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The effect of dehydroepiandrosterone (DHEA) on recognition memory decision processes and discrimination in postmenopausal women

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In this article, the theoretical distinction between recognition memory decision and discrimination processes is used to explore the effect of dehydroepiandrosterone (DHEA) in postmenopausal women. DHEA is an adrenal steroid that diminishes with aging. It has enhanced memory in laboratory animals. An 8-week placebo-controlled, double-blind experiment in which 30 women (ages 39–70) received a 50-mg/day oral dose of DHEA for 4 weeks demonstrated that DHEA made subjects more conservative (i.e., less likely to call test items "old") in their recognition memory decisions and enhanced recognition memory discrimination for items presented briefly. The former result may reflect an empirical regularity (Hirshman, 1995) in which *recent* strong memory experiences make participants more conservative. The latter result may reflect the effect of DHEA on visual perception, with consequent effects on memory. These results suggest the methodological importance of focusing on decision processes when examining the effects of hormones on memory.

Aging impairs a broad range of cognitive functions (Salthouse, 1993). Studies of cognitive aging (e.g., N. Anderson, Craik, & Naveh-Benjamin, 1998) have attempted to identify the underlying theoretical mechanisms contributing to these deficits. This article follows in this tradition, applying constructs derived from signal detection theory (Green & Swets, 1966) to the study of memory in postmenopausal women. Specifically, our experiment examines how administration of the adrenal steroid dehydroepiandrosterone (DHEA) affects recognition memory decision processes and discrimination in postmenopausal women.

General Properties of DHEA

DHEA is a steroid hormone secreted by the adrenal cortex. It is synthesized from pregnenolone, which is also a precursor of cortisol, progesterone, and various mineralocorticoids (Kroboth, Salek, Pittenger, Fabian, & Frye, 1999). DHEA is normally secreted synchronously with cortisol in response to corticotrophin-releasing factor (CRH) and adrenal corticotrophin-releasing hormone (ACTH; Pavlov, Harman, Chrousos, Lorieux, & Blackman, 1986; Rosenfeld et al., 1971). Consistent with this mechanism, serum concentrations of DHEA can vary substantially over brief periods (e.g., 2 h; Kroboth et al., 1998). A second factor that may contribute to variation in serum levels of DHEA is its rapid metabolic clearance rate (Longcope, Bourget, & Flood, 1982).

DHEA can be metabolized to a sulfated version, DHEAS, which is the most abundant circulating steroid hormone in humans, as well as to androgens, such as testosterone and androstenedione (Regelson, Loria, & Kalimi, 1994). These androgens, in turn, can be metabolized to estrogens, making DHEA a precursor to estrogens as well as to androgens (Mortola & Yen, 1990).

Two factors have motivated scientific interest in the biological functions of DHEA. First, its high metabolic clearance rate and broad distribution in plasma, saliva,

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cerebrospinal fluid, liver, kidney, and brain indicate that it is a biologically active and functionally important hormone (Barrou, Charru, & Lidy, 1997). Second, aging has large effects on DHEA levels. The secretion of DHEA in response to administration of ACTH diminishes substantially with age, even though secretion of cortisol, another product of the adrenal cortex, remains approximately constant in older adults (Ohashi, Kato, Nawata, & Ibayashi, 1986). Similarly, plasma concentrations of DHEA show significant decreases with age, peaking in the 20s or 30s and declining thereafter at a rate of 10% to 15% per decade. By age 70, plasma levels of DHEA are only 30% of peak levels (Labrie, Bélanger, Cusan, Gomez, & Candas, 1997; Orentreich, Brind, Rizer, & Vogelman, 1984; Orentreich, Brind, Vogelman, Andres, & Baldwin, 1992). Given this substantial decline, investigators have hypothesized that deficits in DHEA may produce numerous age-related problems, including memory difficulties. In the next section, we detail three specific reasons why supplementation with DHEA might enhance memory.

DHEA and Memory

DHEA affects neural function. DHEA functions as an antagonist of γ-aminobutyric acid (GABA) receptors, whose activity results in hyperpolarization of neuronal membranes and inhibition of neural function (Hanson, Fjalland, & Jackson, 1999). This GABA antagonism may be functionally significant because there is a large concentration of GABA receptors in the hippocampus, an area generally regarded as critical to learning and memory (Squire, 1992). In agreement with this hypothesis, Wigstrom and Gustaffson (1985) demonstrated that DHEA and other GABA antagonists facilitate long-term potentiation in the hippocampus, a process hypothesized to be a mechanism of learning. Reinforcing this view further, benzodiazepines, which function as GABA agonists, produce dense amnesia in humans (e.g., Hirshman, Passannante, & Arndt, 1999). Thus, DHEA's function as a GABA antagonist provides a specific mechanism for enhancing learning and memory.

DHEA metabolizes into estrogens and androgens. DHEA metabolizes into estrogens and androgens, and these steroid hormones may affect memory and cognition. A number of investigators have proposed that estrogen replacement therapy may enhance memory and cognition (LeBlanc, Janowsky, Chan, & Nelson, 2001; Sherwin, 1997). In keeping with these proposals, postmenopausal women have long reported difficulties with memory and concentration (E. Anderson, Hamburger, Liu, & Rebar, 1987), women administered estrogen replacement therapy have reported improved memory (Campbell & Whitehead, 1977), and physiological studies have demonstrated that estrogen enhances the functioning of hippocampal cells (Gould, Woolley, Frankfurt, & McEwen, 1990; Wong & Moss, 1992). (See the meta-analyses by Hogervorst, Williams, Budge, Riedel, & Jolles, 2000, and LeBlanc et al., 2001, for comprehensive reviews of the effects of estrogen on cognition.)

Initial evidence for the role of testosterone in cognition has come from rodent studies demonstrating that testosterone injections alleviate age-related deficits in learning and memory tasks, such as foot-shock avoidance (e.g., Flood, Farr, Kaiser, La Regina, & Morley, 1995). In humans, Moffat and Hampson (1996) and Neave, Menaged, and Weightman (1999) demonstrated that salivary testosterone is positively correlated with performance on spatial tasks in women. Gouchie and Kimura (1991) demonstrated that levels of salivary testosterone are correlated with performance on spatial and mathematical tasks in women, and Postma et al. (2000) demonstrated that testosterone injection enhances memory for object locations. Although studies of the effects of androgen replacement on cognition in women are sparse, Sherwin (1988) demonstrated that pharmacological levels of androgen replacement therapy maintain memory and reasoning performance in oophorectomized women, relative to oophorectomized women who received placebos.

DHEA and memory in rodents. Numerous studies have demonstrated that supplementation using DHEA can facilitate memory performance in rodents (Flood, Morley, & Roberts, 1992; Flood, Smith, & Roberts, 1988; Frye & Sturgis, 1995; Melchior & Ritzmann, 1996; Reddy & Kulkarni, 1998; Rhodes, Li, Burke, & Johnson, 1997). For example, Reddy and Kulkarni demonstrated that a subcutaneous injection of DHEA prior to training improved memory performance in a passive-avoidance step-down task. Caution is necessary, however, in interpreting the preceding studies, because rodents produce low levels of DHEA endogenously (Vinson, Whitehouse, & Goddard, 1978).

Focus on Postmenopausal Women

Our initial study focused on postmenopausal women because estrogen and testosterone deficiency associated with menopause (Morales, Nolan, Nelson, & Yen, 1994; Rubino et al., 1998), in combination with declining DHEA levels, may sensitize this population to the effects of supplementation with DHEA. This situation contrasts with that found in elderly men with relatively intact levels of gonadal steroids and in young men and women in whom levels of DHEA and gonadal steroids are substantially higher. The combination of low DHEA, estrogen, and testosterone in postmenopausal women may enhance DHEA's effects as a GABA antagonist, with concomitant effects on cognitive performance. One would also expect estrogen- and androgen-mediated effects of DHEA to be especially pronounced in postmenopausal women who have low levels of these steroid hormones (Morales et al., 1994; Rubino et al., 1998).

Focus on Recognition Memory

We focused on recognition memory because prior work in signal detection theory (Banks, 1970; Donaldson, 1992; Green & Swets, 1966; Hirshman, 1995; Parks, 1966; Snodgrass & Corwin, 1988) allowed us to measure decision processes as well as memory discrimination. Deci-

sion processes determine how likely a participant is to judge a test item as old, given a fixed memory representation. The situation with recognition memory contrasts with that found with recall memory (e.g., the Wechsler digit span), for which there is no well-developed theory of decision processes.

We emphasize the importance of decision processes because we believe that they can provide a more sensitive measure of hormonal effects on memory processes than measures of memory discrimination can. To understand this claim, note that Kroboth et al. (1998) demonstrated that serum levels of DHEAS can vary substantially over brief periods (e.g., 2 h) in response to oral administration of DHEA. This variation raises the possibility that beneficial effects of DHEA on memory discrimination will vary over brief periods. Such variations may make it difficult to identify, a priori, an appropriate time for testing DHEA's effects on memory discrimination. DHEA's metabolism into estrogens and androgens, coupled with the possibility that these hormones might mediate its effects on memory discrimination, may exacerbate this problem.

Measuring decision processes can help alleviate the problem of identifying an appropriate testing time, because measures of decision processes can be influenced by recent memory experiences, not just by current levels of memory discrimination (Hirshman, 1995). Specifically, Hirshman demonstrated that if recent memory experiences have been strong, participants become more conservative in their decision processes (i.e., they are less likely to call items "old"). Hirshman (1995, Experiment 4) demonstrated this regularity by comparing memory for two types of study lists. In one type of list, items were presented for 500 msec at study. In the other type of list, half of the items were presented for 500 msec and the remaining items were presented for 2 sec, with a stronger memory trace presumably produced for the latter set of items. For both types of study lists, participants received test lists consisting of old items that had been presented for 500 msec at study, and new items. There was an equal number of old and new items on the test lists, and participants were asked to make an old–new recognition memory judgment for each test item.

The results of Hirshman's (1995) Experiment 4 are presented in Table 1.

Note that both hit rates and false alarm rates are lower for the mixed list, in which half of the study items were presented for 2 sec [$F(1,39) = 6.06, MS_e = 0.008, p < .05$, and $F(1,39) = 3.85, MS_e = 0.012, p < .06$, respectively]. This conservatism is reflected in a higher value of C, a standard measure of criterion placement, in the mixed list [$F(1,39) = 6.85, MS_e = 0.056, p < .05$]. This increased conservatism occurred even though the stronger-memory-trace (2-sec) items from the mixed list were not presented during the recognition memory test and, as indicated in Table 1, had no measurable effect on d', a measure of memory discrimination.

In summary, measures of recognition memory decision processes (i.e., C) can be more sensitive than measures of recognition memory discrimination (i.e., d'). Thus, we focused on recognition memory because prior theoretical work has provided a well-articulated procedure for measuring decision processes, and this measurement may enhance our ability to detect the effects of DHEA on memory.

Table 1
Mean Hit Rates for Items Presented for 500 Milliseconds at Study, Mean False Alarm Rates for New Items, and Measures of Memory Discrimination (d') and Decision Processes (C) as a Function of List Type (Pure vs. Mixed) (Hirshman, 1995, Experiment 4)

List Type	Hit Rate	False Alarm Rate	d'	C
Pure	.72	.30	1.27	.00
Mixed	.67	.25	1.25	.14

Note—"Pure" refers to all study list items presented for 500 msec; "mixed" refers to the study list items of which half were presented for 500 msec and half were presented for 2 sec.

Measurement of Recognition Memory: Signal Detection Theory

Although an extensive review of the literature on measuring recognition memory processes is beyond the scope of this article, we describe the specific properties of the signal detection model that are relevant to the present experiment and analyses. The model is represented graphically in Figure 1.

The signal detection model assumes that probability density distributions of memory strength for old and new items underlie recognition memory. Memory strength is represented on the x-axis in Figure 1. The mean strength of old items is generally assumed to be greater than the mean strength of new items, and the old and new distributions are often assumed to be normal with equal variance.

In the model, decisions are made by placing a criterion on the memory-strength axis so that a participant will call an item "old" if the memory strength of the item is greater than the criterion and will call it "new" otherwise. In this context, a participant who moves his or her criterion up on the memory-strength axis is making a more conservative decision (i.e., he or she is less likely to say "old"). The algebraic representation associated with the classic signal detection model allows one to compute d', a measure of memory discrimination, and C, a measure of decision processes, from the observed hit rate (the proportion of old items called "old") and the observed false alarm rate (the proportion of new items called "old"). The measure d' denotes the distance between the means of the old and new distributions scaled relative to the constant variance of the two distributions. C denotes the distance of the criterion placement from the point of intersection of the old and new distributions, scaled relative to the common variance of the distributions. More positive values of C represent more conservative decisions.

Considering that a significant number of researchers (Donaldson, 1992; Hirshman & Hostetter, 2000; Snodgrass & Corwin, 1988) have questioned the equal-variance

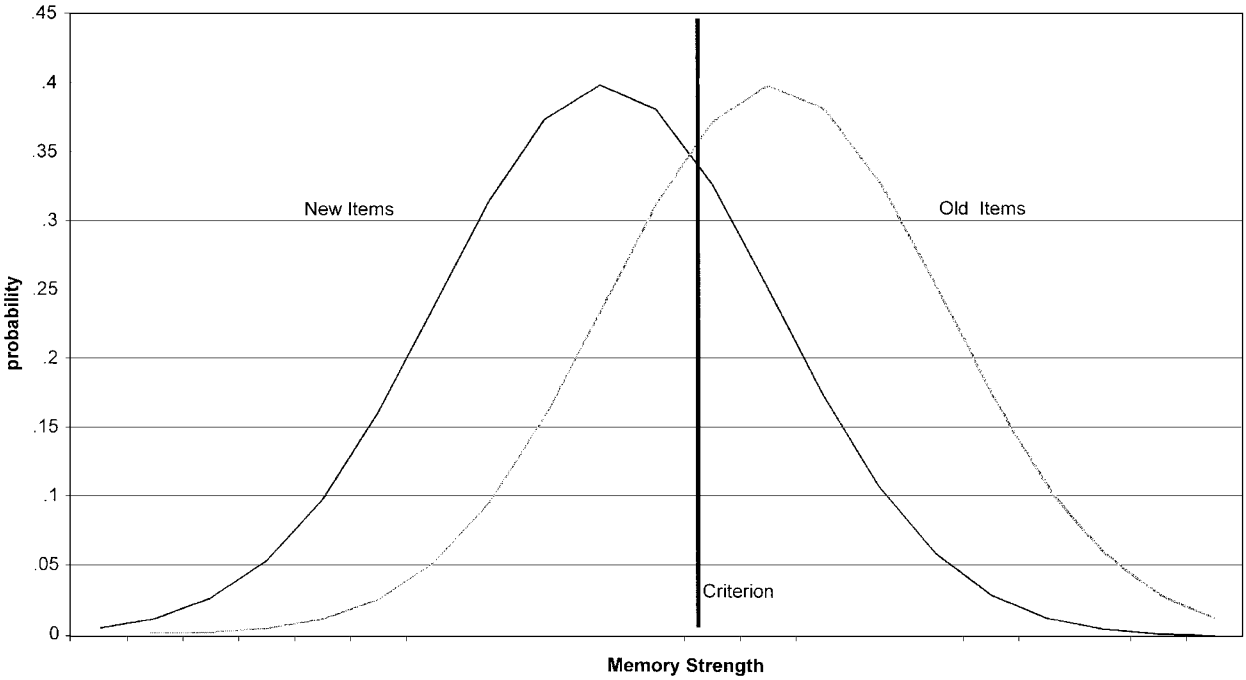

Figure 1. Signal detection model of recognition memory.

assumption in the classic signal detection model, we also conducted analyses using A' and B'', measures of discriminability and decision processes, derived from nonparametric assumptions (Donaldson, 1992, 1994). Donaldson (1994) demonstrated that A' is a more accurate estimate of discriminability than d' when the variance of the old and new distributions differ, and that it approximates the value of A_z, derived from an unequal-variance model under a broad range of discriminabilities, relative variances, and criterion placements (see Table 1 in Donaldson, 1994).

Results of Prior Studies

The results of prior studies of the effects of DHEA on cognition are mixed. We focused on postmenopausal women in our review, given the nature of the experiment presented below. Huppert, van Niekerk, and Herbert (2000) conducted an extensive review of 415 DHEA-replacement studies and identified two studies (Wolf, Kudielka, Hellhammer, Hellhammer, & Kirschbaum, 1998; Wolf et al., 1997) that examined the effects of DHEA supplementation on cognitive performance in postmenopausal women. Neither of those studies examined the effect of DHEA on recognition memory. Wolf et al. (1997) demonstrated in a crossover design that women who received 50 mg of oral DHEA daily for 2 weeks showed increases in immediate and delayed picture recall relative to women in a placebo condition. Endocrine studies (Wolf et al., 1997) demonstrated that levels of DHEA and androstenedione approximately doubled in women who received DHEA. Testosterone levels increased 500%. This large percentage change is likely to have arisen due to low baseline levels of testosterone in postmenopausal women. Despite these endocrine changes, DHEA did not enhance performance in visual search, the Stroop test, or digit span memory, raising the possibility that the recall findings may be Type I errors (Wolf et al., 1997).

Wolf et al. (1998) examined the effect of DHEA supplementation on cognition following a stressful event (i.e., public speaking) in a sample of 37 older women. Twenty of the women were given a daily dose of 50 mg of DHEA orally for 2 weeks prior to testing, and the remaining women were given daily placebos during this period. After exposure to the stressful event, the women were given a list of pictures to study, followed by a visual selective attention task and a recall test for the studied pictures. Wolf et al. (1998) demonstrated that visual attention was superior in the DHEA condition following the stressful event. This finding is relevant to the issues addressed here because attention may play a role in memory encoding (Hasher & Zacks, 1979). However, recall performance was lower in the DHEA condition for material learned following the stressful event, raising further questions about DHEA's effect on memory.

Observational studies of normal aging also produced mixed results. Berkman et al. (1993) demonstrated that elderly participants who scored higher on a composite measure of cognitive and physical fitness had higher DHEAS levels than those who scored in the intermediate or low ranges on that measure. Barrett-Connor and Edelstein (1994) demonstrated a prospective relationship between DHEA levels and performance on the Buschke

recall test, but failed to demonstrate a relationship between DHEA levels and verbal fluency or visual reproduction. The failure to demonstrate effects of DHEA on the latter measures suggests that the results on the Buschke recall test may reflect a Type I error (Barrett-Connor & Edelstein, 1994).

At present, two contrasting interpretations of DHEA's effects on cognition in postmenopausal women remain viable: (1) DHEA has no reliable effects on cognition in this population; (2) the effects of DHEA on cognition in postmenopausal women are reliable and depend on a variety of factors, such as testing circumstances and the specific cognitive processes involved. We present empirical evidence in favor of the second interpretation next.

METHOD

Overview

In the present study, we compared the effect of a daily oral dose of 50 mg of DHEA over 4 weeks and the effect of a daily placebo over 4 weeks. In the first 4-week period, participants received DHEA or placebo daily and participated in a study–test session at the end of the 4 weeks. They then received the alternative treatment for another 4 weeks, followed by a second study–test session. The 50-mg/day dose was selected because prior studies (Morales, Haubricht, Hwang, Asakura, & Yen, 1998; Morales et al., 1994; Wolf et al., 1997) had demonstrated that this dosage (1) is safe in short-term clinical trials, (2) is sufficient to alter levels of DHEA metabolites (e.g., estradiol and testosterone), and (3) can produce effects on memory performance. We chose a 4-week period of supplementation to ensure increases in serum levels of DHEA and its metabolites. Thus, our study used an 8-week placebo-controlled, double-blind, crossover design to examine the effect of DHEA on recognition memory performance.

In each study–test session, we presented participants with a study list consisting of individual words, followed by a recognition memory test. We also manipulated presentation duration during study. Items were presented during study for 300, 500, 800, 1,200, or 2,500 msec. We manipulated presentation duration because of Wolf et al.'s (1998) finding that DHEA enhanced visual attention. The first three presentation durations (300, 500, and 800 msec) bound the normal range of latencies for word perception (e.g., Folk, 1999; Gerhand & Barry, 1998). The latter two durations (1,200 and 2,500 msec) are substantially longer than the normal latencies for word perception. We hypothesized that effect of DHEA on memory would be more likely to occur at the former durations. At these durations, the hypothesized effect of DHEA on visual attention could enhance word perception, with corresponding effects on later memory.[1] Last, we asked subjects to complete a Beck Depression Inventory (BDI; Steer, Cavalieri, Leonard, & Beck, 1999) following memory testing in each session. Examination of BDI scores allowed us to consider whether any memory effects produced by DHEA are mediated by its effect on depression.

Participants

Thirty postmenopausal women participated in the experiment. The participants met the World Health Organization's criterion for postmenopausal status of 1 year's absence of menses or bilateral oophorectomy that preceded the study by one year. Potential participants were excluded from the study if they reported a serious mental illness (e.g., schizophrenia, depression), a serious physical illness within the last year (e.g., cardiac arrest), a history of drug or alcohol abuse, or current use of benzodiazepines, narcotics, or amphetamines.

Demographic characteristics of the sample of participants are presented in Table 2. The mean, standard deviation, and range are presented for the continuous variables of age, years of education, and BDI scores in the top panel of the table. BDI scores are from the placebo condition. In the bottom panels, frequency counts are presented for the categorical variables of hormone replacement status and racial/ethnic identification. (One woman did not report her HRT status.) The participants were primarily older (more than 75% over the age of 50 years), Caucasian (90%), and well educated (100% of the participants had high school educations). In addition, the participants demonstrated little evidence of depressive symptomatology (no BDI scores greater than 11), and a majority of the participants were taking some form of estrogen as part of a hormone replacement therapy regimen. Furthermore, there were no significant correlations between any of the three continuous variables (all $ps > .05$).

All participants were volunteers recruited by newspaper advertisement, and they were paid $100 for their participation. The experimental protocol was approved by the medical internal review board of the University of North Carolina at Chapel Hill.

Experimental Design and Dependent Measures

The experiment used a 2×5 within-subjects design. Type of drug (DHEA vs. placebo) was manipulated within subjects in a crossover design. Participants received DHEA for one 4-week period and placebo for the other 4-week period. Order of treatment was counterbalanced across participants. Presentation duration of study items (300 vs. 500 vs. 800 vs. 1,200 vs. 2,500 msec) was manipulated within subjects in each study–test session. Items in a presentation-duration condition were blocked in the study list, and serial order of these blocks was counterbalanced across participants. Because we used a crossover design, we also examined the effect of testing session (first session vs. second session) to evaluate practice effects.

Hit rates were computed for each presentation-duration condition during each test session, and false alarm rates were computed for each test session. Given these scores, the classic signal detection model (which applies to normal, equal-variance distributions) was used to derive d' for the 10 conditions representing the orthogonal combinations of the type of drug and presentation-duration variables, and C was computed for the two levels of the type-of-substance variable. Although one can also compute C for each presentation duration, the computation of multiple criteria assumes that participants use separate criteria for items presented for different presentation durations during study. This use of multiple criteria seems extremely unlikely, because there is no reliable way for participants to identify the presentation duration of items during the test. (Our substantive conclusions about decision processes are identical if C is calculated separately for each presentation duration.) Nonparametric measures of discrimination (A') and decision processes (B'';

Table 2
Demographic Characteristics of the Participants

Mean, Standard Deviation, and Range of Age, Education, and Beck Depression Inventory (BDI)

Variable	Mean	Standard Deviation	Range
Age (years)	54.30	7.07	39–70
Education (years)	14.93	1.87	12–18
BDI score	3.07	3.04	0–11

	Hormone Replacement Status			
	Estrogen	Estrogen + Progesterone	Estrogen + Testosterone	None
No. of Participants	15	5	1	8

	Racial/Ethnic Identification	
	Caucasian	African-American
No. of Participants	27	3

Donaldson, 1992, 1994) were also computed. Finally, scores on the BDI were computed in the DHEA and placebo conditions.

Materials

The recognition memory test used 600 medium- to high-frequency words. These 600 items were divided into two sets of 300 items each, with each set of 300 items used in one of the two study–test sessions. Each 300-item set used in a study–test session was, in turn, divided into two subsets of 150 items each. One subset of 150 items was presented as old items, and the other was presented as new items to a given participant. Of the 150 old items, 30 were presented in each of the five presentation-duration conditions. Items were counterbalanced across participants so that all items occurred equally often as old and as new items in each of the type-of-drug conditions and in each of the five presentation-duration conditions.

The BDI was used. The inventory consists of 21 self-report questions examining a participant's hedonic state and physiological functioning. The participant's response to each self-report question is scored, and scores are added, with higher scores being more indicative of depression. Although no unambiguous cutoff can be set to indicate the presence of clinical depression, scores below 10 generally do not motivate further clinical inquiries.

Procedure

The participants who responded to the advertisement gave separate informed consent prior to the first session. After signing the informed consent forms, the participants were each assigned a counterbalancing number that determined whether they would receive DHEA or placebo first. They were given a pillbox containing a 28-day supply of placebo or DHEA and a diary sheet. Daily doses of DHEA and placebo consisted of two white pills. For the DHEA condition, these were 25-mg tablets, and for the placebo condition, they were lactose tablets. The participants were instructed to take two pills each morning with breakfast and to write any significant adverse events or reactions that occurred on their diary sheets on the corresponding day. No adverse events were reported.

An appointment with the participant was made for memory testing in 28 days, and the participant was instructed to take the pills 2 h prior to her arrival for testing on that day. To control for any effects of time of day on cognitive performance (see May & Hasher, 1998), each participant was tested at the same time of day in the two type-of-drug conditions. The experimenter called each participant on the evening prior to her test and reminded her of the test session and the need to take her pills 2 h before arrival at the test session.

On the day of testing, the participants were asked to bring their pillboxes with them, and pills were counted as a measure of compliance. The participants then entered the laboratory, and they were told that they would receive a 150-word list presented on a computer monitor. They were told that their task was to try to remember those items. Blocks of 30 items were then presented on the computer monitor for each of the five presentation durations. Immediately following the recognition memory study period, the participants engaged in memory distractor tasks for approximately 30 min. The recognition memory test followed the retention interval. The recognition memory test presented 300 items in random order. One hundred fifty of these items were old and 150 were new. The participants were instructed to press the "Y" key for "yes" if the item was from the study list and the "N" key for "no" if the item was not on the study list. The computer recorded the responses for computation of the discrimination and decision-processes measures.

After the recognition memory test, the participants were given the BDI. The instructions that accompany the BDI were used. They instruct the participants to read a series of self-descriptive statements on a number of psychological/physiological topics (e.g., feelings of regret, sleep habits) and, for each topic, to pick the statement that best represented them. The completion of the BDI concluded the first session. At the end of this session, participants were given the appropriate pills for the second session and new diary sheets. An appointment was then made for memory testing in 28 days. As with the first testing session, the participants received a reminder call prior to the second session. The test procedures for the second session were identical to those used for the first session, with the notable exception that participants were debriefed at the end of the second session.

RESULTS

We begin by presenting the derived scores representing decision processes and memory discrimination. Analyses of C and B'' led to identical results, as did analyses of d' and A'. Consequently, we present only analyses of the measures from the classic model (C and d') here. We then present analyses of the false alarm rates and hit rates, followed by an analysis of participants' scores on the BDI. There were no effects of or interactions involving the factor of testing session in any of these analyses. This result indicates there were no practice effects on the present measures. Consequently, we collapsed across the factor of testing session (first session vs. second session) in this presentation. The alpha level for all statistical comparisons was .05.

Decision Processes

Our most important finding is that participants' criterion placements were substantially more conservative in the DHEA condition than in the placebo condition [C = .3, B'' = .13 in the DHEA condition and C = .08, B'' = .04 in the placebo condition, $F(1,29) = 8.10$, $MS_e = 0.088$, $p < .01$]. In the context of Figure 1, these results indicate that the participants placed their criteria higher on the memory strength (x) axis relative to the intersection of the old and new distributions in the DHEA than in the placebo condition. Thus, they required more memory information before they called an item "old" in the DHEA condition. In light of the memory discrimination results presented below, it is important to emphasize that C is computed relative to the intersection of the old and new distributions in a given condition (Snodgrass & Corwin, 1988), ensuring that the greater value of C in the DHEA condition is not simply a consequence of greater memory discrimination in that condition. Given the wide range of our subjects' ages, we examined whether DHEA's effect on C might be larger in older subjects. There was no compelling evidence for this hypothesis (Pearson's $r = -.23$, $p > .20$). One plausible explanation of this null effect is that almost all of our participants are likely to have already experienced substantial reductions in circulating levels of DHEA (Labrie et al., 1997).

Memory Discrimination

Recognition memory discrimination scores, as represented by mean d' and mean A', are presented in Table 3. The primary result on the discrimination scores is that the effects of type of drug and presentation duration interacted [$F(4,116) = 2.89$, $MS_e = 0.08$, $p < .05$]. On the

Table 3
Mean Recognition Memory Discrimination Scores (d' and A') and Standard Deviations (SD) as a Function of Type of Drug (DHEA vs. Placebo) and Presentation Duration During Study

	Presentation Duration									
	300 msec		500 msec		800 msec		1,200 msec		2,500 msec	
Type of Drug	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
					d'					
DHEA	.41	.43	.37	.42	.63	.36	.55	.49	.87	.44
Placebo	.24	.35	.33	.29	.41	.41	.65	.41	.82	.77
					A'					
DHEA	.63	.10	.62	.10	.69	.08	.66	.12	.74	.08
Placebo	.58	.09	.61	.06	.63	.10	.69	.08	.71	.12

basis of our hypothesis that the effect of type of drug would be more pronounced at brief presentation durations, we examined the effect of type of drug separately for the brief (300, 500, and 800 msec) and longer (1,200 and 2,500 msec) presentation durations. As discussed in the overview, the former durations bound the normal range of latencies in word perception (Folk, 1999; Gerhand & Barry, 1998), whereas the latter durations are substantially longer than the normal range of latencies in word perception. DHEA produced better memory discrimination than the placebo did at the brief presentation durations [$F(1,29) = 5.48$, $MS_e = 0.097$, $p < .05$, .47 vs. .32]. Memory discrimination was approximately equal in the DHEA and placebo conditions at the long presentation durations [$F(1,29) = 1.27$, .71 vs. .74, $.30 > p > .25$]. We also conducted comparisons in each presentation-duration condition. Memory discrimination was greater for the DHEA condition than for the placebo condition at the 300-msec and 800-msec presentation durations [$F(1,29) = 5.86$, $MS_e = 0.072$, $p < .05$, and $F(1,29) = 7.01$, $MS_e = 0.101$, $p < .05$, respectively]. Effects in the 500-, 1,200-, and 2,500-msec conditions did not approach the traditional criterion for significance (all ps > .15). In addition to the finding just mentioned, increasing presentation duration at study improved memory [$F(4,116) = 24.56$, $MS_e = 0.108$, $p < .01$, .33 vs. .35 vs. .52 vs. .60 vs. .85]. The effect of type of drug (DHEA vs. placebo) approached the traditional criterion for significance [$F(1,29) = 2.93$, .57 vs. .49, $.05 < p < .10$].[2]

Given the wide range of our subjects' ages, we examined whether DHEA's effect on d' might be larger in older subjects. We measured differences in d' produced by DHEA by averaging the effect of DHEA on d' in the 300- and 800-msec presentation-duration conditions (i.e., the conditions that produced significant effects on the paired comparisons). There was no evidence that age correlated with differences in d' produced by DHEA (Pearson's $r = -.01$).

False Alarms and Hits

There were fewer false alarms in the DHEA condition than in the placebo condition [$F(1,29) = 7.73$, $MS_e = 0.013$, $p < .01$, .31 vs. .40]. The mean hit rates are presented in Table 4 as a function of type of drug (DHEA vs. placebo) and presentation duration (300 vs. 500 vs. 800 vs. 1,200 vs. 2,500 msec). As in the analysis of memory discrimination, there was an interaction of the effects of type of drug and presentation duration [$F(4,116) = 3.36$, $MS_e = 0.008$, $p < .05$]. As with the d' scores, we examined the effect of type of drug separately for the brief (300-, 500-, and 800-msec) and longer (1,200- and 2,500-msec) presentation durations. Hit rates were greater in the placebo condition than in the DHEA condition for both brief and long presentation durations [$F(1,29) = 4.61$, $MS_e = 0.027$, $p < .05$, and $F(1,29) = 13.79$, $MS_e = 0.022$, $p < .001$, respectively). The interaction effect on the hits parallels the finding from the memory discrimination scores. In the discrimination scores, an advantage occurred for the DHEA condition in the brief presentation-duration conditions. In the hit scores, the placebo advantage was smaller in these conditions than in the longer presentation conditions. In addition to the interaction effect, there was an effect of type of drug, in which hits were greater in the placebo condition than in the DHEA condition [$F(1,29) = 5.95$, $MS_e = 0.045$, $p < .05$, .54 vs. .50], and an effect of presentation duration, in which hits increased with presentation duration [$F(4,116) = 23.02$, $MS_e = 0.013$, $p < .01$, .46 vs. .47 vs. .53 vs. .56 vs. 63].

Table 4
Mean Recognition Memory Hit Rates as a Function of Type of Drug (DHEA vs. Placebo) and Presentation Duration During Study

	Presentation Duration									
	300 msec		500 msec		800 msec		1,200 msec		2,500 msec	
Type of Drug	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
DHEA	.45	.23	.43	.22	.52	.21	.50	.21	.61	.21
Placebo	.47	.23	.50	.22	.53	.23	.61	.21	.66	.22

BDI Scores

Scores on the BDI ranged from 0 to 11 in the placebo condition and from 0 to 10 in the DHEA condition. Consistent with our selection criteria, these scores are generally considered to be within the normal range. Mean scores on the BDI were 3.12 in the DHEA condition and 3.06 in the placebo condition ($p > .50$).

DISCUSSION

Decision Processes

The effect of DHEA on decision processes provides clear evidence that DHEA supplementation affects cognitive processes in postmenopausal women. The effect is also consistent with the hypothesis that DHEA influences brain processes, although it does not imply this conclusion, given that metabolites of DHEA might mediate the present effect. From a cognitive perspective, we believe that the effect of DHEA on decision processes reflects DHEA's recent influence in producing strong memories. As discussed in the introduction, prior work on decision processes (Hirshman, 1995) demonstrated that criterion placement becomes more conservative following recent "strong" memory experiences. Thus, the conservative criterion in the DHEA condition is consistent with the view that DHEA had recently produced strong memory experiences. It is also important to note that there is no compelling reason to believe that other factors affecting criterion placement, such as payoffs or knowledge of the prior probability of old items (Healy & Kubovy, 1978; Hirshman & Henzler, 1998), differ systematically across the DHEA and placebo conditions. DHEA's effect on criterion placement has important methodological implications. It indicates that studies of the effects of DHEA on memory should include measures of decision processes because null effects of DHEA on memory discrimination do not necessarily imply that DHEA has no effect on memory processes.

Memory Discrimination

DHEA enhanced recognition memory discrimination, but only at brief presentation durations. This finding converges with the decision-processes results to demonstrate that supplementation with DHEA affects cognitive processes in postmenopausal women. The finding raises the question of why DHEA's enhancement of memory discrimination is limited to brief presentation durations. One possible explanation arises from Wolf et al.'s (1998) finding that supplementation with DHEA can enhance visual attention in postmenopausal women. Enhanced visual attention could improve later memory in two ways when presentation durations are brief. First, it could increase the probability of successful word perception during study. Second, it could reduce the latency of word perception, allowing additional time for postperceptual processing. The effects of both of these factors will be minimized at longer presentation durations because the probability of word perception is near 1, and there is already substantial time for postperceptual processing in these conditions.

There are two important cautions to be taken regarding this account. First, the paired comparisons did not indicate a significant advantage for the DHEA condition in the 500-msec presentation duration. This result raises questions about the reliability of our findings at brief presentation durations. Second, Wolf et al.'s (1998) finding was obtained only following the experience of a psychosocial stressor, raising questions about the plausibility of DHEA's enhancing visual attention in the present study. Providing further evidence of the effect of DHEA on visual attention would support the explanation above.

False Alarms and Hits

Examination of the false alarm and hit results demonstrates the importance of using the signal detection model to examines effects on memory discrimination and decision processes. If one examined only the false alarm and hit rates of our study, one would be led to the paradoxical conclusion that DHEA *enhances* memory by reducing false alarms and *harms* memory by reducing hits. By applying the signal detection model, we were able to understand that these results reflect DHEA's large effect on decision processes, coupled with its modest effect on memory discrimination.

BDI Scores

The BDI scores suggest that the alleviation of depressive symptoms did not mediate the memory effects reported here. These results do not suggest that DHEA never alleviates depressive symptoms, nor that such alleviation cannot influence memory. Furthermore, our results do not imply that DHEA does not produce mood changes in nondepressed subjects. DHEA may produce subtle or alternative types of mood changes that the BDI cannot detect.

Limitations of the Present Study

From the perspective of identifying the endocrinological mechanisms of DHEA's effects, the present study has two important limitations. First, 21 of the women whom we tested were on estrogen replacement therapy. Thus, it may be that either the effects presented here are limited to women using estrogen replacement therapy, or they would be enhanced for women not using any form of HRT. We cannot resolve this ambiguity in the present experiment. To provide preliminary evidence on this issue, we compared differences in d' and C produced by DHEA for those 21 women who were, and for those 8 women who were not, taking some form of estrogen. (One woman did not disclose whether she was taking estrogen, and her results were excluded from this analysis.) Differences in C and d' produced by DHEA were approximately equal in these two groups of participants (both ps $> .5$). These null effects must be interpreted with extreme caution, given the small number of women in our study who were not taking estrogen. Second, we

did not measure serum levels of DHEA, testosterone, and estradiol in the placebo and DHEA conditions. Given this omission, we can not determine whether it was DHEA or its metabolism into estrogens and/or androgens that was responsible for the cognitive effects reported here.

CONCLUDING REMARKS

Our experiment focused on the hypothesis that administration of DHEA might affect recognition memory in postmenopausal women. Two results were consistent with this hypothesis. First, DHEA made the participants more conservative in recognition memory tests. This effect is consistent with the hypothesis that DHEA had recently produced strong memory experiences. Second, DHEA enhanced memory discrimination when items were presented briefly during study. This effect may reflect DHEA's influence on visual perception. Overall, these results provide motivation for further explorations of the effects of DHEA on memory in postmenopausal women and suggest the methodological importance of measuring decision processes in such studies.

REFERENCES

Anderson, E., Hamburger, S., Liu, J. H., & Rebar, R. W. (1987). Characteristics of menopausal women seeking assistance. *American Journal of Obstetric Gynecology*, **156**, 428-433.

Anderson, N., Craik, F. I. M., & Naveh-Benjamin, M. (1998). The attentional demands of encoding and retrieval in younger and older adults: Evidence for divided attention's costs. *Psychology & Aging*, **13**, 405-423.

Banks, W. P. (1970). Signal detection theory and human memory. *Psychological Bulletin*, **74**, 81-99.

Barrett-Connor, E., & Edelstein, S. (1994). A prospective study of dehydroepiandrosterone sulfate and cognitive function in an older population: The Rancho Bernardo Study. *Journal of the American Geriatric Society*, **42**, 420-423.

Barrou, Z., Charru, P., & Lidy, C. (1997). Dehydroepiandrosterone (DHEA) and aging. *Archives of Gerontology & Geriatrics*, **24**, 233-241.

Berkman, L., Seeman, T., Albert, M., et al. (1993). High, usual and impaired functioning in community-dwelling older men and women: Findings from the MacArthur Foundation Research Network on Successful Aging. *Journal of Clinical Epidemiology*, **46**, 1129-1140.

Campbell, S., & Whitehead, M. (1977). Œstrogen therapy and the menopausal syndrome. *Clinical Obstetrics & Gynecology*, **4**, 31-47.

Donaldson, W. (1992). Measuring recognition memory. *Journal of Experimental Psychology: General*, **121**, 275-277.

Donaldson, W. (1994). Accuracy of d' and A' as estimates of sensitivity. *Bulletin of the Psychonomic Society*, **31**, 271-274.

Flood, J. F., Farr, S. A., Kaiser, F. E., La Regina, M., & Morley, J. E. (1995). Age-related decrease of plasma testosterone in SAMP8 mice: Replacement improves age-related impairment of learning and memory. *Physiology & Behavior*, **57**, 669-673.

Flood, J. F., Morley, J. E., & Roberts, E. (1992). Memory-enhancing effects in male mice of pregnenolone and steroids metabolically derived from it. *Proceedings of the National Academy of Sciences*, **89**, 1567-1571.

Flood, J. F., Smith, G. E., & Roberts, E. (1988). Dehydroepiandrosterone and its sulfate enhance memory retention in mice. *Brain Research*, **447**, 269-278.

Folk, J. (1999). Phonological codes are used to access the lexicon in silent reading. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, **25**, 892-906.

Frye, C. A., & Sturgis, J. D. (1995). Neurosteroids affect spatial/reference, working, and long-term memory of female rats. *Neurobiology of Learning & Memory*, **64**, 83-96.

Gerhand, S., & Barry, C. (1998). Word frequency effects in oral reading are not merely age-of-acquisition effects in disguise. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, **24**, 267-283.

Gouchie, W., & Kimura, D. (1991). The relationship between testosterone levels and cognitive ability patterns. *Psychoneuroendocrinology*, **16**, 323-334.

Gould, E., Woolley, C. S., Frankfurt, M., & McEwen, B. S. (1990). Gonadal steroids regulate dendritic spine density in hippocampal pyramidal cells in adulthood. *Journal of Neuroscience*, **10**, 1286-1291.

Green, D., & Swets, J. (1966). *Signal detection theory and psychophysics*. New York: Wiley.

Hanson, S. L., Fjalland, B., & Jackson, M. D. (1999). Differential blockade of gamma-aminobutyric acid type A receptors by the neuroactive steroid dehydroepiandrosterone sulfate in posterior and intermediate pituitary. *Molecular Pharmacology*, **55**, 489-496.

Hasher, L., & Zacks, R. T. (1979). Automatic and effortful processes in memory. *Journal of Experimental Psychology*, **108**, 356-388.

Healy, A., & Kubovy, M. (1978). The effects of payoffs and prior probabilities on indices of performance and cutoff location in recognition memory. *Memory & Cognition*, **6**, 544-553.

Hirshman, E. (1995). Decision processes in recognition memory: Criterion shifts and the list-strength paradigm. *Journal of Experimental Psychology: Learning, Memory, & Cognition*, **21**, 302-313.

Hirshman, E., & Henzler, A. (1998). The role of decision processes in conscious recollection. *Psychological Science*, **9**, 61-65.

Hirshman, E., & Hostetter, M. (2000). Using ROC curves to test models of recognition memory. *Memory & Cognition*, **28**, 161-166.

Hirshman, E., Passannante, A., & Arndt, J. (1999). The effect of midalzolam on the modality-match effect in implicit memory. *Cognitive Brain Research*, **7**, 473-493.

Hogervorst, E., Williams, J., Budge, M., Riedel, W., & Jolles, J. (2000). The nature of the effect of female gonadal hormone replacement therapy on cognitive function in post-menopausal women. *Neuroscience*, **101**, 485-512.

Huppert, F. A., van Niekerk, J. K., & Herbert, J. (2000). Dehydroepiandrosterone (DHEA) supplementation for cognition and well-being. *Cochrane Database of Systematic Review* [Computer file], **2**, CD000304.

Kroboth, P. D., Frye, R., Linares, A., Folan, M., Hakala, C., Stone, R., & Kroboth, F. (1998). Gender differences in pharmacokinetics of DHEA and DHEA-S following single and multiple dose administration of DHEA in healthy older adults [Abstract]. *Journal of Neuroscience*, **24**, 345.

Kroboth, P. D., Salek, F. S., Pittenger, A. L., Fabian, T. J., & Frye, R. F. (1999). DHEA and DHEA-S: A review. *Journal of Clinical Pharmacology*, **39**, 327-348.

Labrie, F., Bélanger, A., Cusan, L., Gomez, J.-L., & Candas, B. (1997). Marked decline in serum concentrations of adrenal C19 sex steroid precursors and conjugated androgen metabolites during aging. *Journal of Clinical Endocrinology & Metabolism*, **82**, 2396-2402.

LeBlanc, E., Janowsky, J., Chan, B., & Nelson, H. (2001). Hormone replacement therapy and cognition: Systematic review and meta-analysis. *Journal of the American Medical Association*, **285**, 1489-1499.

Longcope, C., Bourget, C., & Flood, C. (1982). The production and aromatization of dehydroepiandrosterone in postmenopausal women. *Maturitas*, **4**, 325-332.

May, C., & Hasher, L. (1998). Synchrony effects in inhibitory control over thought and action. *Journal of Experimental Psychology: Human Perception & Performance*, **24**, 363-379.

Melchior, C. L., & Ritzmann, R. F. (1996). Neurosteroids block the memory-impairing effects of ethanol in mice. *Pharmacology, Biochemistry, & Behavior*, **53**, 51-56.

Moffat, S. D., & Hampson, E. (1996). A curvilinear relationship between testosterone and spatial cognition in humans: Possible influence of hand preference. *Psychoneuroendocrinology*, **21**, 323-337.

Morales, A. J., Haubricht, R. H., Hwang, J. Y., Asakura, H., & Yen, S. S. C. (1998). The effect of six months treatment with a 100 mg daily dose of dehydroepiandrosterone (DHEA) on circulating sex

steroids, body composition and muscle strength in age-advanced men and women. *Clinical Endocrinology*, **49**, 421-432.

Morales, A. [J.], Nolan, J., Nelson, J., & Yen, S. (1994). Effects of replacement dose of dehydroepiandrosterone in men and women of advancing age. *Journal of Clinical Endocrinology & Metabolism*, **78**, 1360-1367.

Mortola, J. F., & Yen, S. S. C. (1990). The effects of oral dehydroepiandrosterone on endocrine-metabolic parameters in postmenopausal women. *Journal of Clinical Endocrinology & Metabolism*, **71**, 57-62.

Neave, N., Menaged, M., & Weightman, D. R. (1999). Sex differences in cognition: The role of testosterone and sexual orientation. *Brain & Cognition*, **41**, 245-262.

Ohashi, M., Kato, K., Nawata, H., & Ibayashi, H. (1986). Adrenocortical responsiveness to graded ACTH infusions in normal young and elderly human subjects. *Gerontology*, **32**, 43-51.

Orentreich, N., Brind, J. L., Rizer, R. L., & Vogelman, J. H. (1984). Age changes and sex differences in serum dehydroepiandrosterone sulfate concentrations throughout adulthood. *Journal of Endocrinology & Metabolism*, **59**, 511-555.

Orentreich, N., Brind, J. L., Vogelman, J. H., Andres, R., & Baldwin, H. (1992). Long-term longitudinal measurements of plasma dehydroepiandrosterone sulfate in normal men. *Journal of Endocrinology & Metabolism*, **75**, 1002-1004.

Parks, T. (1966). Signal detectability theory of recognition memory performance. *Psychological Review*, **73**, 44-58.

Pavlov, E. P., Harman, S. M., Chrousos, G. P., Lorieux, D. L., & Blackman, M. R. (1986). Responses of plasma adrenocorticotropin, cortisol, and dehydroepiandrosterone to ovine corticotropin-releasing hormone in healthy aging men. *Journal of Clinical Endocrinology & Metabolism*, **62**, 767-772.

Postma, A., Meyer, G., Tuiten, A., Van Honk, J., Kessels, R. P., & Thijssen, J. (2000). Effects of testosterone administration on selective aspects of object-location memory in healthy young women. *Psychoneuroendocrinology*, **25**, 563-575.

Reddy, D. S., & Kulkarni, S. K. (1998). The effects of neurosteroids on acquisition and retention of a modified passive-avoidance learning task in mice. *Brain Research*, **791**, 108-116.

Regelson, W., Loria, R., & Kalimi, L. R. (1994). Dehydroepiandrosterone (DHEA)—the "mother steroid": I. Immunologic action. In W. Pierpaoli, W. Regelson, & N. Fabris (Eds.), *The aging clock: The pineal gland and other pacemakers in the progression of aging and carcinogenesis. Third Stromboli Conference on Aging and Cancer.* (Annals of the New York Academy of Sciences, Vol. 719, pp. 533-563). New York: New York Academy of Sciences.

Rhodes, M. E., Li, P. K., Burke, A. M., & Johnson, D. A. (1997). Enhanced plasma DHEAS, brain acetylcholine and memory mediated by steroid sulfatase inhibition. *Brain Research*, **773**, 28-32.

Rosenfeld, R. S., Hellman, L., Roffwarg, H., Weitzman, E. D., Fukushima, D. K., & Gallagher, T. F. (1971). Dehydroepiandrosterone is secreted episodically and synchronously with cortisol by normal man. *Journal of Clinical Endocrinology*, **33**, 87-92.

Rubino, S., Stomati, M., Bersi, C., Casarosa, E., Luisi, M., Petraglia, F., & Genazzani, A. (1998). Neuroendocrine effect of a short-term treatment with DHEA in postmenopausal women. *Maturitas*, **28**, 251-257.

Salthouse, T. (1993). The processing speed theory of adult age differences in cognition. *Psychological Review*, **103**, 403-428.

Sherwin, B. (1988). Estrogen and/or androgen replacement therapy and cognitive functioning in surgically menopausal women. *Psychoneuroendocrinology*, **13**, 345-357.

Sherwin, B. (1997). Estrogen effects on cognition in menopausal women. *Neurology*, **48**, S21-S26.

Snodgrass, J. G., & Corwin, J. (1988). Pragmatics of measuring recognition memory: Applications to dementia and amnesia. *Journal of Experimental Psychology: General*, **117**, 34-50.

Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans. *Psychological Review*, **99**, 582-594.

Steer, R. A., Cavalieri, T. A., Leonard, D. M., & Beck, A. T. (1999). Use of the Beck Depression Inventory for primary care to screen for major depression disorders. *General Hospital Psychiatry*, **21**, 106-111.

Vinson, G., Whitehouse, B., & Goddard, C. (1978). Steroid 17-hydroxylation and androgen production by incubated rat adrenal tissue. *Journal of Steroid Biochemistry*, **9**, 677-683.

Wigstrom, H., & Gustaffson, B. (1985). On long-lasting potentiation in the hippocampus: A proposed mechanism for its dependence on coincident pre- and postsynaptic activity. *Acta Physiologica Scandinavica*, **123**, 519-522.

Wolf, O. T., Kudielka, B. M., Hellhammer, D. H., Hellhammer, J., & Kirschbaum, C. (1998). Opposing effects of DHEA replacement in elderly subjects on declarative memory and attention after exposure to a laboratory stressor. *Psychoneuroendocrinology*, **23**, 617-629.

Wolf, O. T., Neumann, O., Hellhammer, D. H., Geiben, A. C., Strasburger, C. J., Dressendörfer, R. A., Pirke, K. M., & Kirschbaum, C. (1997). Effects of a two-week physiological dehydroepiandrosterone substitution on cognitive performance and well-being in healthy elderly women and men. *Journal of Clinical Endocrinology & Metabolism*, **82**, 2363-2367.

Wong, M., & Moss, R. L. (1992). Long-term and short-term electrophysiological effects of estrogen on the synaptic properties of hippocampal CA 1 neurons. *Journal of Neuroscience*, **12**, 3217-3225.

NOTES

1. Enhanced word perception could improve later memory in two ways when presentation durations are brief. First, it could increase the probability of successful word perception during study. Second, it could reduce the latency of word perception, allowing additional time for postperceptual processing. The effects of both of these factors would be minimized at the 1,200- and 2,500-msec presentation durations, because the probability of word perception is near 1 and there is already substantial time for postperceptual processing in these conditions.

2. To allay concerns that the present discrimination results arise from estimation errors associated with differential criterion placement in an unequal-variance model, we examined the percentage error in A' (relative to A_z) given the criterion placements and discrimination values used in the present experiment, and we used .8 as a measure of the slope of the z-transformed ROC curve (Hirshman & Hostetter, 2000). Given these parameters (see Table 1 in Donaldson, 1994), A' represents approximately a 4% overestimate of A_z in the placebo condition and approximately a 6% overestimate of A_z in the DHEA condition. Thus, the estimation errors in the DHEA and placebo conditions are modest and similar, ensuring that the present effects of DHEA on memory discrimination are not due to errors in estimation associated with differential criterion placement in an unequal-variance model.

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