settings, which induce lower levels of SNS activation. Finally, the unexpected finding that women with low sexual desire and anorgasmia differed in their physiologic sexual responses to SNS activation strongly suggests that future research on sexually dysfunctional women should consider these women as separate experimental groups. Categorization of women with a variety of sexual difficulties into 1 heterogeneous group may disguise potentially important differences in response patterns between subgroups of women with sexual difficulties.

In summary, a number of preliminary conclusions may be drawn from the findings of these studies: (1) moderate levels of SNS activation facilitate physiologic sexual arousal in sexually functional women and in women with low sexual desire; (2) there may be an optimal level of SNS activation for facilitation of sexual arousal in sexually functional women; (3) decreasing SNS activity during heightened nervous system arousal inhibits subjective and physiologic sexual arousal in sexually functional women; and (4) SNS activation has a differential influence on women with and without orgasmic difficulties.

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