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Cortisol Variation in Humans Affects Memory for Emotionally Laden and Neutral Information

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In a test of the effects of cortisol on emotional memory, 90 men were orally administered placebo or 20 or 40 mg cortisol and presented with emotionally arousing and neutral stimuli. On memory tests administered within 1 hr of stimulus presentation, cortisol elevations caused a reduction in the number of errors committed on free-recall tasks. Two evenings later, when cortisol levels were no longer manipulated, inverted-U quadratic trends were found for recognition memory tasks, reflecting memory facilitation in the 20-mg group for both negative and neutral information. Results suggest that the effects of cortisol on memory do not differ substantially for emotional and neutral information. The study provides evidence of beneficial effects of acute cortisol elevations on explicit memory in humans.

Cortisol elevations are one mechanism through which stress affects learning and memory. Research, primarily in rats, has shown that mild glucocorticoid[1] elevations enhance memory and extreme deficiencies or elevations disrupt memory (see McEwen & Sapolsky, 1995 for review). Circulating glucocorticoids readily cross the blood–brain barrier, and extensive research has revealed that glucocorticoids alter functioning of hippocampal neurons (for reviews, see Lupien & McEwen, 1997; McEwen & Sapolsky, 1995). For instance, an inverted U-shaped function characterizes the relation between glucocorticoids and long-term potentiation in hippocampal neurons (Filipini, Gijsbers, Birmingham, & Dubrovsky, 1991). This effect is due to differential activation of the two types of corticosteroid receptors, that is, mineralocorticoid receptors (MRs, with high affinity for cortisol) and glucocorticoid receptors (GRs, with substantially lower affinity for cortisol; for review, see McEwen & Sapolsky, 1995). The effects of glucocorticoids on memory depend on both MR and GR activation, with memory facilitation occurring when MRs are fully occupied and GRs are only partially activated. It is only when GRs become highly saturated (e.g., during stress) that deficits in memory related to elevated glucocorticoids are observed (de Kloet, Oitzl, & Joels, 1999; Oitzl & de Kloet, 1992; Roozendaal, Bohus, & McGaugh, 1996).

Consistent with the animal research, studies in humans have also shown various effects of cortisol on memory. Although most human studies have shown deficiencies in memory performance associated with acute glucocorticoid elevations (see Lupien & McEwen, 1997 for review), a few studies have shown facilitation with mild cortisol elevations (Beckwith, Petros, Scaglione, & Nelson, 1986; Buchanan & Lovallo, 2001; Lupien et al., 2002). Human data demonstrate that glucocorticoids affect hippocampally mediated learning but have few effects on nonhippocampally mediated cognitive tasks, such as implicit memory testing or vigilance (e.g., Kirschbaum, Wolf, May, Wippich, & Hellhammer, 1996; Newcomer et al., 1999; Wolkowitz et al., 1990). Thus, GR activation in the hippocampus has been suggested to underlie the effects of cortisol on memory in humans (for review, see Lupien & Lepage, 2001). However, recent data suggest that significant species differences exist in the concentrations of GR receptors in the hippocampus. For instance, using in situ hybridization, Sanchez, Young, Plotsky, and Insel (2000) recently found very low concentrations of GR mRNA in the hippocampus of the rhesus monkey, but Patel and colleagues (2000) found high concentrations of GR mRNA in the squirrel monkey hippocampus. The density of GRs in the human hippocampus is currently unknown (for review, see Lupien & Lepage, 2001). These data call into question whether the hippocampal model accounts for all of the observed findings and highlight the importance of expanding the neural model of glucocorticoids' effects on memory (Lupien & Lepage, 2001).

The amygdala is an additional brain region known to mediate the effects of glucocorticoids on memory (Roozendaal, 2000). In some memory tasks, the basolateral nucleus of the amygdala is

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[1] Glucocorticoids are corticosterone in most rodents, and cortisol in primates.

important in mediating the effects of glucocorticoids or GR agonists infused directly into the hippocampus (for review, see Roozendaal, 2000). For instance, in rats, bilateral lesions of the basolateral nucleus of the amygdala block the memory-enhancing effects of the specific GR agonist 28362 administered directly into the hippocampus after training on an inhibitory avoidance task (Roozendaal & McGaugh, 1997). Furthermore, lesions of the basolateral nucleus of the amygdala that, alone, do not impair retention block the enhancing effects of systemic injections of glucocorticoids immediately after inhibitory avoidance training in rats (Roozendaal & McGaugh, 1996). These and other studies have shown that the effects of glucocorticoids on learning and memory are importantly mediated by activity not only in the hippocampus, but also in the basolateral nucleus of the amygdala (Roozendaal, 2000).

The Amygdala and Emotionally Based Memories

It is well established that emotional information tends to be remembered better than neutral information (Cahill & McGaugh, 1995; Heuer & Reisberg, 1990). For instance, when study participants are presented with both emotionally laden and neutral stimuli (e.g., words like *pain* vs. *cabinet*, or pictures of scenes such as a car accident vs. a boat on a quiet lake), memory tests generally show superior performance for emotionally arousing, compared with neutral, stimuli (Bradley, Greenwald, Petry, & Lang, 1992; Phelps, LaBar, & Spencer, 1997). Animal and human studies have suggested that the amygdala mediates the effects of emotion on learning and memory. For instance, activity in the amygdala underlies aversive classical conditioning in humans and animals (e.g., LaBar, LeDoux, Spencer, & Phelps, 1995; LeDoux, Cicchetti, Xagoraris, & Romanski, 1990). Human neuroimaging and brain lesion data have confirmed a role for the amygdala in the superiority of memory for emotional information (Cahill et al., 1996; Hamann, Ely, Grafton, & Kilts, 1999). For instance, using functional magnetic resonance imaging, Canli, Zhao, Brewer, Gabrieli, and Cahill (2000) found that event-related activation in the left amygdala during encoding predicted memory performance only for highly emotionally evocative scenes, suggesting a relatively specific role for the amygdala in memory of emotional, but not neutral, information. Furthermore, two patients with selective bilateral damage to the amygdala failed to show normal enhancement of memory for emotionally arousing information (Adolphs, Cahill, Schul, & Babinsky, 1997).

Thus, the amygdala is involved in the superiority of memory for emotional information, and glucocorticoids are one of several molecular mechanisms contributing to the amygdala's role in memory (which also importantly includes β-adrenergic activation of basolateral amygdala neurons; for review, see Roozendaal, 2000). As a consequence of the differential roles of the amygdala and hippocampus in emotional versus nonemotional learning (Bechara et al., 1995; Cahill et al., 1996; Canli et al., 2000), the dose–response curves for the effects of glucocorticoids on memory may vary for emotionally arousing and neutral information.

One study examining these issues (Buchanan & Lovallo, 2001) showed memory facilitation associated with acute cortisol elevations for emotionally arousing, but not for neutral, stimuli. They found that 20 mg cortisol caused memory facilitation for emotionally arousing stimuli and no effect for neutral stimuli, and thus concluded that cortisol facilitates memory only for emotional information. However, other investigators have found cortisol-related memory facilitation for neutral information (e.g., Beckwith et al., 1986; Lupien et al., 2002; Lupien, Gillin, & Hauger, 1999). Thus, the conclusion that cortisol facilitates memory only for emotionally arousing material but has no effect or causes impairments for neutral information may be oversimplified. A primary goal of the current study was to further characterize the dose–response curves for cortisol's effects on emotional versus neutral information in humans.

Memory and Glucocorticoids: Dose–Response Relationship

On the basis of studies in animals, it is known that an inverted U-shaped function characterizes the relation between memory and glucocorticoids. However, human studies have yet to replicate these effects for explicit memory. Human studies have shown *either* facilitation or impairment in explicit memory associated with cortisol elevations. Thus, for the current study, two doses of exogenously administered cortisol were chosen, one hypothesized to cause memory facilitation and another hypothesized to cause impairment.

With few exceptions (e.g., Buchanan & Lovallo, 2001; de Quervain, Roozendaal, Nitsch, McGaugh, & Hock, 2000), most investigators who have studied the effects of pharmacologically manipulated cortisol levels on memory have tested memory retrieval while glucocorticoid levels were still pharmacologically elevated. It has therefore been difficult to distinguish cortisol's effects on memory formation from its effects on retrieval in humans. Thus, in the current study, memory testing was performed both during the same session as encoding and two evenings later, when cortisol levels were no longer manipulated. Data from Session 2 allow examination of cortisol's effects on memory formation independent from its effects on retrieval.

In the current study, participants were given either placebo or a single administration of one of two doses of hydrocortisone. The doses of hydrocortisone were chosen to elevate cortisol to levels observed during mild-to-moderate (20 mg) or extreme (40 mg) acute stress. Drug administration occurred in the evening, when endogenous cortisol levels are minimal. Participants were presented with words and pictures (i.e., photographs) that varied with respect to their emotional content. Free-recall and recognition memory for these stimuli were tested on the same evening and two evenings later. Recognition is considered a relatively pure measure of memory storage because it is not affected by processes that alter generation or retrieval of items stored in memory, which are involved in free-recall. Certain variables affect recall and recognition differently (sometimes even in opposite directions, such as word frequency; for review, see Brown, 1976). Furthermore, for certain tests of memory, it is known that verbal encoding of material can be deleterious for memory performance (e.g., Schooler & Engstler-Schooler, 1990). It is currently unknown exactly what aspects of explicit memory are affected by glucocorticoids. Thus, word and picture recall and recognition were assessed with the goal of fully examining the effects of cortisol on explicit memory processes.

Method

Participants

Ninety paid healthy male volunteers (aged 18–33), weighing between 140–200 lbs (63.5–90.7 kg), were recruited. Individuals who met any of the following exclusionary criteria were excluded from participation: previous exposure to the slides used in the study (i.e., International Affective Picture System; Lang, Bradley, & Cuthbert, 1998); non-native English speaking; medical illness within the prior 3 weeks; asthma; endocrine disorders; history of psychopathology; current alcohol or substance abuse; daily tobacco use; cardiac disorders; hypertension; neurological disorders; history of head trauma; night-shift work; allergies or sensitivities that would preclude administration of the study drug; or treatment with psychotropic medications, narcotics, beta-blockers, or steroids. Participants were additionally screened upon arrival to the laboratory for vision problems (i.e., worse than 20/40 vision) and hypertension (i.e., blood pressure $>$ 160/95). Written informed consent was obtained in accordance with the University of Wisconsin Health Sciences Human Subjects Committee guidelines.

Every participant who completed Session 1 also completed Session 2. Data from two placebo participants and one 20-mg participant were excluded from data analyses because of extremely high salivary cortisol values.[2]

Procedure

Eligible participants were invited into the lab for two sessions: an initial session, which always began at 7 p.m. (Session 1), followed two evenings later by Session 2, which began any time between 5 and 8 p.m. Participants were instructed to eat a light dinner at least 1 hr prior to the initial session and to refrain from eating, exercising, and drinking anything but water for the hour prior to both sessions. Participants were also instructed to refrain from drinking alcohol for the 24 hr prior to both sessions. Individuals who were occasional smokers (i.e., $<$ 1 pack per month) were instructed not to smoke for the week prior to the sessions. Participants were tested individually, and tasks were administered on a computer, with the exception of self-report questionnaires and the free-recall tasks.

Session 1

Drug administration. Participants were orally administered placebo or 20 or 40 mg hydrocortisone (which is identical to the hormone cortisol). Drug administration was randomized[3] and double-blind, using identical opaque capsules. Hydrocortisone tablets (Hydrocortone; Merck & Co, Whitehouse Station, NJ) were encapsulated along with lactose, and placebo capsules contained only lactose. After drug administration, participants sat quietly for 40–43 min while the drug was absorbed. During the rest period, participants watched an informative video about American cities, *Rand McNally Celebrated Cities of America* (International Video Network; San Ramon, California). This neutral to slightly positively valenced video was shown to control, to whatever extent possible, the participant's activities during the drug-absorption rest period.

Saliva sampling. Salivary cortisol samples were collected with the Salivette sampling device (Sarstedt, Rommelsdorf, Germany). During Session 1, saliva samples were obtained at the following time points: 10 min after arrival at the laboratory (i.e., immediately prior to drug administration), approximately every 20 min thereafter for the first 2 hr of the session, and approximately every 25 min during the last hour of the session (Figure 1). Samples were stored frozen at −80 °C until processing.

Measurement of emotional state. To examine the relation between cortisol levels and subjective emotional experience, current emotional state was measured three times during Session 1: approximately 50, 100, and 160 min after drug administration. Ratings were obtained on the 20 adjectives from the Positive Affect and Negative Affect Schedule (PANAS—State Version; Watson, Clark, & Tellegen, 1988) and on 11 additional emotional adjectives (Feldman Barrett & Russell, 1998), which allow separation of the valence and arousal dimensions of affective space.

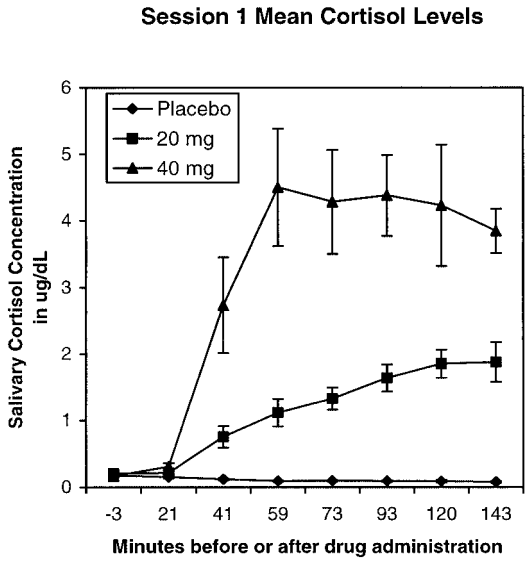

Figure 1. Mean salivary cortisol elevations for each group prior to and following drug administration (at approximately 7:13 p.m.). Salivary cortisol levels among the groups did not differ at the time of the baseline sample (3 min before drug administration). Error bars represent *SEM*. The apparent lack of error bars for the placebo group is due to the minimal variation in cortisol concentration in this group. To convert to nanomoles per liter, multiply values in micrograms per deciliter by 27.6.

Encoding of negative and neutral stimuli: Rating tasks. Approximately 43 min after drug administration, all participants performed a word-rating task followed by a picture-rating task, which exposed them to negative and neutral stimuli.[4] Words were chosen from the Affective Norms for English Words (ANEW; Bradley & Lang, 1999). Pictures (i.e., photographs) were chosen from the International Affective Picture System (IAPS; Lang et al., 1998). For both the picture- and word-rating tasks, two sets of stimuli (deemed Sets A and B) were developed to allow for counterbalancing of targets and distracters in later tests of recognition memory. Because counterbalancing adds another factor to the study design and introduces variability, we chose to limit counterbalancing of variables

[2] The 2 excluded placebo participants had salivary cortisol levels of 0.93 and 1.17 μg/dl, compared with the placebo group range of 0.03–0.29 μg/dl. On a test day information sheet, these 2 participants indicated that they sleep into the very late morning on a regular basis, suggesting that these participants may have had altered circadian rhythmicity of cortisol. Furthermore, 1 participant in the 20-mg group had chewed the capsule containing the hydrocortisone tablet. His extremely high observed salivary cortisol level of 22.7 μg/dl was assumed to have resulted from hydrocortisone residue left in his mouth and/or from an increased absorption rate.

[3] For the first 30 participants, the doses used for the current study were 5 and 20 mg cortisol, and drug administration was truly randomized (i.e., 1:1:1 = placebo: 5 mg: 20 mg). However, the 5-mg dose was found to produce insufficient cortisol elevations and was thus discarded, and a 40-mg group was added. After this point, drug administration was pseudo-randomized (i.e., 2:2:3 = placebo: 20 mg: 40 mg).

[4] Rating tasks were administered a few minutes following the third (Minute 41) and before the fifth (Minute 73) saliva samples.

to the recognition memory task. Recognition memory targets and distracters were considered the most important items to counterbalance in order to ensure that memory effects were not related merely to a particular set of stimuli. Thus, other variables, such as order of presentation of the rating tasks, were kept constant for all participants.

Both picture sets included 56 pictures (28 negative and 28 neutral) that were matched on average normative ratings of pleasantness and arousal (Lang et al., 1998). See Table 1 for average normative ratings. To facilitate free-recall testing, content overlap among pictures was minimized within each set. Both word sets included 44 words (22 negative and 22 neutral) that were matched on average normative ratings of pleasantness and arousal (Bradley & Lang, 1999; Table 1). Word sets were also matched on frequency of usage ($ps < .71$; Carroll, Davies, & Richman, 1971), and length ($ps < .28$).

During the rating tasks, participants were instructed to rate pictures or words on the basis of how they felt while viewing each stimulus, and were not told that they would later be asked to recall the stimuli. Participants rated pictures (5-s stimulus presentation duration) and words (4-s presentation duration) on two 9-point numeric scales assessing pleasantness and arousal.

Continuous performance test. After the rating tasks were completed, the degraded stimulus continuous performance test (DS-CPT) developed by Nuechterlein and Asarnow (1999) was administered as a control task to test for potential differences in vigilance as a result of hydrocortisone administration.

Memory assessment. Explicit memory was assessed for the stimuli in the word- and picture-rating tasks. Participants were not given feedback on their performance for any of the memory tests.

Free-recall. Participants completed separate free-recall tasks for words and pictures, in which they were instructed to list all the words or briefly describe all the pictures they could remember from the rating tasks. Participants were given 7 min to complete the word free-recall and 11 min to complete the picture free-recall tasks. In addition to number of correct responses, free-recall tasks were also scored for intrusive errors, that is, errors of commission, which were responses that were not presented in the word rating task or descriptions of pictures that were not presented in the picture rating task. Because scoring the free-recall lists for pictures entailed a degree of subjectivity, interrater reliability was computed for the first 30 participants' data. All remaining picture free-recall lists were scored by one person (Heather C. Abercrombie), as interrater reliability was found to be extremely high (intraclass correlation coefficients $> .98$).

Recognition memory. After the free-recall tasks were completed, separate recognition memory tests for words and pictures were administered. The tasks involved use of a two-button "yes" or "no" response pad to indicate whether or not test stimuli were presented during the rating tasks. Half of the test stimuli were targets (previously viewed), and half were distracters (new stimuli). Instructions emphasized both speed and accuracy. Distracters were pictures or words from the alternate set of stimuli not presented during encoding (i.e., A or B, accordingly). Only half of the stimuli from each Set A and B were used for the Session 1 recognition memory tasks. Testing only a subset of the total pool of stimuli during Session 1 made available a set of distracters for Session 2 that were completely new, and targets that had been viewed only during the encoding tasks, allowing for a Session 2 recognition memory not contaminated by practice effects from the Session 1 recognition tests. The subsets of stimuli chosen for the recognition tests from Sets A and B were psychometrically matched on normative ratings. Comparisons between the Set A and B subsets (within valence) revealed no differences (for pleasantness, frequency, and word length, $ps > .50$ for pictures and $ps > .45$ for words; for arousal, $ps > .18$).

The participant's ability to discriminate between previously presented and new items, (i.e., "sensitivity") served as the dependent variable for recognition memory. The sensitivity index Pr was used (Snodgrass & Corwin, 1988). Pr is the proportion of old items (targets) endorsed minus the proportion of new items (distracters) endorsed, that is, hits minus false alarms, with positive scores reflecting more hits than false alarms. This metric does not require that the data be normally distributed, and it provides a measure of sensitivity that is independent from bias (Snodgrass & Corwin, 1988). Cortisol dose was not hypothesized to be related to bias or reaction time, and these data are therefore excluded.

Session 2

At Session 2, no drug was administered. Three saliva samples (approximately 25 min apart) were collected according to methods identical to those of Session 1. Participants' memory for stimuli viewed during the Session 1 rating tasks was again assessed, and order of presentation of the memory tests was identical to Session 1. In Session 2, recognition memory measures were derived from the sets of test stimuli not used during Session 1 (see explanation above).

Table 1
Stimuli Sets A and B: Average Normative Ratings

	Negative stimuli		Neutral stimuli	
Stimuli	Set A	Set B	Set A	Set B
		Picture rating task		
IAPS				
Pleasantness	2.38 ± 0.42	2.42 ± 0.41	4.89 ± 0.37	4.91 ± 0.33
Arousal	6.00 ± 0.60	5.99 ± 0.58	2.57 ± 0.32	2.50 ± 0.36
		Word rating task		
ANEW				
Pleasantness	2.59 ± 0.53	2.58 ± 0.57	5.12 ± 0.56	5.09 ± 0.57
Arousal	5.59 ± 0.88	5.58 ± 0.72	3.90 ± 0.30	3.94 ± 0.39

Note. Values are reported as means (± *SD*). Pleasantness and arousal values are average normative ratings for stimuli used in each set (pleasantness: 1 = *highly unpleasant*, 5 = *neutral*, 9 = *highly pleasant*; arousal: 1 = *low*, 9 = *high*). Comparisons between Sets A and B (within valence) revealed no differences: for the words, $ps > .71$; for the pictures, $ps > .47$. IAPS = International Affective Picture System; ANEW = Affective Norms for English Words.

Processing of Saliva Samples

Prior to the cortisol assay, samples were centrifuged at 4500 rpm for 10 min, and the supernatant was transferred to 2-ml tubes for storage (−70 °C) until assayed. Cortisol was assayed with the ^{125}I Cortisol RIA kit (Pantex, Santa Monica, CA) modified for saliva. Individuals performing cortisol assays were unaware of group assignment (i.e., dose). The detection limit of the assay (ED_{80}) was 0.03 μg/dl. The mean interassay and intra-assay variation was 7.4% and 3.8%, respectively (for additional details, see Smider et al., 2002).

Primary Analyses

Effects of dose and stimulus valence on memory performance. To test for the effects of dose and stimulus valence (i.e., negative or neutral) on free-recall correct responses and recognition memory sensitivity (and to ensure that these effects did not vary for the alternate stimulus sets[5]) mixed three-way analyses of variance (ANOVAs) were computed with dose (placebo, 20 mg, and 40 mg), stimulus valence (negative or neutral), and set (A or B) as variables. Significant effects of dose were followed up with comparisons among individual means and trend analyses to test for the predicted quadratic trend (Keppel, 1991).

For errors of commission (i.e., intrusive errors) in the recall tasks, mixed two-way ANOVAs were computed with dose and set as variables. Commission error scores were not separated by stimulus valence because errors were not always easily scored as negative or neutral, and because errors, by definition, did not correspond to the negative or neutral stimuli obtained from the ANEW or IAPS normative sets. Thus, stimulus valence was not included as a variable in the analyses of errors.

Correlational analyses between cortisol levels and memory performance. In order to take advantage of the within-group variation in cortisol levels, we tested correlations between observed salivary cortisol levels and memory scores within each group separately, allowing further examination of the relation between cortisol and memory. Correlational analyses were conducted using the average of cortisol samples taken after drug uptake was regressed on the cortisol concentrations for Sample 1 to remove variance related to baseline cortisol levels. The residualized scores are hereafter referred to as the "postdrug cortisol levels."

Additional Analyses

Effects of dose on vigilance levels. The DS-CPT task provides signal detection metrics for overall performance and for performance broken down into three blocks. A one-way, between-group ANOVA was performed to test for effects of dose (placebo, 20 mg, and 40 mg) on overall DS-CPT scores (i.e., DS-CPT scores collapsed across block). To test the effects of dose on vigilance decrements over time, a two-way mixed ANOVA was performed with dose and block (DS-CPT Blocks 1, 2, and 3) as variables. In addition, one-way ANOVAs were computed for each block separately to adequately test for any effects of dose.

Effects of dose on emotional ratings. The effects of dose on emotional ratings of stimuli viewed during encoding tasks, and the effects of dose on current emotional state were examined with one-way ANOVAs.

Results

Salivary Cortisol Levels

Baseline salivary cortisol levels did not differ among the three groups: 3 min before drug administration, $F(2, 84) = 0.51$, *ns*. See Figure 1 for time course and magnitude of salivary cortisol elevations following drug administration. Cortisol levels in the 20-mg group were commensurate with endogenous elevations occurring during moderate behavioral stressors (e.g., final exam) or moderate exercise stress (e.g., 30 min on a stationary bicycle). The cortisol levels observed within the 40-mg group remained within the physiological range of cortisol, but such levels would be seen only during extreme stress, such as a marathon run or surgery (Kirschbaum & Hellhammer, 1989, 1994).

Analyses were performed within the placebo group to test for the presence of endogenous cortisol elevations associated with viewing emotional stimuli. Within-group *t* tests for the placebo group, examining the differences between the average of the three samples prior to the encoding tasks and each sample thereafter, revealed only declining cortisol values ($ts > 3.0$, $ps < .01$). Thus, viewing negative pictures and words did not cause endogenous cortisol elevations.

No significant differences between groups in cortisol levels occurred at any Session 2 time point ($Fs < 1.02$).

Vigilance

No effects of dose were found for DS-CPT performance analyzed across block or separately by block (highest $F = 0.92$).

Rating Tasks: Pleasantness and Arousal Ratings of Words and Pictures During Encoding

Pleasantness

There were no effects of dose on pleasantness ratings of negative or neutral words or pictures ($Fs < 1.33$).

Arousal

There were no effects of dose on arousal ratings (for negative stimuli: $Fs < 1.32$). However, marginally significant effects of dose were found for arousal ratings of neutral stimuli for both pictures, $F(2, 81) = 2.76$, $p = .07$, and words, $F(2, 81) = 3.08$, $p < .06$. Comparisons of individual means revealed that the 40-mg group rated neutral stimuli as more arousing than both the placebo group: pictures, $t(56) = 1.90$, $p = .06$; words, $t(56) = 2.23$, $p < .05$, and the 20-mg group: pictures, $t(57) = 2.28$, $p < .03$; words, $t(57) = 2.17$, $p < .05$.

Current Emotional State

No main effects or interactions of dose were found for any of the current emotional state indices ($Fs < 2.08$). Thus, emotional state was not significantly altered by cortisol elevations.

Session 1 Memory Results

Analyses of free-recall correct responses for both picture and word free-recall at Session 1 revealed no main effects of dose or Dose × Stimulus Valence interactions ($Fs < 1.86$). See Table 2 for comparison of free-recall correct responses versus errors of commission.

[5] Because the effects of set rarely interacted with the effects of dose, significant effects of set are reported as footnotes.

Table 2
Comparison of Free-Recall Correct Responses and Errors of Commission

Measures	Session 1			Session 2		
	Placebo	20 mg	40 mg	Placebo	20 mg	40 mg
			Picture free-recall			
Correct responses						
Negative pictures	16.52 ± 3.86	17.38 ± 3.76	18.03 ± 4.22	16.15 ± 3.72	17.00 ± 3.76	16.55 ± 3.84
Neutral pictures	10.11 ± 3.11	11.24 ± 2.64	10.97 ± 2.53	10.15 ± 3.29	11.17 ± 3.50	11.48 ± 3.42
Pictures: Errors of commission	1.11 ± 1.03	0.66 ± 0.86	0.53 ± 0.94*	0.63 ± 0.88	0.66 ± 0.86	0.79 ± 1.11
			Word free-recall			
Correct responses						
Negative words	5.50 ± 2.62	5.93 ± 2.49	5.62 ± 2.24	4.33 ± 2.18	5.17 ± 2.67	4.66 ± 2.24
Neutral words	2.39 ± 1.59	3.38 ± 1.47	3.20 ± 2.06	2.81 ± 2.00	3.69 ± 2.02	2.79 ± 1.70
Words: Errors of commission	3.36 ± 2.70	1.83 ± 1.67*	1.89 ± 1.42*	3.04 ± 2.07	2.76 ± 2.28	2.37 ± 2.00

Note. Values are reported as means (± *SD*).
*$p \leq .05$, Session 1 reduction in errors related to cortisol elevations.

Analyses of errors of commission for picture recall at Session 1 revealed a main effect of dose, $F(2, 79) = 3.07$, $p = .05$ (see Figure 2 and Table 2). The 40-mg group made fewer errors than the placebo group, $t(56) = 2.22$, $p < .05$. The 20-mg group showed a trend toward fewer errors than the placebo group, $t(55) = 1.80$, $p = .08$. The effect size for the difference between the 40-mg and placebo groups was 0.58, and between the 20-mg and placebo groups, the effect size was 0.48.

Similarly, a main effect of dose was found for Session 1 word recall errors, $F(2, 78) = 3.28$, $p < .05$ (see Figure 2 and Table 2). Both the 20-mg group, $t(55) = 2.58$, $p < .02$, and the 40-mg group, $t(55) = 2.57$, $p < .02$, made fewer errors than the placebo group. Effect sizes for the differences between the 20-mg and placebo groups and between the 40-mg and placebo groups were both 0.68. For sensitivity in the picture and word recognition tests at Session 1, no main effects or interactions of dose were found (Fs < 1.7).

Session 2 Memory Results

Free-Recall

No effects of dose on errors of commission were found for Session 2 (Fs < 1.47).[6] Analyses of free-recall correct responses for both picture and word free-recall at Session 2 revealed no main effects of dose or Dose × Stimulus Valence interactions (Fs < 1.82).[7]

Picture Recognition

For picture recognition memory at Session 2, a main effect of dose on sensitivity was found, $F(2, 78) = 6.37$, $p < .01$, but a Dose × Stimulus Valence interaction was not found, $F(2, 78) = 0.08$, *ns* (see Figure 3). The predicted quadratic trend was found across stimulus valence, $F_{quadratic} = 6.58$, $p < .02$. However, both the 20-mg group, $t(54) = 3.51$, $p < .01$, and the 40-mg group, $t(53) = 2.28$, $p < .05$, performed better than the placebo group. The effect size for the difference between the 20-mg and placebo group was 0.94, and between the 40-mg and placebo group, the effect size was 0.61. As expected, negative pictures were better recognized than neutral pictures across dose levels, $F(1, 78) = 19.36$, $p < .01$.

Word Recognition

For word recognition at Session 2, a main effect of dose was found, $F(2, 78) = 3.21$, $p < .05$. Again, no Dose × Stimulus Valence interaction emerged, $F(2, 78) = 1.06$, *ns*. The predicted quadratic trend was found across Stimulus Valence, $F_{quadratic} = 5.8$, $p < .05$ (see Figure 3). Across negative and neutral words, the 20-mg group performed better than the placebo group, $t(54) = 2.15$, $p < .05$ (effect size: $d = 0.57$), and marginally significantly better than the 40-mg group, $t(55) = 1.91$, $p = .06$. There was no difference between the 40-mg and placebo groups, $t(53) = .30$, *ns*. There was a trend toward a main effect of stimulus valence, reflecting unexpectedly better performance for recognition of neutral words than negative words, $F(1, 78) = 3.6$, $p < .07$.[8]

Misses Versus False Alarms

Misses and false alarms were analyzed separately to determine whether errors of omission or errors of commission solely caused the effects of dose on recognition memory. Of the four recognition memory tests (i.e., Sessions 1 and 2, pictures and words), only the Session 2 pictures revealed a main effect of dose for false alarms,

[6] Likely due to the fact that negative words were more semantically related than were neutral words. See the Discussion.

[7] For errors of commission in the word free-recall task during Session 2, a Dose × Set interaction was found, $F(2, 78) = 5.08$, $p < .01$, such that an effect of dose on errors emerged for Set B, $F(2, 39) = 4.03$, $p < .05$, but not for Set A, $F(2, 40) = 1.96$.

[8] For word free-recall correct responses at Session 2, a Dose × Set interaction was found such that only Set B showed the predicted quadratic relationship between dose and number of words recalled: for Set B, $F(2, 39) = 6.32$, $p < .005$, but for Set A, $F(2, 40) = 0.75$.

$F(2, 78) = 3.80$, $p < .05$, as well as a marginally significant main effect of dose on misses, $F(2, 78) = 2.92$, $p = .06$. No other effects of dose were found for analyses conducted separately on misses and false alarms. The ability to correctly accept targets and correctly reject distracters must both be taken into account for the effects of dose to emerge. Thus, for recognition memory, neither misses (errors of omission) nor false alarms (errors of commission) alone accounted for the effects of dose.

Correlations Between Observed Salivary Cortisol Levels and Memory Performance

Within the placebo and 40-mg groups, postdrug salivary cortisol levels were not correlated with memory performance (*p*s > .21). However, within the 20-mg group, postdrug salivary cortisol levels were negatively correlated with performance on free-recall tests (i.e., correct free-recall responses; see Table 3). Scatter plots confirmed that correlations were not due to outliers. Furthermore, for word recall, scores for negative stimuli alone were significantly related to cortisol levels, after variance related to memory for neutral stimuli had been removed (Session 1 increment in $R^2 = .22$, $p < .05$; Session 2 increment in $R^2 = .16$, $p < .05$). Thus, within the 20-mg group, higher cortisol levels predicted worse recall performance, especially for negative stimuli.

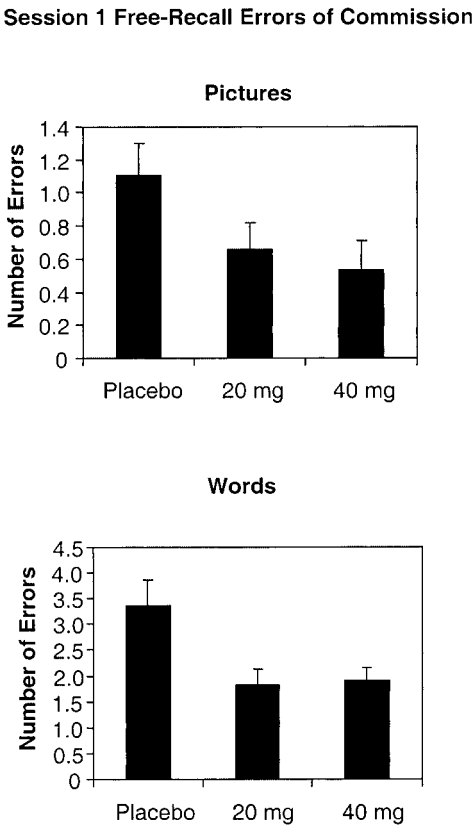

Figure 2. Graphs representing group means for Session 1 free-recall errors of commission. For words, participants in both the 20- and 40-mg groups made fewer errors than placebo group subjects (*t*s > 2.55). For pictures, participants in the 40-mg group made fewer errors than placebo group subjects ($t = 2.20$, $p < .05$), and participants in the 20-mg group made marginally fewer errors than the placebo group ($t = 1.80$, $p = .08$). Error bars represent *SEM*.

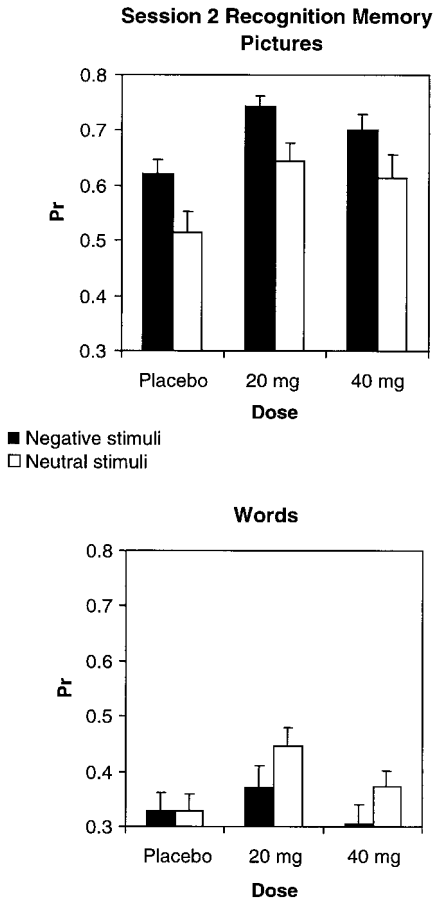

Figure 3. Graphs representing group means for Session 2 recognition memory tasks. For both words and pictures, main effects of dose were found (*F*s > 3.21). Error bars represent *SEM*.

Discussion

The current study replicates and extends previous research showing that acute glucocorticoid elevations affect explicit memory performance, in the absence of effects on other types of cognitive measures, such as vigilance (Kirschbaum et al., 1996; Newcomer et al., 1999; Wolkowitz et al., 1990). In the present study, memory tests were administered at two time points, once during the same session as encoding of stimuli, while cortisol levels were concurrently elevated (Session 1), and two evenings after the encoding session, when cortisol levels were no longer manipulated (Session 2). Memory effects differed for the two sessions. Compared with placebo, single doses of either 20 or 40 mg cortisol administered 40–45 min prior to encoding caused fewer errors of commission (i.e., intrusive errors) on a free-recall test during Session 1. However, during Session 2, effects emerged for recognition memory tests. An inverted-U quadratic trend was found across negative and neutral stimuli, with memory facilitation observed most predominantly in the 20-mg group, and less facilitation or none at all in the 40-mg group.

Table 3
Correlations Between Cortisol Levels and Free-Recall Performance Within the 20-mg Group

Session and task	All	Negative	Neutral
Session 1			
Word recall	−.47*	−.48**	−.15
Picture recall	−.31	−.21	−.22
Session 2			
Word recall	−.42*	−.47*	−.23
Picture recall	−.45*	−.39*	−.33

Note. Data represent *r* values for correlations between postdrug cortisol levels and free recall correct responses (for all stimuli, collapsed across negative and neutral, and separately for negative and neutral stimuli).
* $p < .05$. ** $p < .01$.

Glucocorticoids and Emotional Memory

In the current study, no interaction was found between stimulus valence and dose, which suggests that the effects of cortisol on memory do not differ substantially for negative and neutral information. However, within the 20-mg group, higher cortisol levels predicted poorer free-recall performance, primarily for negative stimuli. For the words, poorer recall for negative stimuli was related to higher cortisol levels, even after performance for neutral stimuli was accounted for. Thus, across memory tests, the 20-mg group showed memory facilitation, but within this group, poorer memory (especially for negative stimuli) was associated with higher cortisol levels. For negative information, the peak of the hypothetical dose–response curve between explicit memory formation and cortisol levels may have resided in the lower cortisol elevations in the 20-mg group. These findings suggest the speculative conclusion that there may exist a more lawful relation between decline in memory performance and increasing cortisol levels for negative, compared with neutral, information. The drop-off in memory performance that occurs with extreme cortisol elevations may occur more reliably for negative information than for neutral information, and the signal-to-noise ratio between glucocorticoids and memory may be enhanced for negative, compared with neutral, information. Together, the results from the current study suggest that an inverted-U-shaped function characterizes the relation between cortisol elevations and delayed recognition memory for both negative and neutral information, and that marked differences in the effects of cortisol on memory for emotional and neutral information do not exist. However, the findings are possibly suggestive of subtle valence-related differences in dose–response curves, namely, that the decline in memory associated with elevated cortisol may be more reliable for negative, compared with neutral, information. Future studies should specifically address this hypothesis.

The results obtained by Buchanan and Lovallo (2001), of cortisol-related memory facilitation only for emotionally arousing information, might be explained by a shift in the hypothetical dose–response curve for negative information. In animals, dose–response curves for exogenous administration of glucocorticoids vary on the basis of the inherent stressfulness of the task (Roozendaal, 2000). A leftward dose–response shift for stressful tasks is at least partially caused by differences in endogenous cortisol elevations. For tasks that produce very small glucocorticoid responses, moderate doses cause facilitation, but for tasks that elicit a strong endogenous glucocorticoid response, moderate glucocorticoid doses cause memory impairment (Roozendaal, 2000). However, passive viewing of aversive stimuli is typically not sufficient to cause endogenous cortisol elevations (Hubert & de Jong-Meyer, 1991; Kirschbaum & Hellhammer, 1994), and in the current study, no cortisol elevations associated with viewing stimuli were found in the placebo group. It is possible that other mechanisms in addition to differences in endogenous cortisol responses might cause a subtle dose–response shift, such as the combined effects of cortisol and the differential roles of the amygdala and hippocampus in emotional and nonemotional memory (e.g., Bechara et al., 1995).

Inverted-U-Shaped Dose–Response Function in Humans

The current study demonstrates in humans the hypothesized inverted U-shaped relation between cortisol and explicit memory, with facilitation occurring primarily at the 20-mg dose (which produced cortisol levels commensurate with endogenous elevations during moderate stress). However, the 40-mg dose (commensurate with extreme stress) was hypothesized to be sufficient to cause acute impairment in memory, but it did not cause performance deficits. Other studies have shown memory impairments at doses even lower than the moderate 20-mg dose in the current study (e.g., Kirschbaum et al., 1996). Across different studies, identical cortisol elevations have caused opposite effects on memory performance. These differences in findings may be explained by the circadian rhythmicity of cortisol, given that the timing of studies has differed (e.g., the Kirschbaum et al., 1996 study occurred in the late morning/early afternoon, whereas both the current study and the Buchanan & Lovallo, 2001 study occurred in the late afternoon and evening). Early in the day, GRs are already moderately saturated because of high endogenous morning cortisol levels, and it is likely that a small cortisol dose (which would cause no deficits or facilitation in the evening) would oversaturate GRs, causing memory impairment. This view is supported by an abundance of animal and human research showing the importance of time of day in relation to centrally mediated glucocorticoid effects (e.g., Bradbury, Akana, & Dallman, 1994; Fehm-Wolfsdorf, Reutter, Zenz, Born, & Lorenz, 1993; Lupien et al., 2002).

Additional factors also may account for the differences among studies. For instance, doses that do not affect memory after 1 day of exposure have been found to cause memory impairments after multiple days of treatment (e.g., Newcomer et al., 1999). The rate of rise of cortisol levels may also be an important factor. In the current study, the rate of rise of cortisol was relatively slow compared with that seen in some other studies. For instance, in the Kirschbaum et al. (1996) study, subjects peaked at a mean salivary cortisol concentration of 2.3 μg/dl within 90 min after administration of a 10-mg hydrocortisone tablet, whereas 90-min cortisol elevations of only 1.6 μg/dl (which were continuing to increase) were found in the current study after a 20-mg encapsulated oral dose. The relatively slow increase in the current study was likely due to a time-release effect caused by encapsulation of hydrocortisone tablets. It is known that the negative feedback effects of glucocorticoids vary depending on the rate of rise of plasma concentrations (Keller-Wood & Dallman, 1984). It is possible that

study procedures that led to slower rate of rise of cortisol may have contributed to the observations of beneficial effects on explicit memory processes in humans (Beckwith et al., 1986; Buchanan & Lovallo, 2001). Examination of this issue would require memory testing after systematic variation of rate of rise of cortisol by means of intravenous infusion. It is clear that there does not exist a simple dose–response relation between cortisol levels and memory performance. Various factors (such as time of day, rate of rise of cortisol, or type of task) moderate cortisol's role in memory.

Differential Effects of Cortisol on Memory Formation Versus Retrieval

The different findings from Session 1 and 2 in the current study provide further clarification of glucocorticoids' differential roles in memory formation and retrieval. Because memory effects were found at Session 2 when cortisol levels were not manipulated, the study provides definitive evidence in humans that cortisol has effects on memory formation that are independent from its effects on retrieval (de Quervain et al., 2000). Not only did results from the current study differ for the types of memory tasks in Session 1 and 2 (free-recall errors vs. recognition memory), but the shapes of the dose–response curves also differed for Session 1 and 2. Unlike the Session 2 recognition memory tasks, no quadratic function was apparent for the group differences in Session 1 errors of commission. This suggests that different neuropsychological processes account for the Session 1 and Session 2 results.

One could speculate that effects of glucocorticoids primarily on retrieval or generative processes might account for the Session 1 results. McEwen (1982) argued that glucocorticoids affect the capacity of the hippocampus to filter out task-irrelevant stimuli, and it is known that glucocorticoids modulate the strength of a fear response to a context, but not to a specific cue (Pugh, Fleshner, & Rudy, 1997). Thus, glucocorticoids may affect selection of contextually appropriate responses and filtering of internally generated responses. For Session 1 free-recall tasks, hydrocortisone may have facilitated inhibition of incorrect answers, filtering out inappropriate information during retrieval. In addition to the current study, previous studies have also found effects of glucocorticoids on errors of commission in the absence of effects on errors of omission (Wolkowitz et al., 1990). Furthermore, a recent study (de Quervain et al., 2000) provided evidence that cortisol has effects on retrieval that are independent of its effects on memory formation. de Quervain and colleagues found deficits in memory performance when cortisol was given before testing only, rather than before encoding (although these findings were for correct responses rather than errors). Thus, it is known that glucocorticoids affect retrieval processes, and it is plausible that effects isolated to generative processes during retrieval primarily accounted for group differences in Session 1 errors of commission in the current study.

Furthermore, the observation of no differences for recognition memory during Session 1 in the current study suggests that consequential differences among the dose groups in encoding processes did not occur. If group differences in encoding solely accounted for recognition memory results at Session 2, then recognition memory findings as strong as those seen during Session 2 should have been apparent in Session 1. Furthermore, direct effects of dose on retrieval cannot account for the Session 2 findings (because cortisol levels were not manipulated at Session 2, and cortisol levels among the groups did not differ at Session 2). Thus, effects on encoding and retrieval most likely do not account for the effects of dose on Session 2 recognition. The current study therefore suggests that hydrocortisone affects consolidation processes, which is highly consistent with the animal literature. In rats, systemic injections of glucocorticoids have their strongest effects when given in a narrow time window following training, with low posttraining doses facilitating, and high posttraining doses impairing, performance on various delayed tests of memory occurring when glucocorticoid levels are no longer manipulated (Lupien & McEwen, 1997; Roozendaal, 2000). Thus, the Session 1 and 2 results together suggest that cortisol has separable effects on consolidation and retrieval processes.

Cortisol and Current Emotional State

In the current study, dose was not related to current emotional state or to pleasantness ratings of stimuli. These data suggest that at these doses, cortisol is not strongly related to variation in positive or negative affect. However, the current study showed a trend toward higher arousal ratings of neutral stimuli for participants administered 40 mg hydrocortisone, which suggests that extreme elevations in cortisol may be associated with feeling aroused in response to stimuli that are objectively nonarousing. However, these findings should be interpreted with caution. Not only are the effects marginally significant, but the group difference occurred only in the 40-mg group, whose salivary cortisol levels on average were > 4 μg/dl while rating the stimuli. Endogenous cortisol increases of this magnitude do occur, for example, after a marathon, during surgery, or after extreme trauma (Kirschbaum & Hellhammer, 1989, 1994; Resnick, Yehuda, Pitman, & Foy, 1995). However, they do not constitute normal variation in cortisol levels. Prior studies have shown that pharmacologically administered glucocorticoids can increase negative or positive mood and activation (Plihal, Krug, Pietrowsky, Fehm, & Born, 1996; Schmidt, Fox, Goldberg, Smith, & Schulkin, 1999). However, doses used are typically outside the physiological range. For instance, the dose of cortisol used in the Plihal study (10 mg/hr for 9 hr overnight) would likely produce cortisol concentrations outside of the physiological range. Thus, evidence exists that cortisol by itself can affect subjective state, but endogenously occurring variation likely accounts for a relatively small portion of the variance in mood-related variables.

Limitations and Future Directions

A limitation of both the current study and the Buchanan and Lovallo (2001) study is that the same study participants were presented both neutral and emotional stimuli. It may be that viewing neutral stimuli in the context of negative stimuli moderates cortisol's effects on memory. Furthermore, although the study was adequately powered to detect the basic treatment effect of cortisol on memory, it may not have been sufficiently powered to detect valence-related differences in the effects of cortisol on memory. Important follow-up research includes a placebo-controlled dose–response study with stimulus valence as a between-subjects variable (in which participants view only neutral or only emotionally arousing stimuli). To examine the role of

endogenous cortisol elevations in human emotional memory, investigators must study tasks that elicit cortisol elevations, such as social stress tasks (e.g., Kirschbaum, Pirke, & Hellhammer, 1993), and test memory for emotionally laden and neutral stimuli learned during endogenous cortisol elevations. Decreasing cortisol or its ability to interact with GR (e.g., with metyrapone or RU486), as well as examining interactions with noradrenergic effects on emotional memory (e.g., O'Carroll, Drysdale, Cahill, Shajahan, & Ebmeier, 1999), will each provide further clarification of the role of stress hormones in emotional memory. Furthermore, the role of glucocorticoids in declarative memory for emotional information may be quite different from their role in aversive associative learning. It is also known that glucocorticoids are differentially involved in cue conditioning versus hippocampally based context conditioning (Pugh et al., 1997). The varying effects of stress-related elevations in hormones on different types of emotional learning must be further studied in humans.

Furthermore, if inverse correlations between cortisol levels and recall of negative stimuli were apparent in both the 20- and 40-mg groups (i.e., not just in the 20-mg group) in the current study, then the speculative conclusion that the drop-off in memory that occurs with increasing cortisol levels is more reliable for negative than for neutral information could be stated with more confidence. Possibly studies with intravenous infusion and detection of cortisol, which keep tighter control on circulating cortisol levels than oral administration, will allow the opportunity to more precisely examine the very subtle differences that appear to characterize the dose–response relations for emotional and neutral information.

This line of research will provide important data regarding processes involved in traumatic emotional memories. It must be determined whether cortisol increases during traumatic events play a role in the formation of traumatic memories. It may be the case that extreme elevations in cortisol are protective against too strong a memory trace. This interpretation is consistent with data showing that inadequate cortisol elevations following trauma is predictive of posttraumatic stress disorder (PTSD; McFarlane, Atchison, & Yehuda, 1997; Resnick et al., 1995), which necessarily includes tenacious recollections or reexperiencing of the traumatic event. Noradrenergic mechanisms are also implicated in PTSD (Yehuda, Southwick, Giller, Ma, & Mason, 1992). Future research is needed to elucidate the role of both cortisol and noradrenergic mechanisms in traumatic memory.

Psychological processes indirectly related to memory may account for some of the current findings. For instance, reductions in errors of commission in the free recall tasks during Session 1 may have been due to effects of cortisol on impulsivity, reducing the amount of guessing during the tasks. Evidence exists which suggests that endogenous cortisol levels under various conditions may be negatively correlated with trait impulsivity (Bruce, Davis, & Gunnar, 2002; King, Jones, Scheuer, Curtis, & Zarcone, 1990; Moss, Vanyukov, & Martin, 1995), and the possibility exists that cortisol plays a causal role in reducing impulsive behavior. The relations among cortisol, impulsivity, and generation of responses on cognitive tasks must therefore be further studied. In addition, it cannot be stated definitively that effects of cortisol on consolidation processes accounted for the recognition memory effects at Session 2. To precisely determine the role of cortisol in memory consolidation in humans, studies must vary the timing of cortisol administration with respect to encoding of stimuli, including a study condition of cortisol administration soon after encoding. Likewise, studies should be designed to examine the relation between cortisol and the rate of forgetting (e.g., using "savings scores") to more fully investigate cortisol's role in learning and memory consolidation.

Another limitation of the current study is that the inference can only be made tentatively that results depend on glucocorticoid activity in the brain. For instance, glucocorticoids affect biosynthesis of catecholamines in the adrenal medulla (Axelrod & Reisine, 1984). Thus, the results of the current study may be a result of glucocorticoid interactions with noradrenergic mechanisms, and only secondarily related to cortisol levels. Future studies of the relation between cortisol and memory should study interactions with noradrenergic mechanisms. Furthermore, it remains to be validated whether emotional stimuli such as the ones used in this study can be used to test hypotheses about the effects of glucocorticoids in the amygdala's role in memory. Neuroimaging studies should be conducted to test whether activation in the hippocampus, amygdala, and other brain areas is related to glucocorticoid-induced variation in memory. Furthermore, glucocorticoids inhibit transport of glucose into hippocampal neurons and glia, which is a mechanism implicated in certain glucocorticoid actions (Horner, Packan, & Sapolsky, 1990). However, this effect is dose- and time-dependent, with sustained (4 hr) elevations needed for inhibition, and is limited by abundant circulating glucose (Horner et al., 1990; Virgin et al., 1991). Thus, it is unlikely that the single administration of cortisol in the current study significantly affected glucose transport. In addition, participants were instructed to eat a light dinner 1 hr before Session 1, and were therefore likely in a variety of postprandial states, which would have limited any glucose-mediated effects of cortisol administration.

Another limitation of the current study was that several effects of stimulus set (Sets A and B) were apparent, that is, the two sets did not produce exactly the same pattern of results. Fortunately, none of the main effects or interactions of hydrocortisone dose were ever called into question by interactions with set. Word sets were also limited in that the negative words appeared to have a higher degree of semantic relatedness than did the neutral words, causing a spurious reduction in recognition memory performance for negative, compared with neutral, words. It is clear that the careful matching of word sets for multiple psychometric properties in this study was not sufficient. Future studies will need to more extensively match word sets for semantic relatedness and, possibly, other factors in addition to the ones used in this study.

Furthermore, two classes of stimuli (words and pictures) and two types of memory (free-recall and recognition memory) were studied, and corrections for multiple comparisons were not applied. However, some of the memory effects reported here would have survived a more conservative alpha level of .01, and the basic conclusions about emotional memory would not be altered. A benefit of having multiple memory tests is that the different types and timing of memory tests revealed diverse results, providing strong evidence that cortisol differentially affects various aspects of memory functioning. The general consistency of results for pictures and words suggests that these results are generalizable and not due to particulars of a single type of stimuli.

An additional limitation of the current study is that only male participants were included. Evidence now exists suggesting that the effects of cortisol on memory differ for men and women (Wolf,

Schommer, Hellhammer, McEwen, & Kirschbaum, 2001). Thus, future studies must systematically determine whether sex interacts with the various effects of glucocorticoids on memory.

Summary

The current study provides further evidence of specific effects of cortisol on explicit memory processes in humans. The result of an inverted-U-shaped function for Session 2 recognition memory was consistent with the neurobiological model of glucocorticoid effects on corticosteroid receptors. The current study revealed similar results for emotional and neutral stimuli, suggesting that effects of cortisol on memory do not differ substantially for emotional and neutral information. However, findings also suggest that the decline in memory performance with increasing cortisol levels may be more reliable for negative, compared with neutral, information. Differences in the dose–response curves for emotionally arousing and neutral information have been implicated by prior research showing memory facilitation only for emotionally arousing information (Buchanan & Lovallo, 2001). Memory results across studies may be explained by a slightly increased signal-to-noise ratio and/or a subtle leftward shift in the dose–response relation between glucocorticoids and explicit memory for emotional, compared to neutral, information. Future research is needed to specifically address these hypotheses.

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