THE EFFECTS OF HYDROCORTISONE ON FACIAL EMOTION RECOGNITION AND DECISION-MAKING

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ABSTRACT

When exposed to emotionally-arousing information, the stress system, or hypothalamic-pituitary-adrenal (HPA) axis, releases the hormone cortisol, which binds to receptors in brain regions important for emotional processing and decision-making. Evidence exists that HPA-axis manipulation affects memory for emotional items, but not facial expression recognition. Few studies have been conducted on HPA-axis manipulation during decision-making under risk. This study aimed to understand these effects in healthy men and women by administering a high or low dose of hydrocortisone (synthetic cortisol) during one session and a placebo during another session prior to performing a computerized facial emotion recognition task, the Diagnostic Analysis of Nonverbal Accuracy 2, and a decision-making task, the Cambridge Gambling Task. Results indicate facial emotion recognition and decision-making performance was not significantly influenced by hydrocortisone infusion. However, interesting trends were noted for facial emotion recognition and decision-making under conditions of high physiological stress.

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CHAPTER 1

INTRODUCTION

The Neuroendocrine System and the Stress Response

When an organism is confronted with a stressor, a complex network is activated that influences the physiological response of the brain and body through the release of several hormones. Initially, the thalamus and frontal lobes are engaged in the interpretation of the stressor through cognitive appraisal, while the limbic system simultaneously is engaged for evaluation of the stressor and actively recruits the hypothalamic-pituitary-adrenal (HPA) axis if needed (Dickerson & Kemeny, 2004). In the HPA axis, corticotrophin-releasing hormone (CRH) is released from the neurons of the hypothalamus, which signals the pituitary gland to secrete adrenocorticotropin hormone (ACTH), which subsequently signals the adrenal glands to release catecholamines, epinephrine and norepinephrine, and glucocorticoids, specifically cortisol in humans (Lupien, Maheu, Tu, Fiocco, & Schramek, 2007).

Cortisol released naturally during the sleep-wake cycle during relatively non-stressful periods, is important for fundamental physiological processes such as proper cardiovascular functioning (Kirschbaum, Wust, & Hellhammer, 1992). During times of stress, cortisol is crucial in providing energy, assisting in adaptive behavioral changes, and coping with stress (Lupien et al., 2007). Glucocorticoids are at their highest level in the morning and slowly decrease throughout the day, and increase again after a few hours

of sleep (Lupien et al., 2007). Cortisol is able to cross the blood-brain barrier, and receptors to which it binds are located throughout the brain allowing this hormone to influence a number of cognitive and emotional processes (Lupien et al., 2007). The two receptor subtypes are mineralocorticoid (MR), located primarily in the limbic system, and glucocorticoid (GR), found in cortical regions such as prefrontal cortex and subcortical structures associated with the limbic system such as the hippocampus (Lupien et al., 2007). The locations of MRs and GRs in the brain allow these different areas to be functionally affected by increased glucocorticoid secretion and, consequently, permit cortisol binding to influence cognition (Lupien et al., 2007). For example, the binding of receptors located in the amygdala, frontal lobe and the hippocampus influence learning and memory as well as processing of fear-related stimuli and emotional memory, and can do so in a beneficial or detrimental manner (Lupien et al., 2007).

Physiological differences exist between men and women in regards to the stress system. Men aged 24 years and older have more CRH neurons than women, and these numbers increase with age (Bao, Meynen, & Swabb, 2008). Higher levels of ACTH are secreted over 24 hours in men than women, but a similar amount of cortisol is released (Horrocks, Jones, Ratcliff, Holder, White, Holder, Ratcliff, & London, 1990). This implies that the female adrenal cortex is more sensitive to ACTH levels than males (Kajantie & Phillips, 2006).

Sex differences in the neuroendocrine stress response are also reported. A review of the literature indicates that after stimulation by a psychological stressor, there are higher responses of the autonomic system (eg. heart rate and blood pressure) and HPA axis in men than women (Kajantie & Phillips, 2006). Importantly, this difference only applies to

women who are between puberty and menopause (Kajantie & Phillips, 2006). An early study by Kirschbaum et al. (1992), that did not account for the phase of the menstrual cycle reported higher cortisol levels in men than women. However, a later study found that when presented with a psychological stressor, similar levels of free cortisol was released in men and in women during the luteal phase, but not the follicular phase, of their menstrual cycle (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999).

Corticosteroid-binding globulin (CBG) and estrogen are other factors that may contribute to the differences between men and women in the stress system. When cortisol is released, most binds to CBG, while the unbound portion is available during a stress induced response (Kajantie & Phillips, 2006). Estrogen has been shown to play an enhancing role in the production of this globulin (Moore, Kawagoe, Davajan, Nakamura, & Mishell, 1978). Because of the higher levels of estrogen in women, there are higher levels of CBG in premenopausal women than in men (Fernandez-Real, Pugeat, Grasa, Broch, Vandrell, Brun, & Ricart, 2002). However, studies on the role of estrogen in cortisol production have varying results. A group of postmenopausal women given estrogen replacement therapy and presented with a psychosocial stressor produced higher levels of total cortisol (Burleson, Malarkey, Cacioppo, Poehlmann, Kiecolt-Glaser, Berntson, & Glaser, 1998), while another similar sample of postmenopausal women showed a decrease in both free and total cortisol levels (Kudielka, Schmidt-Reinwald, Hellhammer, & Kirschbaum, 1999).

Facial Emotion Recognition

Facial recognition of emotions is a vital part of everyday human communication and social interaction, and is important in judging the character, intentions, and

trustworthiness of an individual. Charles Darwin's, "The Expression of the Emotions in Man and Animals" states that emotions are inherited and essential for survival (Purves, Augustine, Fitzpatrick, Hall, La-Mantia, McNamara, & White, 2008). Darwin also asserts that emotions are universal and people interpret emotions the same way (Breedlove, Rosenzweig, & Watson, 2007), which was later supported by Paul Ekman's cross-cultural studies of emotional face processing (Ekman, Sorenson, & Friesen, 1969). Numerous studies support categorizing facial emotions into happiness, sadness, fear, anger, surprise and disgust (Ekman et al., 1969), and those that are used most in everyday life are happiness, sadness, anger, and fear (Nowicki & Duke, 1994). Recognition of these emotions occurs by early childhood (Herba & Phillips, 2004). The ability to judge others' emotions and reacting to them appropriately is important in maintaining social friendships and ties.

The ability to recognize facial emotions is subserved by several brain regions. The amygdala and associated amygdala-based circuits, which contain receptors to which cortisol binds, contribute to the processing of facial expression recognition (Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003), and the amygdala is essential in preconsciously registering a threat and, in the case of facial emotions, providing a connection between the emotion that is seen and the significance of that emotion (Adolphs, 2002). Other brain regions engaged during facial emotion recognition include the insula, basal ganglia (Heberlein, Padon, Gillihan, Farah, & Fellows, 2008), fusiform gyrus, orbitofrontal cortex (OFC), superior temporal gyrus, and relevant somatosensory cortices (Adolphs, 2002). Several studies confirm the role of these areas in facial emotion recognition (Shmuelof & Zohary, 2005; Lotze, Heymans, Birbaumer, Veit, Erb, & Flor,

2006; Heberlein et al., 2008) and more specifically in the recognition of specific emotions. Iidaka and colleagues (2001) conducted an fMRI study that found negative facial emotion recognition, compared to the ability to differentiate shapes, primarily activated the right and left temporal cortices, the left amygdala, and the right inferior frontal cortex, while positive facial emotions activated the right posterior temporoparietal area. Reports of the effects of amygdala lesions on facial emotion recognition are inconclusive. A study by Adolphs et al. (2000) found that damage to the amygdala led to deficits in the facial recognition of fear but no other basic emotions. However, deficits in the recognition of several more negative emotions (fear, sadness, anger, and disgust) was reported elsewhere (Adolphs, Tranel, Hamann, Young, Calder, Phelps, Anderson, Lee, & Damasio, 1999), while another study found deficits in these emotions as well as recognition of happiness (Canli, Sivers, Whitefield, Gotlib, & Gabrieli, 2002). More areas of the amygdala become active during the recognition of fear than other emotions (Zald, 2003).

Past studies have also found differences between men and women in their ability to recognize facial emotions. In healthy individuals, women are better than men overall at correctly identifying facial emotions (McClure, 2000; Mufson & Nowicki, 2001). In particular, women are better at identifying negative expressions (Miura, 1993; Mufson & Nowicki, 2001); positive emotions are more easily identified than negative emotions (Ekman, 1982; Russell, 1994). An fMRI study by Lee and colleagues (2002) showed a lateralization effect, with men showing greater activation in left hemisphere regions while viewing happy faces compared to a baseline crosshair, and increased activation in right hemisphere regions during sad face viewing compared to a crosshair. Women, however,

showed greater activation in left hemisphere regions while viewing both happy and sad faces. In females, the amygdala shows greater activation when negative pictures of high intensity are viewed compared to neutral pictures and when both low and high intensity positive images are viewed compared to neutral pictures (Garavan, Pendergrass, Ross, Stein, & Risinger, 2001). Moreover, subjects rated the high intensity, negatively valenced images as more arousing than the low intensity images (Garavan et al., 2001). Guapo et al. (2009) investigated the sex difference by exploring the influence of hormones on emotion processing during the three stages of the menstrual cycle and comparing performance to men. Women had higher accuracy in recognition of fear and sadness during the follicular phase, characterized by low levels of estrogen, than women in other phases of the menstrual cycle and men (Guapo, Graeff, Zani, Labate, Reis, & Del-Ben, 2009). However, in another study women in the luteal stage, characterized by high estrogen levels, recognized more faces displaying fear, compared to women in the follicular phase (Pearson & Lewis, 2005). Testosterone administration in women led to deficits in the recognition of anger but not facial expressions of fear, disgust, sadness, or happiness (Von Honk & Schutter, 2007). High stress levels can decrease testosterone production (Chichinadze & Chichinadze, 2008) which can then have an impact on the empathy experienced by men that can then influence facial emotion recognition (Van Honk & Schutter, 2007). Thus, sex hormones appear to have a role in the recognition of emotions.

The "tend-and-befriend" theory provides a different perspective on sex differences in emotion recognition. Taylor et al. (2000) suggests that the female stress system can more appropriately be characterized as tend-and-befriend than fight or flight. The tend-

and-befriend theory implies that women's greater parental function and role in survival of their children makes them better at emotion recognition, especially happier emotions, because of the influence of their higher levels of estrogen and oxytocin (Taylor, Klein, Lewis, Gruenewald, Gurung, & Updegraff, 2000). In this case, "tending" removes a child from the situation that is causing the emotion of fear (Taylor et al., 2000). "Befriending" refers to a process in which women use social groups to reduce the harms from stressful conditions (Taylor et al., 2000). Along the same lines as "tend-and-befriend," Baron-Cohen (2002) discusses several variables that distinguish men and women and suggests that women can be characterized more as empathizers and thus would have more advantages in aspects of emotional processing.

Little information is available on the effect of cortisol on facial emotion recognition in healthy subjects; the existing literature on the acute effects of HPA-axis manipulation on memory of emotional items provides information on the valance of emotional stimuli detected and any dose dependent effects that may exist. Cortisol binds to regions in the hippocampus that are recruited during learning and memory (de Kloet, Oitzl, & Joëls, 1999), and the amygdala plays a critical role in this process by indicating the emotional salience of a stimulus or event (Abercrombie, Kalin, Thurow, Rosenkranz, & Davidson, 2003) and influences the actions of glucocorticoids (Roozendaal, 2000). This was supported by a study conducted by Buchanan and Lovallo (2001) in which 20 mg of hydrocortisone was administered to healthy subjects one hour prior to stimulus exposure. Subjects recalled emotional pictures, both pleasant and unpleasant, at a higher rate than neutral stimuli. Subjects who were administered cortisol gave lower arousal ratings to the unpleasant pictures than did those who were not. Although some studies show beneficial

effects of cortisol on memory for only emotional stimuli (Buchanan & Lovallo, 2001; de Quervain, Roozendaal, Nitsch, McGaugh, & Hock, 2000), others show benefits on memory for neutral stimuli (Lupien, Gillin, & Hauger, 1999; Lupien, Wilkinson, Briere, Menard, Ng King Kin, & Nair, 2002). A 20 mg oral dose of hydrocortisone, a low to moderate dose, led to good recall and recognition of both negative and neutral words and pictures, while a higher-dose administration of 40 mg hydrocortisone led to good recall but poorer recognition of both negative and neutral words and pictures in men (Abercrombie et al., 2003).

This study sought to investigate the influence of hydrocortisone administration on facial emotion recognition in healthy subjects. Because of similarities in the brain regions affected by cortisol and those recruited during facial expression recognition, hydrocortisone administration may impact facial emotion recognition on the Diagnostic Analysis of Nonverbal Accuracy 2 (DANVA2) task. It is hypothesized that subjects will more accurately identify positive (happy) than negative emotions, and that women will show more accuracy than men on negative emotion identification. Hydrocortisone administration will improve negative emotion identification accuracy. A low dose of hydrocortisone will improve overall accuracy and a high dose will decrease accuracy.

Decision-making

The decision-making process is an important factor in survival, and disturbances in rational decision-making can create social and financial problems (Bechara, Damasio, Damasio, & Anderson, 1994). Decision-making occurs when multiple potential responses are available and it is not clear which option is the best choice (Damasio, 1994). This leads to the evaluation of the pros and cons, often with limited time to do so (Damasio,

1994). An individual considers the probability that the option will yield the desired outcome as well as the emotional consideration of selecting a certain choice (Ernst & Paulus, 2005). These steps then allow for the carrying out of appropriate actions (Ernst & Paulus, 2005). Finally, according to the somatic marker hypothesis, the decision that was carried out is analyzed to aid in making more beneficial decisions in the future. (Bechara & Damasio, 2005).

Several factors can differentiate the decision-making process that occurs in different individuals. Selecting an optimal choice involves not being excessively cautious nor exceedingly risky (Fecteau, Pascual-Leone, Zald, Liguori, The´oret, Boggio, & Fregni, 2007). When making a risky decision, the available probabilities or possible outcomes that could be generated are considered against the reinforcement received from them (Rogers, Owen, Middleton, Williams, Pickard, Sahakian, & Robbins, 1999b.). Some individuals will choose the risky option while others will choose a safer option. Risk takers may not appreciate the possible losses that could occur with making a risky decision. Impulsivity is another factor involved in differential decision-making (Deakin, Aitken, Robbins, & Sahakian, 2004). This occurs when the available options are not evaluated and a hasty decision is made without taking into account the ramifications of the decision (Gerbing, Ahadi, & Patton, 1987). This lack of restraint can lead to a loss of a possible opportunity to receive a bigger reward associated with waiting.

A number of brain regions are engaged during the decision-making process. The ventromedial prefrontal cortex is important for decision-making (Clark, Bechara, Damasio, Aitken, Sahakian, & Robbins, 2008) and damage to this area can cause impulsiveness, reduced judgment, and improper social behavior (Berlin, Rolls, &

Kischka, 2004). The amygdala and the OFC are involved in punishment and reward processing (Bechara, Damasio, Damasio, & Lee, 1999) and, in conjunction with the nucleus accumbens and striatum (Augustine, 1996; Reynolds & Zahm, 2005), may also play a role in the emotional aspects of decision-making (Bechara & Damasio, 2005) and in mediating behaviors that attain rewards while evading punishment (Kolb & Whishaw, 2003). The striatum is also recruited during the prediction and expectation of a reward (Schultz, 2000). The OFC and ventral prefrontal cortex receive information that allows them to modify future decision-making or subsequent actions on trials (O'Doherty, Critchley, Deichmann, & Dolan, 2003). Lastly, the thalamus (Krain, Wilson, Arbuckle, Castellanos, & Milham, 2006) and the insular cortex, important for risk adjustment, are also involved in decision-making (Clark et al., 2008). Glucocorticoids act on these regions (Lupien et al., 2007), thereby playing a role in decision-making processes.

The OFC is recruited during risky decision-making as opposed to decision-making under ambiguity (Krain et al., 2006). The Cambridge Gambling Task (Rogers et al., 1999b.) is an example of a decision-making task under risk, in which the outcomes are unknown but the probabilities are known (Camerer & Weber, 1992). When probabilities are known, a subject who chooses the riskier choice will have a decreased chance of receiving the reward but if he or she does receive the reward, it will be a greater reward, and vice versa for choosing rewards that are not as risky (Bechara et al., 1994). The Iowa Gambling Task (IGT) (Bechara et al., 1994) is an example of a decision-making task under ambiguity in which neither outcomes nor probabilities are known (Clark, et al., 2008) and the dorsolateral prefrontal cortex is more engaged (Huettel, Stowe, Gordon, Warner, & Platt, 2006).

In decision-making processes that involve uncertainty, studies have found that emotion is involved (Hsu, Bhatt, Adolphs, Tranel, & Camerer, 2005; Kuhnen & Knutson, 2005), This is shown by deficits in the physiological processing of emotions leading to a decline in decision-making ability (Bechara et al., 1999). Emotion may play a role in decision-making before a decision is made or in considering the ramifications of one option over the other (Weller, Levin, Shiv, & Bechara, 2007). Choices are evaluated based on whether they will yield positive or negative outcomes. When a decision will most likely yield a positive effect, the nucleus accumbens is greatly involved and often leads to riskier behavior, while a negative effect activates the insular cortex and produces decisions based on risk-aversion (Kuhnen & Knutson, 2005).

Emotional feedback from prior decisions contributes to making future decisions (Starcke, Wolf, Markowitsch, & Brand, 2008). The ventromedial prefrontal cortex receives emotional information from the amygdala (Damasio, 1994) and integrates this with cognitive information (Weller et al., 2007). Damage to the amygdala prevents this information from being received, leading to a deleterious effect on decision-making (Purves et al., 2008). The somatic marker hypothesis suggests that decision-making benefits with the help of internal somatic signals that correspond to the valence and intensity of stimuli as well as provide feedback from prior similar situations (Bechara & Damasio, 2005). The formation of these somatic signals are prevented by stress (Preston, Buchanan, Stansfield, & Bechara, 2007), which can then lead to impairments in decision-making (Starcke et al., 2008).

Several studies conducted using gambling tasks reported sex differences, while others found no effect. For example, on the Cambridge Gambling Task women showed

less risk adjustment but men and women did not differ in the other aspects of decision-making (Deakin et al., 2004). Conversely, other studies using the IGT showed that men are better at decision-making compared to women (Bolla, Eldreth, Matochik, & Cadet, 2004; Reavis & Overman, 2001). In addition to the sex differences in decision-making, a study conducted by Reavis & Overman (2001) found an inverse relationship between testosterone levels in men and decision-making on the IGT but did not find any similar results for women during different stages of the menstrual cycle. Accordingly, women who had the highest levels of testosterone performed better on the decision-making task than men who had the highest levels of testosterone (Reavis & Overman, 2001). Similarly, administering testosterone to women led to unfavorable decision-making (Von Honk, Schutter, Hermans, Putman, Tuiten, & Koppeschaar, 2004). This may be caused by a decrease in punishment sensitivity and an increase in reward dependency (Bechara et al., 1999). These results may be reflective of hemispheric differences in males versus females during decision-making. Bolla and colleagues (2004) found that the left dorsolateral prefrontal cortex, temporal lobe, and left medial frontal gyrus were more engaged during a decision-making task for women than men, while the right lateral OFC was more active in men.

Decision-making by men and women is influenced by cortisol concentrations. Acutely administered 40 mg cortisol to men completing motivated decision-making resulted in more risky decision-making for high rewards by enhancing reward sensitive behavior and reducing punishment sensitive behavior and thus decreasing risk avoidance behavior (Putman, Antypa, Crysovergi, & Van der Does, 2010). Similar results were found in a study by Van den Bos et al. (2009) using the IGT and the Trier Social Stress

Test to acutely induce stress. Men and women with a high response to the stressor and thus higher cortisol levels would make decisions that were high in reward but also in punishment, thus showing a reduced sensitivity to punishment compared to those with low cortisol levels. In men, there was a direct relationship between performance and cortisol levels. However, in low responding women there was an increase in performance while those with high cortisol levels showed a decrease in performance. Women who were stressed were also quicker to complete the decision-making task.

This study sought to investigate the influence of cortisol using the Cambridge Gambling task, a decision-making task under risk. Because the brain regions engaged in this process contain receptors to which cortisol binds, hydrocortisone infusion may affect performance on this task. Based on previous research, it is hypothesized that a low dose of hydrocortisone will increase advantageous choices made by women while a high dose will negatively affect performance in men and women. Hydrocortisone administration will also decrease decision-making response time.

CHAPTER 2

EXPERIMENT

Method

Participants

Participants were recruited through National Institutes of Mental Health protocol 03-M-0102. Participants were compensated financially for their participation. Men and women between the ages of 19 and 50 participated in this study. Subjects for the DANVA2 task included 23 men that ranged from ages of 19 to 50 (mean:28.61, SD:8.669) and 20 women that ranged from ages of 19 to 41 (mean:29.15, SD:6.643). The Cambridge Gambling Task consisted of 19 men with ages ranging from 22 to 48 (mean:29.26, SD:8.608) and 15 women with ages ranging from 20 to 41 (mean:29.13, SD:6.424). Individuals with a neurological disorder, conditions that could have an effect on HPA-axis function, and irregular menstrual cycles were excluded. Subjects did not have a history or current presence of axis I disorders, substance abuse within the last year, substance dependence history, a history or current presence of mood disorders in first-degree family members, or thoughts of suicide in the past six months. Women were tested in the luteal phase of the menstrual cycle because of comparable salivary cortisol levels between men and women during this time (Kajantie & Phillips, 2006).

Materials

The Diagnostic Analysis of Nonverbal Accuracy 2 (DANVA2)

The DANVA2 (Nowicki & Duke, 1994) consists of the Adult Faces 2 subtest from the DANVA. Test-retest reliability ($r = .84$, $n = 45$) was accounted for by Nowicki and Carton (1993). The task investigates the ability to recognize facial expressions of different emotions by presenting 24 adult facial expressions photographs. The photographs represent emotions at low or high intensities of happiness, sadness, anger, and fear. Participants are verbally given the following instructions: "I am going to show you some people's faces, and I want you to tell me how they feel. I want you to tell me if they are happy, sad, angry, or fearful (scared). Please use your mouse to click on the emotion you think is best." Participants are then shown a photograph on the computer screen for 3 seconds, after which they identify the facially expressed emotional state from a list of possible emotions. The participant can continue to the next picture without choosing a response.

The Cambridge Gambling Task

The Cambridge Gambling Task (Rogers, Everitt, Baldacchino, Blackshaw, Swainson, & Wynne, 1999) is administered on a computer with a touch screen and takes about thirty minutes to complete. Blue and red boxes in ratios of 9:1, 8:2, 7:3, and 6:4 are presented. The participant must choose the color of the box behind which he or she believes a token is hidden. The token is randomly placed and is not dependent on any previous or later placing. Once the participant touches the color of their choosing, they place a bet based on their confidence that they have chosen the right color. Bets include

5%, 25%, 50%, 75%, or 95% of the total points they currently have. Each percentage appears on the screen for 5 seconds and the participant chooses the bet when it appears. Thirty six trials have bets increasing in order and thirty six trials have bets decreasing in order. Subjects begin with 100 points each for the ascending and descending conditions. Lastly, the computer indicates "You Win!" or "You Lose!" and shows what box the token is under. The score is also adjusted accordingly. The number of times a color box of majority is chosen is recorded and only bets placed when the participant chooses the majority colored box is taken into consideration. An individual who takes risks would choose the higher bets no matter what order the bets were presented in, while an impulsive person would choose bets presented early on regardless of sequence. The time it takes to choose the blue or red was also recorded. This reaction time allows for gauging the thought put into making the decision. The colors chosen based off of the probabilities and the amount bet allows for gauging of reasoning skills and risk taking behavior that occurred. This task also measures risk adjustment or the change in the amount bet in accordance with the ratio of boxes. For example, a subject may place higher bets when the ratio of boxes is 9:1 as opposed to 6:4.

Design and Procedure

This study is part of a larger research study investigating the neurophysiological and psychological reactions that occur with hydrocortisone administration with the presentation of emotional stimuli. Informed consent was obtained from all participants. Demographic information was collected and subjects were screened to ensure that they fit the criteria for participation in this study. This screening included clinical rating scales,

electrocardiogram (ECG), heart rate and blood pressure monitoring, and a pregnancy test for women. Clinical measures used for exclusionary criteria included the Hamilton Rating Scales, the Structured Clinical Interview for DSM-IV Disorders (SCID), and an unstructured interview with a psychiatrist.

In a randomized design, subjects were administered a bolus of .15 mg/kg (low dose) or .45 mg/kg (high dose) of hydrocortisone during one session and a placebo infusion during the other session. All infusions were performed during late morning (between 11:00 a.m. and noon). Blood plasma levels, through blood draws, were measured at baseline, post-infusion, and pre- and post-testing (+75 minutes and +150 minutes post-infusion) to monitor cortisol levels. After 75 minutes subjects began a test battery that included the DANVA2 and the Cambridge Gambling Task. Subjects first participated in an fMRI procedure and were then administered the neuropsychological test battery designed to assess emotional processing by a trained research assistant. The DANVA2 was administered approximately 15 minutes into the battery (+90 minutes), and the Cambridge Gamble Task approximately 45 minutes into the battery (+120 minutes). Cortisol was measured immediately prior to and following the test battery. The second session was one to four weeks after the first. If hydrocortisone was administered during the first session, a placebo was administered during the second session, and vice versa.

Blood was stored at -70 °C until it was assayed. Cortisol and cortisol binding globulin (CBG) were assayed by a biologist at NIMH (D. Venable). Total cortisol was assayed using the Nichols Advantage®Specialty System (Nichols Institute Diagnostics, San Clemente, CA) and CBG was assayed using the Corticosteroid Binding Globulin IRIA (Radioimmunoassay) Kit (Biosource, Nivelles, Belgium). These

measurements were used by D. Venable to calculate free cortisol by using the equation $U^2 K (1+N) + U (1+N+K) - C = 0$, where U is the molar concentration of unbound cortisol, K is the affinity of transcortin for cortisol at 37°, N is the proportion of albumin-bound to unbound cortisol, and C is the molar concentration of total cortisol. The obtained free cortisol levels were then converted to μM.

Results

Free Cortisol Concentrations in DANVA2 Subjects

A repeated measures ANOVA of free cortisol concentration difference scores (hydrocortisone – placebo) was performed. Results of the analysis indicated a significant main effect of time point ($F(1.523,59.386) = 12.104$, $p=.00$), time point by dose interaction ($F(1.523,59.386) = 6.667$, $p=.005$) (see Figure 1), and an overall effect of dose ($F(1,39) = 11.978$, $p=.001$) with the high dose group having a greater difference in free cortisol levels than the low dose group. Free cortisol levels were not significantly different between men and women.

Post-hoc single-sample t-tests showed significance for time points of pre-infusion ($t(42)= -2.130$, $p= .039$), post-infusion ($t(42)= 3.665$, $p= .001$), and pre-testing ($t(42)= 3.222$, $p= .002$) indicating free cortisol levels are different between the hydrocortisone and placebo sessions. Bonferroni pairwise comparisons of difference scores between the different time points sampled found significance for pre-infusion and post-infusion ($p=.002$), pre-infusion and pre-testing ($p=.004$), post-infusion and post-testing ($p=.003$), and pre-testing and post-testing ($p=.013$). Post-hoc independent t-tests of time points by dose comparisons indicated pre-infusion ($t(23.832)= -2.506$, $p= .019$), post-infusion

(t(41)= -3.164, p= .003), and post-testing (t(41)= -2.141, p= .038) were significant, and approached significance for pre-testing (t(41)= -1.904, p= .064) with all time points having greater differences in free cortisol levels between placebo to hydrocortisone sessions for the high dose group than the low dose group.

Further analysis was conducted to identify differences in free cortisol levels between the placebo session and the corresponding low dose infusion group and between the placebo session and the corresponding high dose infusion group. Single-sample t-tests show that free cortisol following high dose hydrocortisone infusion was significantly different from placebo levels at post-infusion (t(21)=4.643, p= .00) and pre-testing (t(21)=2.999, p= .007) time points and approached significance at the post-testing time point (t(21)=1.904, p= .071) (see Figure 1). Importantly, post-hoc tests did not show a significant difference between free cortisol levels following low dose hydrocortisone infusion, compared to placebo session at post-infusion (t(20)= .633, p= .534), pre-testing (t(20)= 1.434, p= .167), or post-testing (t(20)= -1.038, p= .311).

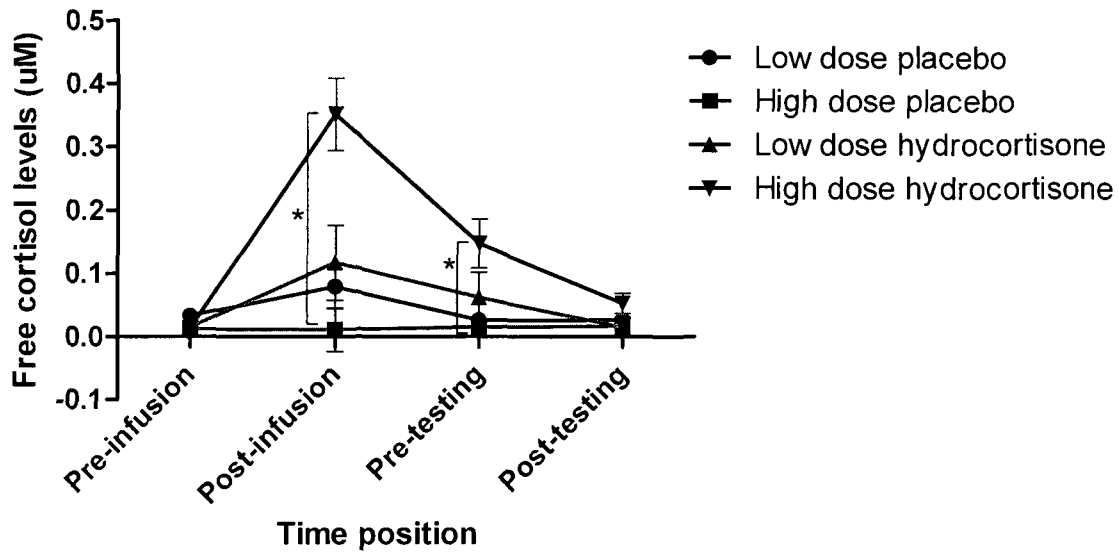

Figure 1 Free Cortisol Levels for All Subjects during Four Time Positions (DANVA2) Error bars represent standard error and * indicate significance at $p<.05$.

Free Cortisol Concentrations in Cambridge Gambling Task Subjects

Because of computer recording errors and outliers, not all participants who completed the DANVA2 were included in the analyses for the Cambridge Gambling Task and vice versa. This resulted in a different sample size, and therefore the analyses reported above were repeated for those who performed the Cambridge Gambling Task during both sessions. Repeated measures ANOVA of difference in free cortisol concentrations between sessions (hydrocortisone – placebo) indicated a significant main effect of time point ($F(1.555,46.659) = 10.128$, $p=.001$) and time point by dose interaction ($F(1.555,46.659) = 4.812$, $p=.019$) (see Figure 2). There was an overall effect of dose ($F(1,30) = 9.164$, $p=.005$) with the high dose group having a greater difference in free cortisol levels than the low dose group. Dose by sex interaction approached

significance ($F(1,30) = 2.912$, $p=.098$) with women in the high dose group having the greatest difference in free cortisol levels between sessions, followed by men in the high dose group.

Post-hoc single-sample t-tests for each time point indicated significant differences in free cortisol levels at pre-infusion ($t(33)= -2.099$, $p= .044$), post-infusion ($t(33)= 2.799$, $p= .008$), and pre-testing ($t(33)= 2.439$, $p= .020$). Similar to the free cortisol levels in DANVA2 subjects, Bonferroni pairwise comparisons of difference scores between the different time points sampled found significance for pre-infusion and post-infusion ($p=.008$), pre-infusion and pre-testing ($p=.013$), and post-infusion and post-testing ($p=.011$). Post-hoc independent t-tests for time points by dose comparisons were significant at pre-infusion ($t(23.871)= -2.441$, $p= .022$) and post-infusion ($t(32)= -2.638$, $p= .013$), and approached significance at post-testing ($t(32)= -1.946$, $p= .06$) between high and low dose hydrocortisone groups, with greater change in free cortisol values between placebo and hydrocortisone sessions for the high dose infusion group.

Further analysis was conducted to identify differences in free cortisol levels between the placebo session and the corresponding low dose infusion group and between the placebo session and the corresponding high dose infusion group. Single-sample t-tests show that free cortisol levels following high hydrocortisone infusion were significantly different from placebo levels at post-infusion ($t(13)=3.920$, $p= .002$) and post-testing ($t(13)=2.257$, $p= .042$) but approached significance at pre-testing ($t(13)=2.155$, $p= .051$) (see Figure 2). Similar to free cortisol levels in DANVA2 subjects, post-hoc tests did not indicate a significant difference in the low dose group free cortisol levels between

hydrocortisone and placebo sessions at post-infusion (t(19)= .646, p= .526), pre-testing (t(19)= 1.274, p= .218), or post-testing (t(19)= 1.678, p= .110).

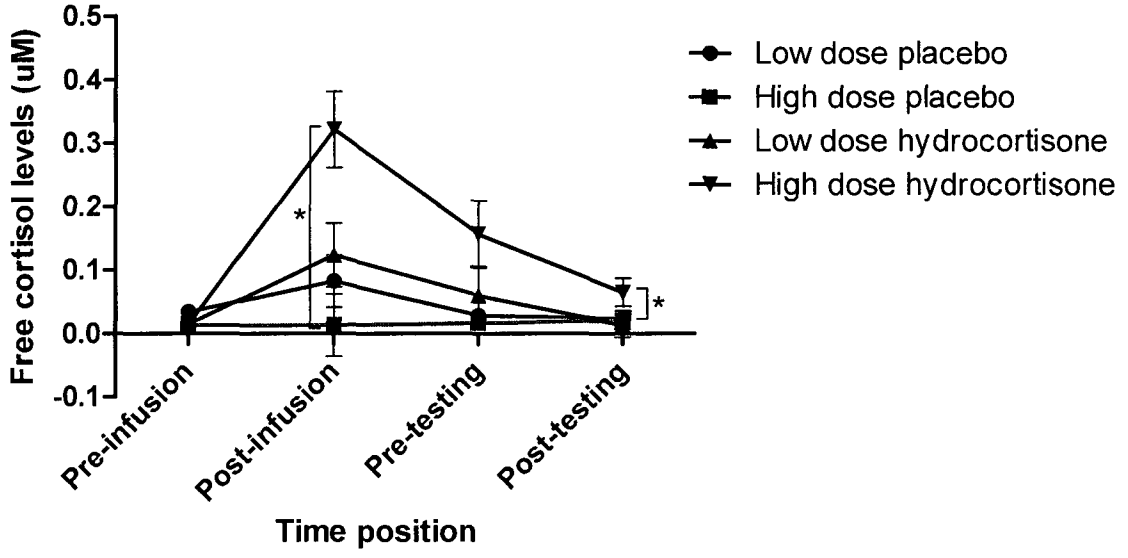

Figure 2. Free Cortisol Levels for All Subjects during Four Time Positions (Cambridge Gambling Task)
Error bars represent standard error and * indicate significance at p<.05.

DANVA2

Emotion

Total correct responses for each of four emotions (happy, sad, fear, anger) were computed, and a repeated-measures ANOVA with emotion as the within-subjects factor, total correct responses for the recognition of emotions as the dependent variable, and sex as the between-subjects factor for all subjects during the placebo condition found a significant main effect of emotion ($F(1,41) = 31.645$, $p<.001$). Bonferroni pairwise comparisons indicated higher recognition of happy emotions compared to sad ($p=.019$), fearful ($p=.001$), and angry faces ($p<.001$).

To investigate the effect of hydrocortisone infusion on emotion recognition,

difference scores (hydrocortisone-placebo) for total correct responses for the four emotions were calculated, and a repeated-measures ANOVA with emotion as the within-subjects factor, net total correct responses as the dependent variable, and dose and sex as the between-subjects factors was performed. The main effect of emotion was not significant, but the emotion by dose interaction approached significance (see Table 1). Post-hoc independent t-tests comparing low and high dose groups on the four emotions were not significant. Single-sample t-tests of hydrocortisone – placebo scores indicated a trend in the low dose group for correctly identifying happy facial expressions ($t(20)= 1.746$, $p= .096$) during low dose hydrocortisone infusion conditions than placebo conditions. The emotion by dose by sex interaction also approached significance (see Table 4). Figure 3 illustrates performance of the subjects and Table 2 indicates significant post-hoc comparisons. These post-hoc tests reflect more accurate recognition of angry emotions by men following high dose hydrocortisone infusion than placebo, compared to change in accuracy of recognizing other emotions in this group, change in accuracy in women, or change in accuracy in the low dose group.

Table 1: Repeated Measures Results for Emotions

Emotion	F value	df	p
Within-subjects Emotion	1.703	1,39	.20
Emotion x dose	3.095	1,39	.086
Emotion x sex	2.697	1,39	.109
Emotion x dose x sex	3.067	1,39	.088
Between-subjects Dose	.018	1,39	.895
Sex	.00	1,39	.990

Table 1 continued

Dose x sex	.014	1,39	.905

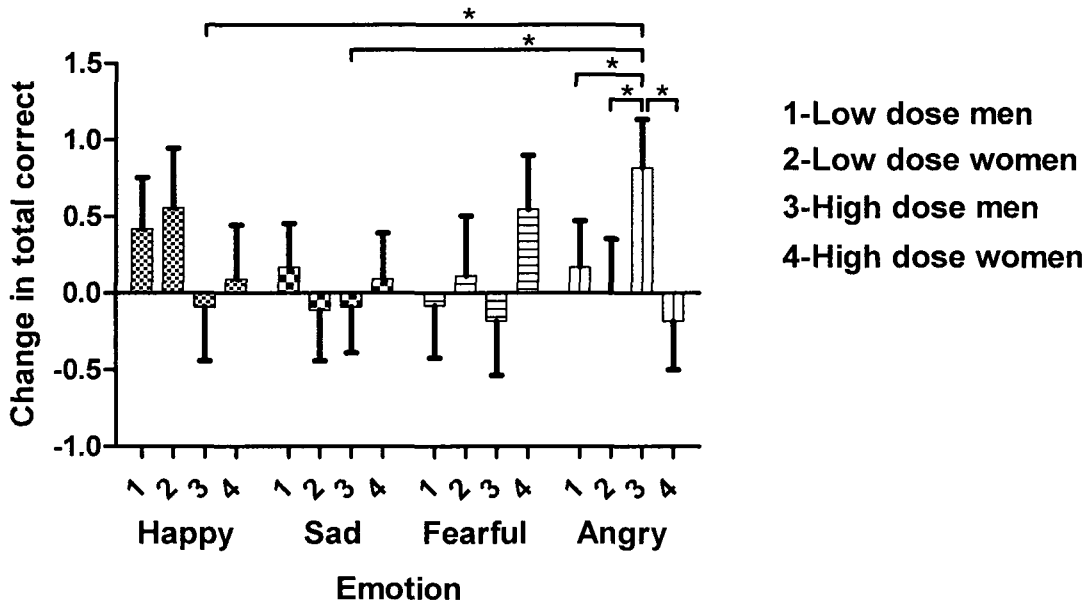

Figure 3. Change in Total Correct Response from Placebo to Hydrocortisone Condition Positive number indicates better performance during the hydrocortisone condition. Error bars represent standard error and * indicate significance at $p<.05$.

Table 2: Post-hoc Tests Identifying Significant Interactions of Emotion by Dose by Sex on DANVA2 Facial Emotion Recognition Performance using Difference Scores (hydrocortisone – placebo sessions)

Comparison (hydrocortisone – placebo scores)	t	df	p
High dose men happy vs. high dose men angry	-3.194	10	.010
High dose men sad vs. high dose men angry	-2.654	10	.024
Low dose men angry vs. high dose men angry	-2.795	18	.012
High dose women angry vs. high dose men angry	-2.389	20	.027
Low dose women angry vs. high dose men angry	-2.795	18	.012

Intensity

Total correct responses for intensity (high and low) were computed. During placebo

conditions, a repeated-measures ANOVA with emotional intensity as the within-subjects factor found the main effect of intensity to be significant ($F(1,41) = 41.121$, $p<.001$). Post-hoc paired t-tests found higher correct recognition of high intensity emotions ($t(42) = 6.518$, $p<.001$).

The effect of hydrocortisone infusion on emotional intensity recognition was analyzed. Difference scores (hydrocortisone-placebo) for total correct for high and low emotional intensity were calculated, and a repeated-measures ANOVA was performed. No significant main effects, interactions, or between-subjects effects were found (see Table 3).

Table 3: Repeated Measures Results for Intensity of Emotions

Intensity	F value	df	p
Within-subjects			
Intensity	.255	1,39	.616
Intensity x dose	.132	1,39	.718
Intensity x sex	1.478	1,39	.231
Intensity x dose x sex	.121	1,39	.730
Between-subjects			
Dose	.018	1,39	.895
Sex	.00	1,39	.990
Dose x sex	.014	1,39	.905

Cambridge Gambling Task

Reaction Time (RT)

RT, defined as the time taken to choose a color, blue or red, irrespective of ascending or descending condition, for the placebo condition was analyzed. Data points greater than three standard deviations from the mean were excluded. A repeated-

measures ANOVA, with ratio condition as the within-subjects factor, RT for each ratio as the dependent variable, and sex as the between-subjects factor was used for analysis. After corrections for violation of Mauchly's Test of Sphericity, the main effect of reaction time (RT) was significant ($F(2.40,76.805) = 4.229$, $p = .013$). Bonferroni pairwise comparisons for RT found significance for 7:3 ratios by 9:1 ratios ($p = .024$) with faster choices made when deciding between color boxes in the 7:3 ratios condition than in the 9:1 ratios condition.

To investigate the effect of hydrocortisone infusion on RT, difference scores between placebo and hydrocortisone infusion conditions were calculated. A repeated-measures ANOVA was used to analyze the net scores (hydrocortisone-placebo) of RT data. After corrections were made for violation of sphericity, the main effect and interactions, excluding net RT by dose which approached significance, were not significant (see Table 4). Post-hoc independent t-tests for each net RT by dose did not show significant differences. Within the high dose group, net RTs for 9:1 and 7:3 ratios were significantly different ($t(13) = 2.425$, $p = .031$), with high dose hydrocortisone infusion resulting in significantly decreased net RTs for the 9:1 ratio condition compared to 7:3 ratio trials. No significant between-subjects effects were found (see Table 4).

Table 4: Repeated Measures Results for Reaction Time

Reaction Time	F value	df	p
Within-subjects			
RT	1.468	2.824,84.734	.231
RT x dose	2.204	2.824,84.734	.097
RT x sex	1.676	2.824,84.734	.181
RT x dose x sex	1.416	2.824, 84.734	.245

Table 4 continued

Between-subjects			
Dose	.045	1,30	.833
Sex	.042	1,30	.839
Dose x sex	.596	1,30	.446

Probability

For placebo sessions, a repeated-measures ANOVA (with corrections for sphericity) found the main effect of probability (defined as the percentage of trails that the subject chose the box color most likely to be rewarded; that is, the color that was most plentiful) to be significant ($F(1.638,52.430) = 7.422$, $p = .003$). Bonferroni pairwise comparisons indicated a significant difference for probability between the 6:4 ratio and the 8:2 ratio conditions ($p = .014$), with more advantageous choices made at 8:2 ratios.

To determine the effect of hydrocortisone infusion on probability, a repeated-measures ANOVA was used to analyze net scores (hydrocortisone – placebo) of probability. Mauchly's Test of Sphericity was violated and corrected values were used. The main effect and interactions, except for net probability by dose, which approached significance, were not significant (see Table 5). To explore this trend, several post-hoc tests were performed and found significant. Figure 4 illustrates performance of the subjects and Table 6 indicates significant post-hoc comparisons. These tests indicated greater net probability of choosing the likely option in the 7:3 ratio conditions following high dose hydrocortisone infusion compared to other ratios (8:2, 9:1) and following low-dose infusion.

No significant between-subjects effects were found for dose by sex but dose was

approaching significance (see Table 5) with the low dose group making fewer advantageous choices during stressed times and the high dose group making greater advantageous choices under the hydrocortisone condition; men showed a trend for making more advantageous choices following hydrocortisone infusion while women made fewer advantageous choices during the hydrocortisone condition.

Table 5: Repeated Measures Results for Probability

Probability	F value	df	p
Within-subjects			
Probability	.194	1.702,51.065	.789
Probability x dose	3.001	1.702,51.065	.066
Probability x sex	1.203	1.702,51.065	.303
Probability x dose x sex	.834	1.702,51.065	.423
Between-subjects			
Dose	3.990	1,30	.055
Sex	3.386	1,30	.076
Dose x sex	.684	1,30	.415

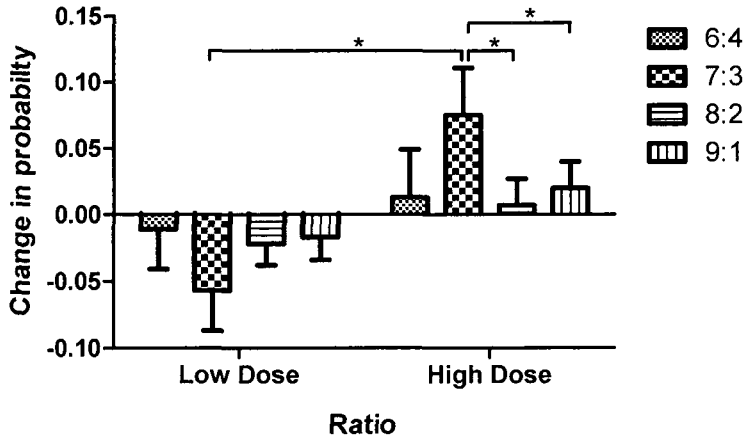

Figure 4. Change in Probability from Placebo to Hydrocortisone Condition
Positive number indicates more advantageous colors chosen during the hydrocortisone condition. Error bars represent standard error and * indicate significance at $p<.05$.

Table 6: Post-hoc Tests Identifying Significant Interactions of Dose by Probability on Cambridge Gambling Task using Difference Scores (hydrocortisone – placebo sessions)

Comparison (hydrocortisone – placebo scores)	t	df	p
High dose 8:2 vs. High dose 7:3	-2.744	13	.017
High dose 9:1 vs. High dose 7:3	-3.341	13	.005
Low dose 7:3 vs. High dose 7:3	-2.835	32	.008

Ascending and Descending Bets

For placebo sessions, a repeated-measures ANOVA (after corrections for violation of sphericity) found the main effect of direction (ascending or descending bets) ($F(1,32) = 75.302$, $p < .001$) and ratio condition ($F(1.467, 46.947) = 43.593$, $p < .001$) to be significant. The Bonferroni pairwise comparison for direction was significant ($p < .001$) with higher bets placed in the descending condition. Bonferroni pairwise comparisons for ratio condition was significant for 6:4 and 7:3 ($p = .003$), 6:4 and 8:2 ($p < .001$), 6:4 and 9:1 ($p < .001$), 7:3 and 8:2 ($p < .001$), and 7:3 and 9:1 ($p < .001$). Direction by sex interaction ($F(1,32) = 4.615$, $p = .039$), direction by ratios interaction ($F(1,32) = 8.843$, $p = .006$), and direction by ratios by sex interaction ($F(1,32) = 5.446$, $p = .026$) were also significant.

The difference in bets chosen (hydrocortisone – placebo) in the ascending and descending conditions (direction) was analyzed using repeated-measures ANOVA with corrections for violation of sphericity. The main effects and interactions were not significant (see Table 7). Between-subjects effects found approaching significance for sex, with men overall making higher bets following hydrocortisone infusion and women placing higher bets in the placebo condition.

Table 7: Repeated Measures Results for Bets during Ascending/descending Conditions

Ascending/descending bets	F value	df	p
Within-subjects			
Direction (Ascending/descending)	2.186	1,30	.150
Direction x dose	.050	1,30	.825
Direction x sex	.488	1,30	.490
Probability x dose x sex	.064	1,30	.802
Ratios (6:4, 7:3, 8:2, 9:1)	.439	1.964,58.931	.644
Ratios x dose	.419	1.964,58.931	.656
Ratios x sex	.753	1.964,58.931	.473
Ratios x dose x sex	.773	1.964,58.931	.464
Direction x ratios	.285	2.158,64.746	.770
Direction x ratios x dose	.927	2.158,64.746	.407
Direction x ratios x sex	.050	2.158,64.746	.959
Direction x ratios x dose x sex	.997	2.158,64.746	.380
Between-subjects			
Dose	.00	1,30	.983
Sex	4.163	1,30	.050
Dose x sex	.972	1,30	.332

CHAPTER 3

DISCUSSION

This study sought to investigate the effects of low and high dose hydrocortisone administration in healthy subjects on facial emotion recognition and decision-making. Hydrocortisone administration increased free plasma cortisol levels while placebo administration did not. Expected effects were found on facial emotion recognition and decision-making for the placebo condition, however no significant effects of hydrocortisone infusion were found; this suggests that healthy people are resilient to the effects of acute hydrocortisone administration on these two cognitive processes. Interesting trends were noted.

As expected, there was an increase in free plasma cortisol concentrations between the placebo and hydrocortisone sessions after infusion, which was maintained when measured prior to the testing session at 75 minutes post-infusion, but was negligible when sampled at post-testing (150 minutes post-infusion). When free cortisol was investigated by dose, high dose hydrocortisone infusion resulted in significantly elevated free cortisol levels post-infusion while low dose hydrocortisone infusion did not result in significant elevation of free cortisol. These results are important when considering the role of low dose hydrocortisone infusion on healthy subjects' performance in this study. The results of analyses did not find sex differences in free cortisol levels following hydrocortisone administration. This lack of significant difference in cortisol response

between men and women may suggest that sex differences in task performance may result from differential receptor distribution or binding patterns in regions that involve both emotional and decision-making processes.

Because cortisol receptors are located in brain regions involved in facial emotion recognition and decision-making processes, it was hypothesized that cortisol would influence these cognitive processes. The results from this study did not completely support the hypotheses. Subjects were not more accurate in identification of positive (happy) than negative emotions (sad, fear, angry) following hydrocortisone administration. Consistent with earlier studies, subjects recognized more happy faces during the placebo condition (Ekman, 1982; Russell, 1994), and this relationship remained following hydrocortisone administration, indicating that change in free cortisol concentrations did not influence recognition of happy faces. However, subjects in the low dose group did show a trend for correctly identifying more happy face trials following hydrocortisone infusion, compared to the placebo condition. Notably, free cortisol levels following low dose infusion were not significantly different from placebo levels, suggesting this trend may not be attributable to cortisol effects. However, genomic effects of acute cortisol elevation may remain in effect for a period of time. Although cortisol concentrations in the periphery are low, this is not an indication that cortisol is no longer binding to receptors in the brain or having an effect on central processes. Second, no sex differences were found during placebo or hydrocortisone administration sessions; women following low or high dose hydrocortisone administration did not show more accuracy than men with similar dose administrations on negative emotion identification. Third, high dose hydrocortisone administration did

not decrease accuracy. Men in the high dose group did show a trend for correctly identifying more angry faces following hydrocortisone than placebo administration compared to men following low dose hydrocortisone administration than placebo (see Table 5). Surprisingly, hydrocortisone administration did not increase or decrease accuracy of facial emotion recognition of either high or low intensities; recognition accuracy was similar to that during placebo conditions in which high intensity emotions were accurately identified more often than low intensity emotions.

On the Cambridge Gambling Task, subjects administered hydrocortisone showed trends for decision-making under risk. Compared to placebo, hydrocortisone administration resulted in a trend for reaction times for 9:1 ratios compared to 7:3 ratios; hydrocortisone led to faster reaction times for 9:1, a ratio that is easily processed, than 7:3. Reaction times for each ratio, 6:4, 7:3, 8:2, and 9:1, were not significantly influenced by hydrocortisone administration. No sex differences in the effects of hydrocortisone administration was found, contrary to the study by Van den Bos et al. (2009) that reported women who had a significant increase in cortisol following a psychological stressor made decisions quicker than men. However, Van den Bos et al. used a decision-making task under ambiguity as opposed to risk, as was used in the current study.

Men and women in the hydrocortisone and placebo sessions were alike in choosing the color of the box present in the greatest amount, i.e. lowest-risk choice. Compared to other ratios, a trend was shown for the more advantageous choice in the 7:3 ratio trials being made following high dose hydrocortisone administration (see Table 12). Specifically, high dose hydrocortisone infusion provided an advantage in choosing the

box color most likely to be rewarded (i.e. the color displayed by seven of the ten boxes), and thus decreased risk-taking behavior, compared to other ratios with both low and high dose hydrocortisone administration, which resulted in riskier decision-making because more disadvantageous choices were made.

Hydrocortisone administration did not lead to a change from placebo in the amount bet in either the ascending or descending conditions. This indicates that there was no significant change in impulsive behavior, that is choosing a bet quickly regardless of whether the choice is likely to be advantageous, and risk-seeking behavior, that is usually placing high bets in either direction, after hydrocortisone administration. Subjects appeared to choose bets using similar risk adjustment strategies when betting on different ratios of boxes.

The ability to appropriately recognize facial emotions has been shown to be important in evolutionary terms as well as for modern day life. Through pan-cultural studies, Ekman et al. (1969) demonstrated that the ability to recognize facial emotions is not as influenced by social factors but more likely based in evolutionary origins. Facial emotion recognition is essential for effective social interactions in which emotional expressions yield nonverbal communication. Facial expressions provide information about the intentions of an individual as well as what others think of us. Positive facial expressions are welcoming while negative expressions, such as fear and anger, signal us to avoid unsafe situations.

Because no significant sex differences were found in free cortisol concentrations, the sex differences in facial emotion recognition may be attributable to other factors. The "tend-and-befriend" theory suggests that recognition of fear may allow a mother under

stress to better provide comfort for her children. Although not significant, women in the high dose hydrocortisone condition did recognize more fearful faces than men in the high dose condition compared to placebo. This study also found that men following high dose hydrocortisone administration compared to placebo were better at recognizing angry faces than women in both dose conditions compared to placebo. From an evolutionary perspective, sensing anger during tense situations would help men prepare for or avoid dangerous situations by leading to a change in their behavior. Testosterone levels can also provide a potential explanation as to why men may be better at recognizing angry faces (Guapo et al., 2009). Because low and high testosterone levels impact facial emotion recognition (Von Honk & Schutter, 2007) and increases in stress can impact testosterone production, future studies that measure testosterone levels would allow for better interpretation of its role in facial emotion recognition during stressful conditions.

Few studies have been conducted on the effect of cortisol on decision-making. Van den Bos, et al. (2009) found an effect of induced stress on decision-making using the IGT, while this study found only minimal effects of hydrocortisone administration. It is important to distinguish the IGT and the Cambridge Gambling Task. Learning and working memory, cognitive processes that are affected by cortisol (Lupien et al., 2007), are essential parts of the IGT, while the Cambridge Gambling Task was carefully constructed to eliminate the need for learning and memory for successful performance (Deakin et al., 2004). Because differences exist in brain regions utilized during performance of each task, it suggests that cortisol may have a greater impact on one verses the other. Also, as previously mentioned, the IGT is a decision-making task under ambiguity and the Cambridge Gambling Task is under risk. These two types of decision-

making tasks activate different brain areas and perhaps these differences also underlie a differential influence of cortisol.

Dopamine levels are influenced by stress (Adler, Elman, Weisenfeld, Kestler, Pickar, & Breier, 2000) and, because of dopamine's role in reward processing, it may influence the decision-making process by reinforcing decisions. It is suggested that subjects experiencing acute stress are risk-seeking (Coates & Herbert, 2008) while chronic stress leads to risk-aversion (Putman et al., 2010). Acute stress seems to increase dopamine activity in the nucleus accumbens of rats (Kalivas & Duffy, 1995) while chronic stress decreases dopamine transmission to this area (Mangiavacchi, Masi, Scheggi, Leggio, De Montis, & Gambarana, 2001). The orbital PFC also receives dopaminergic input (Koob & Bloom, 1988) which may impact decision-making through its rewarding and reinforcing properties. Receiving reinforcement determines which behaviors are repeated, which are not repeated, and which are altered in the future (Cohen, 2008). Although this study did not find an increase in risk-seeking behavior, as is suggested to occur during conditions of acute stress, measures of homovanillic acid levels (HVA) would help in determining the role of dopamine in this study as well as distinguishing the acute and chronic effects of stress on decision-making. In addition, sex differences in decision-making were not found. Gonadal steroid hormones, estrogen, progesterone, and testosterone interact with dopamine and also influence decision-making (Dreher, Schmidt, Kohn, Furman, Rubinow, & Berman, 2007). This hormonal influence is indicated through the differential activation of brain regions involved in decision-making during different stages of the menstrual cycle and the variation of dopamine levels dependent on the phase of the cycle (Dreher et al., 2007). Again,

assaying HVA levels would contribute to a more concrete understanding of the relationship between dopamine and stress.

Studies have shown that emotion influences decision-making, and stress can influence one's emotions; therefore, inducing elevations in cortisol through psychological manipulation may have different outcomes from physiologically induced elevations. In real life situations, emotions could not only be related to the decision-making process but also be an external factor caused by another source. This was imitated by having subjects complete a decision-making task under risk after being told they would be giving an impromptu speech (Starcke et al., 2008). This anticipatory stress interfered with advantageous decision-making (Starcke et al., 2008). Stressful situations invoke emotional responses, usually those associated with a negative mood (Buchanan, al'Absi, & Lovallo, 1999), that are not directly relevant to the decision to be made but still impact effective decision-making by impeding the formation of somatic markers (Bechara & Damasio, 2005).

There were several limitations to this study. First, sample size was reduced due to some participants not returning for the second session, data loss from computer recording errors, and exclusion of outlying data points. Second, results from the low dose group should be considered cautiously because the free cortisol levels following hydrocortisone infusion were not elevated when the testing session began. In the future, administering the tasks soon after infusion may help to provide more direct results between elevations in cortisol levels and cognitive processing. Third, facial emotion recognition was tested in a somewhat artificial fashion. In everyday situations, cues such as environmental situations and the posture of others play a role in the recognition of facial emotions. In

addition, the tasks used in this study may not have been sensitive enough to acute hydrocortisone administration. Fourth, as previously mentioned, physiological manipulation of the HPA axis can have a different effect on cognitive processes than psychological stressors. Psychological stressors are processed first by the limbic system and the prefrontal cortex and then activate the HPA-axis (Herman & Cullinan, 1997), which is similar to the circuitry utilized in facial emotion recognition and decision-making. Physiological stress inducers, such as administration of hydrocortisone, CRH and ACTH, directly activate the HPA-axis (Herman & Cullinan, 1997). Different types of psychological stressors can also lead to differential activity in men and women. For example, knowing that one is going to be evaluated by others led to higher cortisol levels in men than women prior to the event occurring (Kirschbaum et al., 1992). Evaluation by others and lack of control over a situation produces greater and longer lasting stress responses than when tasks involve only one of these factors (Dickerson & Kemeny, 2004). Future studies should compare the effects of psychological and physiological measures to consider the initial differences in processing that psychological stressors produce and the impact this can have on cognitive processes.

APPENDIX A

DESCRIPTIVE STATISTICS

Table A: Sample Size, Mean, and Standard Deviations for Free Cortisol Levels (uM) for Each Time Point and Session for DANVA2 Subjects

Time point and condition	n	Mean free cortisol levels (uM)	SD
pre-infusion			
Placebo			
Low	21	.033	.052
High	22	.012	.016
Hydrocortisone			
Low	21	.015	.022
High	22	.013	.014
post-infusion			
Placebo			
Low	21	.079	.231
High	22	.011	.012
Hydrocortisone			
Low	21	.117	.136
High	22	.351	.351
pre-testing			
Placebo			
Low	21	.026	.045
High	22	.015	.02
Hydrocortisone			
Low	21	.062	.132
High	22	.147	.224
post-testing			
Placebo			
Low	21	.026	.06
High	22	.017	.028
Hydrocortisone			
Low	21	.147	.014

Table A continued

High	22	.053	.102

Table B: Sample Size, Mean, and Standard Deviations for Free Cortisol Levels (uM) for Each Time Point and Session for Cambridge Gambling Task Subjects

Time point and condition	n	Mean free cortisol levels (uM)	SD
pre-infusion			
Placebo			
Low	20	.034	.053
High	14	.013	.02
Hydrocortisone			
Low	20	.015	.023
High	14	.015	.016
post-infusion			
Placebo			
Low	20	.082	.237
High	14	.013	.014
Hydrocortisone			
Low	20	.123	.144
High	14	.321	.306
pre-testing			
Placebo			
Low	20	.028	.046
High	14	.016	.025
Hydrocortisone			
Low	20	.06	.136
High	14	.156	.267
post-testing			
Placebo			
Low	20	.024	.061
High	14	.021	.035
Hydrocortisone			
Low	20	.013	.014
High	14	.065	.127

Table C: Sample Size, Mean, and Standard Deviations for Difference Scores for Each Emotion by Dose

Emotion and Dose	n	Mean Difference (hydrocortisone – placebo)	SD
Happy			
Low Dose	21	.476	1.25
High Dose	22	.00	1.024
Sad			
Low Dose	21	.048	1.071
High Dose	22	.00	.873
Fear			
Low Dose	21	.00	1.095
High Dose	22	.182	1.259
Anger			
Low Dose	21	.095	1.091
High Dose	22	.318	1.086

Table D: Sample Size, Mean, and Standard Deviations for Difference Scores for Intensity by Dose

Intensity and Dose	n	Mean Difference (hydrocortisone – placebo)	SD
High			
Low Dose	21	.429	1.399
High Dose	22	.273	1.579
Low			
Low Dose	21	.190	2.064
High Dose	22	.227	1.66

Table E: Sample Size, Mean, and Standard Deviations for Difference Scores for Reaction Time for Each Ratio Condition by Dose

Ratio Condition and Dose	n	Mean Difference (hydrocortisone – placebo) (ms)	SD

Table E continued

6:4			
Low Dose	20	13.997	902.417
High Dose	14	213.726	876.609
7:3			
Low Dose	20	36.409	636.976
High Dose	14	405.091	1929.814
8:2			
Low Dose	20	-91.279	467.961
High Dose	14	155.552	1171.565
9:1			
Low Dose	20	93.814	1030.258
High Dose	14	-307.883	1691.98

Table F: Sample Size, Mean, and Standard Deviations for Difference Scores for Probability for Each Ratio Condition by Dose

Ratio Condition and Dose	n	Mean Difference (hydrocortisone – placebo)	SD
6:4			
Low Dose	20	-.0042	.165
High Dose	14	.0162	.0959
7:3			
Low Dose	20	-.0540	.1507
High Dose	14	.0791	.1072
8:2			
Low Dose	20	-.0188	.0839
High Dose	14	.0051	.0580
9:1			
Low Dose	20	-.0150	.0735
High Dose	14	.0239	.0752

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