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Cindy M. Meston & Julia R. Heiman

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Acute Dehydroepiandrosterone Effects on Sexual Arousal in Premenopausal Women

CINDY M. MESTON
Department of Psychology, University of Texas at Austin, Austin, Texas, USA
JULIA R. HEIMAN
Department of Psychiatry and Behavioral Sciences, University of Washington, City, State, USA

The present investigation was designed to provide the first empirical examination of the effects of acute dehydroepiandrosterone (DHEA) administration on subjective and physiological sexual arousal in women. The primary purpose was to assess whether DHEA influences vaginal blood flow response in sexually functional women. Subjective (self-report) and physiological (vaginal photoplethysmograph) sexual responses to erotic stimuli were measured following DHEA (300 mg) and placebo administration in 12 sexually functional, premenopausal women, using a single-blind protocol. Acute DHEA significantly increased blood levels of dehydroepiandrosterone sulfate (DHEA-S) 30 min following drug administration but had no significant effect on either vaginal pulse amplitude responses or subjective responses to the erotic films. Acute DHEA does not appear to substantially influence sexual responding among sexually functional, premenopausal women.

In recent years, administration of the adrenal hormone dehydroepiandrosterone (DHEA) has been linked to improvements in a variety of psychological factors, such as mood (Wolkowitz et al., 1997), energy, confidence, interest, activity levels, and in some cases memory (Bonnet & Brown, 1990). Recently, researchers and an endless number of popular self-help books have speculated that DHEA administration also might improve sexual well-being. There are several possible mechanisms by which DHEA could feasibly alter sexual functioning in women. Psychologically, DHEA could enhance sexual desire or global ratings of sexual satisfaction by altering

Address correspondence to Cindy M. Meston, Department of Psychology, University of Texas at Austin, Mezes Hall 330, Austin, TX 78712, USA. E-mail: meston@psy.utexas.edu

negative cognitive or emotional processess. This would be consistent with the findings from a study of depressed 8–16-year-olds, which noted a relationship between high cortisol/DHEA ratios, negative thoughts processes, and subsequent levels of depression (Goodyear, Herbert, & Altham, 1998). In a study of nonclinically depressed women and men ages 40 to 70, Morales, Nolan, Nelson, and Yen (1994) found that 50 mg DHEA, administered nightly for 6 months using a double blind protocol, had a beneficial effect on global ratings of psychological well-being. It did not, however, have any apparent effect on "libido." Similarly, in a large multiple regression study conducted in women ages 40 to 60, Cawood and Bancroft (1996) found that DHEA was positively related to well-being but was unrelated to any of a number of sexuality variables.

DHEA and its sulfate metabolite DHEA-S serve as precursors for testosterone and estrogen. Hormonally, then, DHEA could feasibly impact female sexual functioning by increasing levels of testosterone and estrogen, which may subsequently influence sexual desire and/or arousal processes. Although there is no absolute level of testosterone necessary for sexual desire in women, if testosterone falls below some unspecified critical threshold, as is frequently the case following menopause, oophorectomy, or adrenalectomy, levels of desire may be adversely impacted (Regan, 1999). Testosterone replacement therapy has been shown to improve sexual functioning in women with abnormally low basal testosterone levels due to oophorectomy (Sherwin & Gelfand, 1985; Sherwin, Gelfand, & Brender, 1985). Unlike testosterone, estrogen does not appear to be directly related to sexual desire in women; its role in sexual functioning appears to be more closely associated with sexual arousal. Estrogen is responsible for maintaining vaginal elasticity and lubrication and is believed to be associated with pelvic blood flow (Barbach, 1996). Decreases in vaginal lubrication and blood flow define female sexual arousal disorder, may lead to painful intercourse (and consequent decreased sexual desire), and may be associated with orgasm difficulties (Meston & Gorzalka, 1996).

The present investigation was designed to examine the effects of acute DHEA administration on physiological (vaginal pulse amplitude; VPA) and subjective measures of sexual arousal in premenopausal women. Past research has not found DHEA to be significantly linked to subjective, global ratings of sexual functioning or satisfaction. The present study represents the first empirical investigation of whether DHEA influences a physiological measure of sexual function in women and extends past research of this nature that has relied solely on self-report measures (for a review of the limitations of self-report sex data, see Meston, Heiman, Trapnell, & Paulhus, 1998). Twelve sexually functional women received both placebo and DHEA (300 mg), using a single-blind protocol. Forty-five minutes after each drug/placebo adminstration subjects viewed an erotic film. Sexual responses to the erotic film were measured subjectively using a self-report questionnaire, and physiologically using a vaginal phoroplethysmograph.

METHOD

Subjects

Twelve sexually functional premenopausal women (*M* age = 27.7 years, range = 24–34 years) participated in this investigation. The subjects were recruited via advertisements in the local and universtiy student newspapers. Initial telephone screening inclusion criteria were: ages 21–35 years; no use of any medications including birth control pills, cold, or allergy medications for at least 6 months; no history of treatment for depression, anxiety, or sexual dysfunction; no history of high or low blood pressure, thyroid disorder, diabetes, or cardiovascular problems; and current involvement in a heterosexual relationship. Further medical screening was done by a registered nurse who gave all subjects a brief cardiovascular exam at the beginning of the experimental session. All subjects were free of medication use, were in the normal range of resting heart rate and blood pressure levels, and were nonsmokers.

To screen for absence of sexual dysfunction, profile descriptions of all subjects were obtained via the Derogatis Sexual Functioning Inventory (DSFI; Derogatis, 1978). All subjects employed in the study scored greater than or equal to the 30th percentile (that is, within two *SD*s of the normative mean) on the Sexual Functioning Index (*M* = 53.00), the Drive subscale (*M* = 59.82), and the Information subscale (M = 55.91). The Brief Symptom Inventory (BSI; Derogatis, 1975) subtest of the DSFI was used to screen for absence of generaly psychopathology, and the Affect subtest of the DSFI was used to screen for absence of depression. All subjects scored greater than or equal to the 30th percentile on the BSI scale (*M* = 46.27) and the Affect subtest (*M* = 53.55). Data from the Experience subtest of the DSFT 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 (*M* = 54.09).

Design and Procedure

The study consisted of one 2½-hour experimental session. Subjects were scheduled for the experimental sessions on days when they were not menstruating. All subjects were asked to abstain from caffeine and alcohol and to refrain from engaging in any strenuous physical activity for 24 hours prior to each experimental condition. Because rate of drug absorption may be influenced by food in the stomach, subjects also were asked to refrain from eating for 4 hours prior to the experimental conditions.

During the experimental sessions subjects were first given a placebo capsule that they took orally with approximately 250 ml of water. Blood draws were taken 30 min following placebo adminstration for analyses of the DHEA sulfate metabolite, DHEA-S. All blood analyses were conducted

by SmithKline Beecham Clinical Laboratories. The results were used to validate DHEA treatment effects. Following the ½-hr waiting period, subjects were instructed on how to insert the vaginal photoplethysmograph and were asked to remain as still as possible throughout the condition in order to minimize potential movement artifacts. When the subjects notified the experimentor, via an intercom system, that they had finished inserting the plethysmograph, a 20-min baseline adaptation recording was taken in order to allow the plethysmograph time to adapt to each subject's body temperature. Following the adaptation period, subjects viewed one of two 9-min videotaped sequences that consisted of a 1-min display of the word "relax," followed by a 3-min neutral travelogue film and then a 5-min erotic film. The sequences differed only in the content of the neutral and erotic films. In both sequences, the erotic films depicted a heterosexual couple engaging in foreplay, intercourse, and oral sex. The films were previously shown to reliably elicit physiological and subjective sexual arousal in women (Meston & Heiman, 1998). Immediately following the erotic film, subjects were asked to fill out the subjective rating scale.

Subjects were then given a short break after which they took a 300-mg capsule of DHEA with approximately 250 ml of water. Blood draws were again taken 30 min following DHEA administration for DHEA-S analyses. Past research has shown that 30 min is sufficient time for DHEA to be absorbed into the blood stream and for DHEA-S to show a significant increase (Wolf et al., 1997). Subjects did not know which capsule contained placebo and which capsule contained DHEA. Following blood draws, subjects then viewed the second 9-min videotaped sequence and filled out a second subjective rating scale. Which film they viewed after placebo and DHEA administrations was counterbalanced across subjects. The time from DHEA/placebo ingestion to the onset of the erotic film was approximately 45 min (½-hr waiting period, 10-min baseline, 1-min insertion of the plethysmorgraph, 1-min display of the word "relax," 3-min neutral film). All subjects were paid $50.00 for their participation. The study was approved by the Human Subjects Ethics Committee at the University of Washington, and all subjects gave written consent.

DATA SAMPLING AND REDUCTION

Physiological Measurements

VPA responses were measured using a vaginal photoplethysmograph (Sintchak & Geer, 1975; Behavioral Technology, Inc., Salt Lake City, UT). A sampling rate of 60 samples/s was used for VPA throughout the entire 180 s of neutral film and 300 s of erotic film. The signal was band-pass filtered (0.5–30 Hz) and recorded on a Power Macintosh 6100/60 computer using the software program AcqKnowledge III, Version 3.2 (BIOPAC Systems, Inc., Santa Bar-

bara, CA) and a Model MP 100WS data acquisition unit (BIOPAC Systems, Inc.) for analog/digitial conversion. In accordance with previous studies of this nature (for example, Meston & Heiman, 1998), artifacts caused by movement or contractions of the pelvic muscles were deleted using the computer software program following visual inspection of the data. VPA scores were then computed for both the neutral and erotic films by averaging across the entire 3 min of the neutral and 5 min of the erotic film sequences.

Subjective Measurements

Perceptions of genital change (6 items), autonomic arousal (5 items), anxiety (1 item), positive affect (11 items), and negative affect (11 items) were assessed using a self-report rating scale (Heiman & Rowland, 1983). Immediately following the erotic films, subjects rated, on a 7-point Likert Scale, the degree to which they experienced these sensations, from not at all (1) to intensely (7). Subjective sexual arousal was defined by the following six items on the scale: Warmth in genitals, genital wetness or lubrication, genital pulsing or throbbing, any genital feelings, genital tenseness or tightness, and physical sexual arousal.

Statistical Analysis

A Condition × Film repeated measures analysis of variance (ANOVA) was used to examine the effects of DHEA in comparison with placebo on VPA scores during neutral and erotic films. Planned, paired-samples *t*-tests were conducted on VPA scores between the DHEA and placebo conditions during each of the neutral and erotic film presentations and on subjective ratings of physical sexual arousal, mental sexual arousal, positive affect, negative affect, heart rate, and anxiety between the placebo and ephedrin conditions. An alpha of $p < .05$ is considered statistically reliable for all analyses with the exception of analyses of subjective measures in which a more conservative alpha of .008 ($p < .05/6$) was used.

RESULTS

Blood Analyses of DHEA-S

Paired-samples *t*-tests were conducted on DHEA-S blood assays taken 30 min following placebo and DHEA administrations. There was a significant increased in DHEA-S levels following DHEA administration, $t(11) = -2.09$, $p = .03$, one-tailed. Mean (+/– *SD*) DHEA-S levels 30 min after placebo and DHEA ingestion were 2.63 (1.60) and 2.93 (1.65), respectively. This finding suggests that DHEA had been metabolized by the time sexual arousal was measured.

Analyses of Vaginal Pulse Amplitude (VPA)

Results of the Condition (DHEA versus placebo) × Film (neutral versus erotic) ANOVA revealed a significant effect of film on VPA scores, $F(1, 11) = 49.36$, $p < .001$. This indicates that the experimental stimuli were effective in eliciting sexual arousal. There was no significant effect of condition on VPA scores, $F(1, 11) = 1.81$, $p = .21$, and no significant interaction between condition and film, $F(1, 11) = 1.96$, $p. = .19$. Planned t-tests revealed a nonsignificant trend toward increased VPA scores with DHEA administration during the erotic films, $t(11) = -1.48$, $p = .08$, one-tailed. Five subjects showed an increase with DHEA administration, six showed a decrease, and one showed no change. Visual inspection of the data did not reveal any apparent link between those persons who showed an increase in VPA with DHEA administration and blood levels of DHEA, age, or weight. The small sample size used in the present investigation precluded formal statistical evaluation of these relations. There was no significant difference in VPA scores between DHEA and placebo conditions during the neutral films, $t(11) = -0.67$, $p = .26$, one-tailed. Mean VPA raw scores measured in millivolts (+/– *SD*) during the neutral and erotic films following placebo and DHEA administration were 3.01 (4.71), 3.73 (5.75), 3.11 (4.68), 4.16 (8.95), respectively.

Analysis of Subjective Measures

There was a trend toward higher levels of negative affect with placebo versus DHEA administration, $t(11) = 2.45$, $p = .03$. There were no significant effects of DHEA on subjective perceptions of genital change, $t(11) = .077$, $p = .46$, autonomic arousal, $t(11) = 2.06$, $p = .06$, positive affect, $t(11) = 0.60$, $p = .56$, or anxiety, $t(11) = 1.00$, $p = .34$.

COMMENT

Animal studies as well as recent reports of improvements in a number of psychological domains have supported the hypothesis that DHEA enhances sexual functioning. Results from the present investigation do not support this notion. A single administration of 300 mg of DHEA had no significant effect on either physiological or subjective measures of sexual arousal. Increased plasma concentrations of the DHEA sulfate metabolite DHEA-S at 30 min post-DHEA ingestion assured that the exogenous DHEA was absorbed into the blood and was endrocrinologically active during the testing of sexual responding.

The failure of DHEA to enhance sexual responding is consistent with past research that indicated that chronic (i.e., 3 months) DHEA had no noticeable effect on self-reported "libido" (Morales, Nolan, Nelson, & Yen, 1994) and with research that found DHEA levels to be unrelated to a variety of self-

report sexuality variables (Cawood & Bancroft, 1996). Together, these findings raise serious doubts about an enhancing effect of this adrenal steroid on sexual functioning. It remains open whether the present observations after a single administration of DHEA in premenopausal women would also apply to effects of longer-term replacement in postmenopausal women. It is well known that levels of DHEA and DHEA-S decrease monotonically with age from about 20 years of age until the end of the life span (Orentreich, Brind, Rizer, & Vogenman, 1984). It may be the case that DHEA administration facilitates sexual responding only in those women with decreased baseline levels of this hormone or in women who meet clinical criteria for specific sexual dysfunctions. This would be consistent with findings from other domains that suggest, for example, that acute DHEA facilitates mood and memory performance in elderly depressed individuals (Wolkowitz et al., 1997) but has no effect on such measures in young, healthy adults (Wolf et al., 1997). It is consistent with research that indicates testosterone replacement therapy improves sexual functioning in women with decreased testosterone levels due to menopause or oophorectomy (Sherwin & Gelfand, 1985; Sherwin, Gelfand, & Brender, 1985) but has not noticeable effect on women with unchallenged testosterone levels (Dow & Gallagher, 1989). It also should be noted that although DHEA-S levels were significantly elevated at 30 min post-drug ingestion, it may be the case that when sexual arousal was measured at 45 min post-drug ingestion, blood levels of DHEA-S were not high enough to have impacted genital blood flow measures. Future research is needed to examine potential time course effects of DHEA on sexual arousal as well as the effects of both acute and chronic DHEA administration on physiological and subjective sexual responses in postmenopausal women.

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