THE INTERACTION BETWEEN SALIVARY CORTISOL AND DHEA DURING ACUTE PSYCHOSOCIAL STRESS IN SLEEP DEPRIVED INDIVIDUALS

by

Michaella Anne Petrosky, B.S.

THESIS

Presented to the Faculty of

The University of Houston-Clear Lake

In Partial Fulfillment

Of the Requirements

For the Degree

MASTER OF SCIENCE

in Psychology

THE UNIVERSITY OF HOUSTON-CLEAR LAKE

MAY, 2020

THE INTERACTION BETWEEN SALIVARY CORTISOL AND DHEA DURING ACUTE PSYCHOSOCIAL STRESS IN SLEEP DEPRIVED INDIVIDUALS

by

Michaella Anne Petrosky

APPROVED BY

_____
Georgina Moreno, Ph.D., Chair

_____
Angela Kelling, Ph.D., Committee Member

RECEIVED/APPROVED BY THE COLLEGE OF HUMAN SCIENCES AND HUMANITIES:

_____
Samuel Lyndon Gladden, Ph.D., Associate Dean

_____
Rick Jay Short, Ph.D., Dean

Dedication

I dedicate this thesis to my family, whose never ending support has led me on this beautiful journey. To my mother, Lisa, because your love and support has taken me way beyond what I thought I could achieve. To my father, Thomas, because I know how proud you would be if you were here today. To my sister, Felicia, for showing me how to dream big. To my grandma, Bettie, and my aunt, Autumn, for constantly giving me words of encouragement. Lastly, to all the family members I have lost along the way, I know the encouragement you provided me while alive has helped shaped me today.

Acknowledgements

My deep gratitude goes first to Dr. Georgina Moreno, who expertly guided me through my graduate career. Your unwavering support for my academic and personal success has made my time at UHCL enjoyable. I would not be here today without your countless hours of support outside of the classroom.

My appreciation also extends to my laboratory colleagues. Jacqueline Khamma, Kate Crooks, Ryan McAdams, Allyssa Hashaw and Ellen Scott, thank you for the countless hours spent sleep deprived to ensure this experiment could occur. Thank you to Ping-Hsun Tsai for your help in running the ELISA kits. Thank you Dr. Nick Kelling for letting us take over your laboratory space every weekend. Lastly, thank you to Dr. Angela Kelling, your contribution to my thesis as a committee member has been truly instrumental to finishing.

Lastly, thank you to my friends and family, who came along this journey with me. Thank you for always lending a helping hand and an ear to listen when I needed.

ABSTRACT

THE INTERACTION BETWEEN SALIVARY CORTISOL AND DHEA DURING ACUTE PSYCHOSOCIAL STRESS IN SLEEP DEPRIVED INDIVIDUALS

Michaella Anne Petrosky
University of Houston-Clear Lake, 2020

Thesis Chair: Georgina Moreno, Ph.D.

Sleep deprivation can impair cognitive and emotional processes, especially those regulated by the prefrontal cortex and medial temporal lobe (i.e., hippocampus, amygdala). Stress and increased cortisol levels have been found to have similar detrimental effects. More recently, research has found that dehydroepiandroeterone (DHEA), an antagonist to cortisol, may counter the negative consequences of stress and even provide beneficial results to individuals under stress. However, very little is known regarding the relationship between DHEA and cortisol when individuals are both sleep deprived and stressed. The aim of the current study was to explore the relationship between DHEA and cortisol during an acute psychological stressor in sleep-deprived individuals. It was hypothesized that sleep deprivation would disrupt the protective effects of DHEA, as evidenced by a larger interaction between cortisol and DHEA in sleep deprived individuals after an acute stressor, as compared to controls. Specifically,

high cortisol and low DHEA would be seen in sleep deprived participants compared to low cortisol and high DHEA in control participants. Additionally, it was hypothesized that if such a difference exists between groups, this difference would predict changes in affect. More specifically, individuals with low cortisol and high DHEA would have decreased negative affect, whereas individuals with high cortisol and low DHEA would have increased negative affect. Twenty-eight participants were split evenly between the sleep deprivation group and control group. Sleep deprivation was induced by wakefulness for 24 hours while controls slept for 8 hours. Stress was induced through the Trier Social Stress Test. Saliva samples and the Positive and Negative Affect Scale (PANAS) were collected at three time points—before, immediately after, and 20 minutes after the acute stressor. There was no significant difference observed in the cortisol to DHEA ratio between sleep deprived and non-sleep deprived individuals after an acute stressor. These findings suggested that the combined effects of sleep deprivation and stress did not disrupt the protective effects of DHEA on cortisol. Future research should be conducted to fully elucidate these relationships.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I:

INTRODUCTION

Context of the Problem

Sleep deprivation is a global health problem that has negative effects on the health and well-being of individuals (Killgore, 2010). Sleep is essential and has important implications in emotion regulation (Vandekerckhove & Cluydts, 2010), cognitive performance, and health (Goel et al., 2013). One night of sleep deprivation is found to significantly reduce attention, reaction speed, cognitive processing speed (Louca & Short, 2014), and the experience of positive emotions (Talbot et al., 2010). Moreover, the impact of sleep deprivation on stress, another ubiquitous public health concern, is not fully understood. Studies have found that the less sleep an individual gets, the more anxious they will be in stressful situations (Greenberg et al., 1972; Minkel, et. al., 2014). Cortisol is an important hormone in the hypothalamic-pituitary-adrenal (HPA) axis that is produced in response to stress (Dickerson & Kemeny, 2004). Dehydroepiandroeterone (DHEA), an antagonist to cortisol that plays an important role in modulating immune responses to acute stress (Prall et al., 2017), is suggested to counter the negative effects of stress. That is, lower cortisol to DHEA ratios (i.e., low cortisol and high DHEA) may provide a buffer against the negative effects of stress (Morgan, et. al., 2004). For example, lower cortisol to DHEA ratios during stressful situations are associated with less perceived stress (Qiao, et al., 2017). Interestingly, no research to date has investigated the cortisol to DHEA ratio in sleep-deprived individuals who are acutely stressed. It is important to understand the interaction between sleep deprivation and stress given the prevalence of these issues and because many professions (e.g., medical staff, shift workers) require employees to be awake for extended periods of time.

Purpose of the Study

Although it has been established that there is a relationship between DHEA and cortisol, it is unclear if a low cortisol to DHEA ratio could still buffer the negative effects of stress in acutely (i.e., 24 hour) sleep deprived individuals. The aim of the current study is to determine if there is a difference in the cortisol to DHEA ratio between sleep deprived and non-sleep deprived individuals after an acute stressor. It is hypothesized that there is difference in the cortisol to DHEA ratio between sleep deprived individuals as compared to non-sleep deprived individuals. Specifically, higher cortisol and lower DHEA will be seen in sleep deprived participants compared to control participants. Additionally, it is hypothesized that if such a difference exists between groups, this difference will predict changes in reported affect. More specifically, individuals with low cortisol to DHEA ratios (i.e. low cortisol and high DHEA) will have decreased negative affect, whereas individuals with high cortisol to DHEA ratios (i.e. high cortisol and low DHEA) will have increased negative affect.

CHAPTER II:

LITERATURE REVIEW

Sleep

Sleep is an important process the body goes through and almost one third of a lifetime is spent sleeping (Scullin, 2013). Sleep has two major types of cyclical sleep stages: rapid eye movement (REM) and non-rapid eye movement (NREM), also called slow wave sleep (SWS). EEGs of REM-sleep show the hippocampus and amygdala showing wake-like activity, while the prefrontal cortex shows reduced activity (Rasch & Born, 2013). NREM sleep is the stage where neurons are firing at the lowest point (Bear et al., 2016). Although the average length of sleep for adults is 7.5 hours, sleep times vary and throughout the lifespan the sleep cycle structure changes (Bear et al., 2016; Steiger, 2003). Sleep quality continuously declines with age, with REM sleep decreasing (Ohayon et al., 2011; Steiger, 2003), as well as slow wave sleep (Scullin, 2013) and sleep latency increasing (Ohayon et al., 2011). Although the primary function of sleep is still unknown, sleep seems to have important implications in emotion regulation (Vandekerckhove & Cluydts, 2010), cognitive performance and health (Goel et al., 2013), and consolidation of memory (Diekelmann & Born, 2010).

Throughout sleep, neuronal activity in the brain varies. Research by Tononi and Cirelli (2003) suggests that SWS is important in synaptic homeostasis by promoting the downscaling of synapses during slow wave activity after previous wakefulness increases synaptic weight. The neuronal activity in the amygdala and medial prefrontal cortex varies across the sleep-wake cycle (Vandekerckhove & Cluydts, 2010). During REM sleep, there is enhanced activity in the amygdala and hippocampus, with these activations hypothesized to be related to dreaming during REM sleep (Payne & Nadel, 2004). The emotional and social processes that occur during REM sleep seem to be due to increased

activity in the amygdala, medial prefrontal cortex and anterior cingulate cortex (Maquet et al., 1996). During NREM sleep, there is reduced activity in the prefrontal cortex, hypothalamus, anterior cingulate cortex, basal ganglia and thalamus (Rasch & Born, 2013).

Sleep Deprivation

Although sleep is vital for human functioning, approximately one third of the U.S. population is receiving an insufficient amount of sleep at night (Liu, 2016). Sleep deprivation can either be A) partial or total and B) acute or chronic (Landolt et al., 2014). Partial sleep deprivation, or sleep restriction, is when sleep is restricted to below 7 hours of sleep per 24 hours, while total sleep deprivation is when sleep is completely lost for the 24-hour period (Landolt et al., 2014). Acute sleep deprivation is the short-term loss of sleep, while chronic sleep deprivation is the long term loss of sleep (Landolt et al., 2014). Although sleep needs vary, sleep restrictions of 6 hours a night produce the first signs of daytime sleepiness throughout the day (Friedmann et al., 1977; Horne, 2011). Sleep deprivation of all types have been found to significantly reduce attention, reaction speed, and cognition (Killgore, 2010; Louca & Short, 2014). Additionally, sleep deprivation increases anxiety levels (Vollert et. al., 2011) and slows psychomotor response time, reduces working memory performance, reduces task performance as duration increases and increases involuntary microsleeps (Goel et al., 2009).

Acute Sleep Deprivation

Compared to chronic sleep restriction, acute sleep deprivation induces higher levels of subjective sleepiness (Philip et al., 2012). Total acute sleep deprivation is associated with a decline in cognitive performance and vigilance (Zhong et al., 2005). Military jet pilots show a significant decrease in performance in a flight simulator after 36 hours of sleep deprivation (Van Dongen et al., 2006). Physiologically, total acute

sleep deprivation significantly increases heart rate, sympathetic cardiac and blood pressure modulation, while decreasing baroreflex sensitivity (Zhong et al., 2005) and energy expenditure (Benedict et al., 2011). After a meal, metabolic rate is 20% lower in acute sleep deprived individuals compared to those with a full night's rest (Benedict et al., 2011). Sleep deprivation also leads to an increase in hunger and an increase in caloric intake (Benedict et al., 2011; Benedict et al., 2012).

Partial acute sleep deprivation tends to have similar detrimental effects as total sleep deprivation, with some differences. Similar to total sleep deprivation, partial acute sleep deprivation increases food intake (Brondel et al., 2010) and increases sympathetic cardiac modulation in a manner similar to total acute sleep deprivation (Dettoni et al., 2012). However, partial acute sleep deprivation does not change resting heart rate, blood pressure, respiratory rate, or cholesterol levels (Dettoni et al., 2012). Cognitively, partial acute sleep deprivation leads to working memory impairments (Yeung et al., 2018). Surgeons with four hours or less of sleep show a deterioration in their cognitive ability (O'Brien et al., 2012). Doctors who experience short sleep durations report decreased daytime alertness (Wali et al., 2013) and poorer concentration (Sanches et al., 2015).

Neural Underpinnings of Sleep Deprivation

Positron emission tomography (PET) scans of the brain show that the absolute metabolic rates in the prefrontal cortex, thalamus, basal ganglia and limbic regions reduce greatly after sleep deprivation (Wu et al., 1991; Wu et al., 2006). This reduction leads to a greater deficit in vigilant attention, which is common in acute sleep deprivation (Wu et al., 1991). Functional magnetic resonance imaging (fMRI) show that acute sleep deprivation leads to reduced activity in the prefrontal cortex, (Vandekerckhove & Cluydts, 2010) parietal lobes, and premotor cortex (Drummond et al., 1999), while the thalamus has increased activity (Ma et al., 2015). These changes in brain activity lead to

deficits in normal cognitive functioning such as attention and working memory (Goel et al., 2009).

During sleep debt, the functional connectivity of the amygdala with the superior temporal gyrus decreases and connectivity with the inferior frontal gyrus increases (Motomura et al., 2017). There is also a decrease in the functional connectivity between the amygdala and the medial prefrontal cortex during sleep debt, which leads to lower self-reported mood (Motomura et al, 2017). This functional connectivity between the amygdala and the medial prefrontal cortex is positively correlated to the duration of REM sleep (Motomura et al., 2017), which can explain why deprivation of REM-sleep impacts processing and consolidation of daily experiences (Vandekerckhove & Cluydts, 2010).

Stress

Stress is a state of allostasis caused by intrinsic or extrinsic forces that the body deems as a threat by a distribution of neural connections (McEwen & Gianaros, 2010; Tsigos et al., 2000). The response is mediated by neuroendocrine cellular and molecular infrastructures that are located in both the central and peripheral nervous system (Tsigos et al., 2000). Individual factors such as genetics, environment, and development influence the stress response (McEwen & Gianaros, 2010; Tsigos et al., 2000).

Due to the body creating a stress response to actual or anticipated threatening stimuli, psychological and physiological symptoms occur (Bear et al., 2016). While the stress response is activated in the same manner for various stressful stimuli, there are several different types of stress and stressors. An absolute stressor is that which causes a real threat to one's survival or well-being, such as being confronted by a dangerous animal (Lupien et al., 2007) or a global pandemic. On the other hand, a relative stressor is that which is an implied threat because the situation is interpreted as being novel, unpredictable, or uncontrollable, such as public speaking (Lupien et al., 2007). While an

absolute stressor will elicit a stress response in almost all individuals the first time, a relative stressor only elicits a response in a proportion of individuals (Lupien et al., 2007).

Stress can also be categorized as either acute or chronic. The American Psychological Association (APA; 2017) found that 75% of the population reports at least one symptom of stress in any given month. Symptoms of acute stress include suboptimal decision making (LeBlanc, 2009), an increase in arousal, alertness, and respiratory rate (Tsigos et al., 2000), an increase in cardiovascular response, and an increase in negative emotion (Feldman et al, 1999). An extremely potent or chronic stressor can lead to detrimental effects on reproduction, metabolism, growth and immunocompetence, as well as psychological development (Tsigos et al., 2000).

Acute Stress

Acute stress is the most common form of stress and lasts for short durations. Examples of acute stress are public speaking and arguments with a significant other. Moderate acute stress tends to decrease parasympathetic nervous system and autonomic nervous system activity, while increasing heart rate and sympathetic nervous system activity (Qin et al., 2009). In extreme cases, acute stress can trigger a potentially lethal cardiovascular response (Leor et al., 1996). For example, after a large earthquake, there was a significant rise in cardiac related deaths unrelated to physical activity (Leor et al., 1996). Acute stress can be a risk factor for developing PTSD in extreme cases (Holman et al., 2008).

A well-validated acute psychosocial stressor is the Trier Social Stress Test (TSST), which induces a social-evaluative threat by having participants prepare for a speech, perform a speech, and perform verbal arithmetic (Kirschbaum et al., 1993). The speech and arithmetic tasks are performed in front of two or three people who are acting

as professionals and provide no facial or verbal feedback except to say when to stop (Kirschbaum et al., 1993). Participants are also told that they will be videotaped to evaluate their performance at a later date (Kirschbaum et al., 1993). Physiologically, the TSST has been shown to increase heart rate and mean arterial pressure (Hamidovic et al., 2010) as well as activate the hypothalamus-pituitary-adrenal (HPA) axis and trigger a substantial release of cortisol in 70-80% of participants (Dickerson & Kemeny, 2004).

Stress and Sleep Deprivation

Given the detrimental effects of both acute stress and acute sleep deprivation on the body, it is important to consider the relationship between the two. Studies have found that the less sleep an individual gets, the more psychological and physiological anxiety symptoms will be shown in acutely stressful situations (Greenberg et al., 1972; Minkel et. al., 2014). These anxiety symptoms are because acute sleep deprivation increases cortisol levels in acutely stressful situations (Dickerson & Kemeny, 2004; Joo et al., 2012; Minkel et. al., 2014). It is important to note that sleep deprivation has been shown to possibly act as a stressful situation itself (Joo et al., 2012; Van Reeth et al, 2000). Additionally, acute stress can negatively alter the quality of sleep an individual receives at night (Grossman et al., 2017; Zambotti et al., 2016), while also decreasing the total amount of sleep an individual gets (Bauducco et al., 2016).

Stress and Affect

One of the main ways that perceived stress is measured is through self-reported affect. The specific definition of affect, mood, and emotion is debated and varies by experiment, with many using the terms interchangeably and, others creating separate definitions. Ketai (1975) found that much of the literature supports that emotion includes the physiological involvement of feelings, affect is the sudden and short-lived reaction and mood is the prolonged affect. Within affect, affective state is the momentary feeling

of affect while affective style refers to the typical emotional experience of a person (Cohen & Pressman, 2006). However, both forms of affect are important in measuring the change of state in individuals (Cohen & Pressman, 2006). In the well-validated, self-report affect scale, the Positive and Negative Affect Scale (PANAS), positive affect is described as active, attentive, determined, enthusiastic, excited, interested, inspired, strong and proud (Watson et al., 1988). Negative affect in the PANAS is described as nervous, afraid, hostile, ashamed, distressed, guilty, jittery, irritable, scared and upset (Watson et al., 1988).

In general, all forms of affect are associated with effects in judgements and decision making and the response occurs rapidly (Slovic et al., 2006). Specifically, increased negative affect is associated with acute stressors (Feldman et al., 1999) possibly because higher cortisol responses are associated with negative affect and agitation (Van Eck et al., 1996). Decreased positive affect and increased mood disturbances are associated with the acute psychosocial stressor, the TSST (Childs & de Wit, 2009). Although, one study found that these changes in affect may be short lived, as affect returned to baseline levels 10 minutes after the TSST (Childs & de Wit, 2009).

The prefrontal cortex, amygdala, hippocampus and anterior cingulate cortex are critical in processing affect. A review by Phan and colleagues (2002) of 55 PET and fMRI studies reported that the medial prefrontal cortex is important in general emotional processing, whereas fear highly activates the amygdala (Phan et al., 2002). Moreover, the rostral anterior cingulate cortex is important in emotional regulation (Sripada et al., 2013). When one is anticipating future affect, the ventromedial prefrontal cortex is activated, while immediate negative affect activates the right side of the prefrontal cortex (Davidson, 2000) and the left hippocampus (Sripada et al., 2013).

Sleep and Affect

It is important to note that sleep deprivation can also evoke an exaggeration in affect. Studies have shown that people who get an insufficient amount of sleep show signs of verbal aggression and anger (Randler & Vollmer, 2013), an increase in negative affect during disruptive events (Zohar et al., 2005), and a decrease in the amount of positive emotions an individual feels (Killgore, 2010; Talbot et al., 2010; Vandekerckhove & Cluydts, 2010). Partial acute sleep deprivation leads to on-call doctors reporting a negative affect mood state (Wali et al., 2013). Deprivation of REM sleep reduces the adaptive functioning of emotion compared to those without REM deprived sleep (Vandekerckhove & Cluydts). Total acute sleep deprivation also impacts the functioning of the emotion related brain areas (Motomura et al., 2017). Slept debt over the course of five days increases activity in the amygdala to negative stimuli and decreases subjective mood (Motomura et al., 2013) because the prefrontal cortex loses its ability to properly suppress activity in the amygdala (Motomura et al, 2017).

Neural Underpinnings of Stress

Real or perceived stress triggers a response intended to maintain homeostasis (Russell & Lightman, 2019), mainly through activation of the HPA axis. The HPA axis is activated when an organism is exposed to stress and the central nucleus of the amygdala is active (Bear et al., 2016). First, neurons in the paraventricular nucleus of the hypothalamus releases neurohormones, corticotropin-releasing factor (CRF) and arginine vasopressin, into the blood vessels that connect to the pituitary gland (Stephens & Wand, 2012). Once there, these neurohormones stimulate the anterior pituitary gland to produce and release adrenocorticotropic hormone (ACTH) (Stephens & Wand, 2012). ACTH then causes glucocorticoid synthesis which releases from the adrenal gland (Stephens & Wand, 2012). This process is self-regulated by a negative-feedback loop to ensure the HPA axis is not activated for prolonged periods (Stephens & Wand, 2012). The

prefrontal cortex, amygdala, and hippocampus also regulate the HPA axis. The prefrontal cortex and hippocampus down-regulate the stress response while the amygdala up-regulates it (McEwen & Gianaros, 2010). The hippocampus regulates the amygdala to determine if the fear the amygdala is sensing is appropriate for the given context. Based on an fMRI study by Pruessner and colleagues (2008), in a stressful mental arithmetic task, the left premotor area, medial left prefrontal cortex and occipital lobe are activated. After acute psychosocial stress, PET scans show that there is reduced cerebral blood flow to structures in the limbic system, including the hippocampus, amygdala, and the prefrontal cortex (Pruessner et. al, 2008).

Cortisol

Cortisol is a steroid hormone produced in the adrenal gland associated with stress and the HPA axis (Dickerson & Kemeny, 2004; Stephens & Wand, 2012). Cortisol is synthesized by steroid 17beta-hydroxylase from 11-Deoxycortisol (Nussey & Whitehead, 2001). It is metabolized irreversibly by A-ring reductases and reversibly by 11beta-hydroxysteriod dehydrogenases (Nussey & Whitehead, 2001). Cortisol is released into the blood when there is an elevation of ACTH (Bear et al., 2016; Stephens & Wand, 2012) and the amount of cortisol released is determined by the HPA axis (Bear et al., 2016). The amount of control cortisol has on stress responsivity and emotional reactivity is mediated by mechanisms in the prefrontal cortex (McKlveen et al., 2013).

Cortisol has a diurnal rhythm. Cortisol levels tend to be lower at the onset of sleep (Hansen et al., 2012) and highest in the early morning (Hasegawa-Ohira et al., 2016; Steiger, 2003). Normal salivary cortisol range from 10.2-27.3 nmol/L at 8:00 a.m. and 2.2-4.1 nmol/L at 8:00 p.m. (Laudat et al., 1988). Cortisol concentrations increase rapidly 15-20 minutes after awakening and peak at around 40 minutes after awakening (Hasegawa-Ohira et al., 2016). Higher than normal morning levels of cortisol leads to

impairments in the cognitive process and a decrease in memory (Echouffo-Tcheugui et al., 2018).

Cortisol plays a critical role in metabolism by moving energy reserves and suppressing the immune system (Dickerson & Kemeny, 2004; Bear et al., 2016). In the central nervous system, cortisol alters the excitability of neurons (Nussey & Whitehead, 2001) and when it interacts with different neurotransmitters, cortisol plays a role in cognitive, emotional and behavioral processes (Kamin & Kertes, 2017). Cortisol is associated with increased arousal, vigilance, focused attention, and memory formation (Charney, 2004).

While cortisol levels are cyclical throughout the day, cortisol levels can be affected by stress (Dickerson & Kemeny, 2004; Russell & Lightman, 2019). Cortisol is released due to psychological stress (Charney, 2004) and as the number of social evaluative threats increase, cortisol also increases (Dickerson & Kemeny, 2004). Salivary cortisol levels peak 10 to 20 minutes after acutely stressful situations (Dickerson & Kemeny, 2004; Russell & Lightman, 2019). Not only does actual stress cause a change in cortisol levels, but anticipated stress can also change cortisol levels. Anticipated exhausting exercise has a comparable increase in cortisol as actually completing the exhausting exercise (Lupien et al., 2007).

Cortisol could possibly be beneficial to affect and stress. Low cortisol during acutely psychosocial stressful situations can increase the negative effects of stress (Shirotsuki et al., 2009). Participants who were administered 30 mg of cortisol, orally, reported higher positive affect after the Trier Social Stress Test compared to those who did not (Het & Wolf, 2007).

Effects of Cortisol on the Brain

Higher morning levels of cortisol, without the presence of stress, is associated with lower total cerebral brain volume, occipital volume, and frontal gray matter volumes (Echouffo-Tcheugui et al., 2018). In white matter, high morning cortisol levels are associated with microstructural injuries in several tracts, especially the corpus callosum (Echouffo-Tcheugui et al., 2018). These injuries in the white matter may explain the cognitive impairment associated with high cortisol levels (Echouffo-Tcheugui et al., 2018). When damage is done to the hippocampus, psychological stressors do not result in a cortisol response, suggesting that the hippocampus may have a more important role in cortisol secretion (Buchanan et al., 2009).

Cortisol and Sleep

In the past, acute sleep deprivation was thought to only alter vigilance, mood, and cognitive function, without altering physiological variables (Leproult et al., 1997). However, recent research has shown that sleep deprivation can also impact cortisol levels. In a longitudinal study, low morning and evening cortisol levels were associated with sleep problems (Hansen et al., 2012). Longer sleep latency also leads to reduced cortisol morning levels (Huang et al., 2017). People who experience poorer sleep quality, shorter sleep durations, and lower sleep efficiency exhibit slower cortisol declines later in the day (Hansen et al., 2012; Huang et al., 2017). Sharper declines earlier in the day and a flattened decline later in the day is associated with daytime dysfunction (Huang et al., 2017). These problems include sleepiness when waking and exhaustion from the previous day (Dahlgren et al., 2009).

Acute sleep deprivation increases cortisol levels compared to a restful night of sleep (Minkel et al., 2014), particularly in the morning (Wright et al., 2015). The rate of recovery from acute sleep deprivation is also altered. Compared to a normal night's sleep,

acute sleep deprivation slows the normal daylong decline in cortisol levels, resulting in an elevation of evening cortisol levels (Leproult et al., 1997). During a two-hour nap after sleep deprivation, cortisol levels will decrease, but after the nap, cortisol levels will increase again (Vgontzas et al., 2007), meaning cortisol needs a much longer time to recover from acute sleep deprivation.

Dehydroepiandroeterone

Another hormone associated with acute stress is dehydroepiandrosterone (DHEA), an antagonist to cortisol. DHEA is synthesized and secreted by the adrenal cortex and along with its sulfate ester, is the most abundant steroid hormone in the body (Maninger et al., 2009; Pluchino et al., 2015; Prough et al, 2016). DHEA is synthesized by P450c17, an enzyme cytochrome, from pregnenolone (Maninger et al., 2009). DHEA is secreted from the zona reticularis layer of the adrenal cortex and from the ovary and testis (Maninger et al., 2009). Normal levels of DHEA in the body range from 2–4 ng/mL (Friess et al., 2000). Although DHEA can be secreted by sex organs, concentrations of DHEA is highest in the brain than any other location (Maninger et al., 2009). DHEA is metabolized into active androgens in the gonads, liver, adrenals and peripheral tissues (Prough et al., 2016). Throughout the lifespan DHEA levels decline, with peak concentration in the mid-20s (Maninger et al., 2009). While underproduction of DHEA is associated with age, overproduction of adrenal androgens can lead to disorders associated with hyperandrogenic states, like polycystic ovarian syndrome (Goodarzi et al., 2015).

While the biology of DHEA is known, the mechanisms of action for DHEA are not fully understood. A few theories about its mechanism of action have been proposed. While no specific DHEA nuclear steroid receptor has been found, DHEA does affect glucocorticoid receptors. Two theories that show this are that glucocorticoid receptors are directly modulated by DHEA or that DHEA directly binds to those receptors (Kalimi et

al., 1994). Another theory is that DHEA may mediate some of its action through sex steroid metabolites such as estradiol and testosterone (Maninger et al., 2009). A few of the mechanisms of neurobiological action are documented. In one mechanism, DHEA is mediated through aromatization to estradiol (Hajszan et al., 2004). This action was shown to increase spine synapse density in the hippocampus (Hajszen et al., 2004).

DHEA plays an important role in modulating immune responses to acute stress (Prall et al., 2017). DHEA is also involved in neuroprotection, neurogenesis, apoptosis, and has anti-inflammatory effects (Maninger et al., 2009). As all gonadal steroid hormones do, DHEA influences the growth, differentiation, normal physiology, and aging of the central nervous system (Pluchino et al., 2015). DHEA also plays a role in cognition and emotional and behavioral processes when it interacts with different neurotransmitters (Kamin & Kertes, 2017). Specifically, DHEA decreases negative affect (Sripada et al., 2013) and increases overall subjective mood (Alhaj et al., 2006). DHEA also tends to increase episodic memory recollection during neutral stimuli (Alhaj et al., 2006) while decreasing memory accuracy during emotional stimuli (Sripada et al., 2013).

Neural Underpinnings of DHEA

DHEA levels are positively associated with cortical thickness in the left dorsolateral prefrontal cortex, right temporoparietal junction, right premotor and right entorhinal cortex during the prepubescent ages of 4 through 13 (Nguyen et al., 2013). A postmortem study on DHEA concentrations in the brain of 10 individuals between the ages of 76 and 93 found that DHEA concentrations were highest in the prefrontal cortex, with lower concentrations found in the parietal lobe, temporal cortex, and cerebellum (Lacroix et al., 1987). DHEA has also been linked to changes in brain activity with regards to affect. DHEA decreases activity in the amygdala and hippocampus and

increased activity in the rostral ACC, leading to a reduction in negative affect and an increase in emotional regulation (Sripada et al., 2013).

DHEA and Sleep

DHEA concentrations increase rapidly and reach peak levels immediately after awakening (Hasegawa-Ohira et al., 2016). Much research about the relationship between DHEA and sleep, independent of the awakening response, are contradictory. Some studies have found that sleep quality is inversely related to DHEA levels (Ko, 2013). One study found that an increase in sleep disturbances and waking is associated with an increase in DHEA (Doan et. al, 2018). Other studies indicate that DHEA is beneficial to sleep. One study found that after a night of very poor sleep quality, DHEA levels at awakening were significantly lower than usual (Huang et al., 2017). The level of DHEA at awakening may be related to recovery from fatigue when it comes to sleep quality (Hasegawa-Ohira et al., 2016).

DHEA and Stress

DHEA has been associated with academic stress (Doan et. al., 2018), acute psychosocial stress (Shields et al., 2016), and daily life stressors (Jeckel et al., 2010). Prall and colleagues (2017) found that mean salivary DHEA concentrations were the highest immediately after a psychosocial stressor. Low DHEA levels during acutely stressful situations can lead to an increase in negative mood and decreases in positive mood (Izawa et al, 2008). In another study, DHEA supplements were given to military trainees and the levels of DHEA did not affect the perception of distress during the training activities (Taylor et al., 2012). These mixed results suggest that while increased DHEA is a characteristic of acute stress, the benefits of it are not well documented.

Cortisol and DHEA

Lennartsson and colleagues (2012) found that the magnitude of change in DHEA was positively correlated with the magnitude of change in cortisol. Higher cortisol to DHEA ratios are seen in chronically stressed individuals (Jeckel et al., 2010) and associated with an increase in negative mood (Izawa et al, 2008). It has been suggested that a lower cortisol and higher DHEA may provide a buffer against the negative effects of stress (Morgan et. al., 2004). Studies have found that lower cortisol to DHEA ratios during stressful situations were associated with less perceived stress (Qiao et al., 2017) and less dissociation symptoms (Morgan et. al., 2004). This difference suggests that individuals with lower cortisol to DHEA ratios during stressful situations may have developed ways to protect against the negative effects of stress.

Severely disturbed sleep may interrupt the balance and synchronization between cortisol and DHEA (Huang et al., 2017). Poor sleep quality, as measured by high Pittsburg sleep quality index (PSQI) scores, is associated with elevated cortisol to DHEA ratios at awakening (Huang et al., 2017).

Chapter Summary

Sleep deprivation and stress are associated with impaired cognitive and emotional processes, especially those regulated by the prefrontal cortex and medial temporal lobe (i.e., hippocampus, amygdala). Research suggests that DHEA, an antagonist to cortisol, may buffer the negative effects of stress on affect. However, very little is known regarding the relationship between DHEA and cortisol when individuals are both sleep deprived and stressed. The aim of the current study is to explore the relationship between DHEA and cortisol during an acute psychological stressor in sleep-deprived individuals. It is hypothesized that there is difference in the cortisol to DHEA ratio between sleep deprived individuals as compared to non-sleep deprived individuals. Specifically, higher

cortisol and lower DHEA will be seen in sleep deprived participants compared to control participants. Additionally, it is hypothesized that if such a difference exists between groups, this difference will predict changes in reported affect. More specifically, individuals with low cortisol to DHEA ratios (i.e. low cortisol and high DHEA) will have decreased negative affect, whereas individuals with high cortisol to DHEA ratios (i.e. high cortisol and low DHEA) will have increased negative affect.

CHAPTER III:

METHODOLOGY

Participants

Twenty-eight adults aged 18-45 (*M*=24.68, *SD*=4.84) were recruited for the current study, with no preference towards gender, race, or ethnicity. Participants were 57.1% female and 42.9% male. Participants were 39.3% Hispanic, 35.7% Caucasians, 14.3% Asian, 7.1% mixed race and 3.6% African-American. Participants were recruited from the UHCL online participant pool, via flyers, and through referrals. Health statuses were evaluated before inclusion in the experiment and participants were screened to ensure those chosen were in good general health and free from psychological or psychiatric illness and sleep disorders. Additionally, participants that had more than a 30-minute commute to UHCL were excluded for safety reasons. Monetary and course credit compensation was given at a rate that would not constitute undue coercion for participants.

Experimental Design

Participants were randomly assigned to one of two groups: the sleep deprivation group or the control group. The sleep deprivation group arrived at the laboratory between 9 and 10 p.m. Participants were asked to refrain from taking naps and eating or drinking anything containing caffeine the day before and during testing. The participants were given a battery of tasks at the beginning of the experiment: the Perceived Stress Scale, the Social Interaction Anxiety Scale, the Positive and Negative Affect Schedule, the Epworth Sleepiness Scale, the Stanford Sleepiness Scale, the Karolinska Sleepiness Scale, and the SQL Sleep Quality Assessment. The participants were monitored continuously by the research personnel to ensure wakefulness. Limited stimulating activities, such as reading, playing board games or using electronic devices, were made available to assist with

wakefulness. Informed consent was acquired at the beginning of the study and the screening was repeated to ensure the safety of the participant.

The acute psychosocial stressor, the Trier Social Stress Test (TSST), began eight hours after the participants finished the baseline testing. Saliva samples and the Positive Affect and Negative Affect Scale (PANAS) were collected 5 minutes before the TSST began, right after the TSST and again 20 minutes after the TSST ended, giving a total of three saliva samples. Heart rate was also monitored at 15 minutes before the TSST began, during the TSST and 10 minutes after the TSST ended, giving a total of three heart rate collection times. The sample tubes were stored in a -20°C freezer and cortisol and DHEA were quantified via human enzyme immunoassay (EIA) kits per the manufacturer's instructions (Salimetrics LLC, USA).

For the control group, the procedures are the same as for those in the sleep deprivation group, but participants were allowed to return home following baseline testing and instructed to go to sleep immediately. They reported the time they went to sleep and woke up through messaging the labs phone number. Fitbit technology was also attempted, but no data about sleep was correctly measured. Participants were asked to report back to the laboratory in the morning at approximately 7 a.m. When participants arrived at the lab at 7 a.m., they were administered the same battery of tasks administered to the sleep deprivation group: the TSST, the Perceived Stress Scale, the Social Interaction Anxiety Scale, The Positive and Negative Affect Schedule, the Epworth Sleepiness Scale, the Stanford Sleepiness Scale, the Karolinska Sleepiness Scale, and the SQL Sleep Quality Assessment. Additionally, saliva samples and heart rate recordings were collected.

Trier Social Stress Task

Participants were asked to perform the Trier Social Stress Task (TSST), a psychological task that has been proven to elicit acute stress in participants (Kirschbaum et al., 1993). From a review of over 100 stress studies, the TSST was proven to be one of the best standardized protocols to evoke a stress response (Dickerson & Kemeny, 2004). Participants are read a scenario in which they have been accused of shoplifting and are asked to prepare a speech defending themselves. Participants are then informed that their speech performance will be recorded and judged by an expert panel for content, quality, and duration. Participants are also asked to perform a mental arithmetic task, which they are told will give those who review their performance additional information about their believability and convincingness. Participants are given three minutes to prepare and five minutes to deliver their speech to confederates. Following the speech, participants then performed the mental arithmetic task for an additional five minutes.

Positive and Negative Affect Schedule

The Positive and Negative Affect Schedule (PANAS) (Watson, Clark, & Tellegen, 1988) is a 20-item mood scale developed to measure the two primary mood dimensions. Both mood dimensions have 10 questions associated with them and higher scores for each dimension indicate a greater level of that affect. The PANAS is sensitive to shifts in mood during short time periods. This was essential because the PANAS was taken a total of three times, within an hour and a half window of time.

Perceived Stress Scale

The Perceived Stress Scale (PSS) is a 14-item global appraisal scale that was used to assess self-reported levels of recent life-event stress (Cohen, Kamarck, & Mermelstein, 1983). Higher scores on the PSS indicated more perceived stress felt by the participant. More specifically, scores between 1 and 13 are considered low stress, scores between 14

and 26 are moderate stress and scores between 27 and 40 are considered high perceived stress.

Sleep Quality Assessment

Sleep quality varies by individual so assessing the typical quality and patterns of each participant was essential. The Pittsburgh Sleep Quality Index (PSQI) is a 19-item, self-rated questionnaire that produces information about subjective sleep quality, latency, duration, disturbances, habitual sleep efficiency, use of sleep medication and daytime dysfunctions (Buysse et al., 1989). The PSQI provides a standardized measure to discriminate between different types of quality of sleep. The PSQI gathers a global score about the participants sleep over a one-month period. Generally, scores at or below five are considered good sleep quality scores and scores over five are considered poor.

Sleepiness Scales

Individual sleep needs vary, thus measuring the level of sleepiness a person experiences is crucial and was achieved through the use of three scales, measured only at baseline, at the start of the experiment. The Epworth Sleepiness Scale (ESS) measures general levels of sleepiness during daytime activities by rating how likely participants were to fall asleep in eight daytime activities (Johns, 1991). A popular test used to determine subjective sleepiness is the Karolinska Sleepiness Scale (KSS), which measures subjective sleepiness by asking the individual to rate themselves on their feeling of drowsiness and fatigue on a scale of one to nine (Åkerstedt & Gillberg, 1990; Louca & Short, 2014; Shekleton et al., 2014). Another subjective sleepiness test that reflects circadian variation is the Stanford Sleepiness Scale (SSS), which measures subjective sleepiness by asking the individual to rate the degree they feel sleepy on a scale of one to seven (Goel et al., 2013; Hoddes et al., 1973). All scales interpreted scoring the same: higher scores indicated poor sleep quality.

Data Analysis

Independent *t*-tests were used on baseline data to compare the differences between the sleep deprived and control participants. A 2x3x3 mixed model ANOVA inferential statistical procedure was used to compare the sleep deprived and control participants' PANAS scores to investigate the effectiveness of the TSST. Then, to test the hypothesis that sleep deprived and control participants would have differences in DHEA, a 2x3 mixed model ANOVA were performed. To test the hypothesis that sleep deprived and control participants would have differences in cortisol, a 2x3 mixed model ANOVA were performed. Then, to test the hypothesis that sleep deprived and control participants would have differences in the cortisol to DHEA ratio, a 2x3 mixed model ANOVA was performed. Lastly, to test the hypothesis that the ratio of cortisol to DHEA would impact positive affect in sleep deprived and control participants, a 2x3x3 mixed model ANOVA were performed. To test the hypothesis that the ratio of cortisol to DHEA would impact negative affect in sleep deprived and control participants, a 2x3x3 mixed model ANOVA was performed. All analyses tested for violated assumptions and corrected for any violations that occurred.

CHAPTER IV:

RESULTS

Baseline

At baseline, there were no significant differences between sleep deprived and sleep conditions participants in age, $t(26)=0.423$, $p=0.676$, gender, $\chi^2(1)=0.583$, $p=0.445$, or in scores of PSQI, $t(25)=-0.324$, $p=0.748$, PSS, $t(26)=0.337$, $p=0.739$, Epworth Sleepiness Scale, $t(25)=0.134$, $p=0.894$, Stanford Sleepiness Scale, $t(25)=0.111$, $p=0.913$ or Karolinska Sleepiness Scale, $t(26)=-0.224$, $p=0.825$ (see Table 1).

Table 1

Mean baseline data by condition

Variable	Control	Sleep Deprived
Age	25.0714	24.2857
Gender		
Female	9	7
Male	5	7
PSS	13.7143	13.0714
PSQI	5.2857	5.6154
Epworth Sleepiness Scale	6.8571	6.6923
Stanford Sleepiness Scale	2.4286	2.3846
Karolinski Sleepiness Scale	3.5714	3.7143

Affect Manipulation

Twenty-eight participants were included in the affect (PANAS) manipulation analyses. Positive affect scores ranged from 17.8 to 24.3; negative affect scores ranged from 11.1 to 14.4. A 2x3x3 mixed model ANOVA was performed with the conditions as a between subjects factor, affect (positive and negative) as repeated measures, and time

(pre-TSST, immediately post-TSST 20 minutes post-TSST) as repeated measures. After correcting for sphericity, there was a significant interaction between time, affect and condition, $F(1.781,46.295)=4.359$, $p=0.022$, indicating that the relationship between time point and affect was significantly different between conditions, with the sleep condition group having higher positive affect scores than the sleep deprived condition across all three time points (See Figure 1). Additionally, for negative affect, the sleep deprived participants had higher negative affect scores Pre-TSST that declined across all time points while the control condition started with lower negative affect scores at Pre-TSST that increased immediately Post-TSST, then declined to level with the experimental condition 20 minutes Post-TSST (See Figure 2).

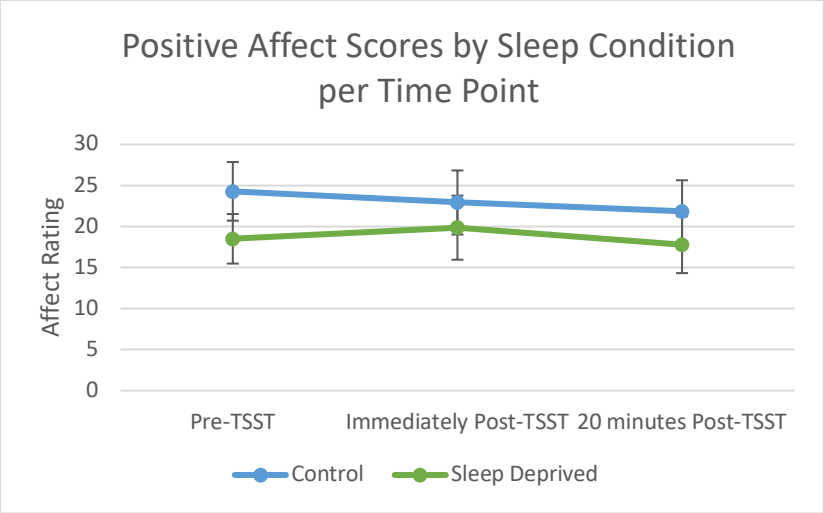

Figure 1
Positive Affect Scores by Sleep Condition per Time Point

Mean scores of positive affect as measured by PANAS, grouped by sleep condition and time point. Error bars represent standard deviations.

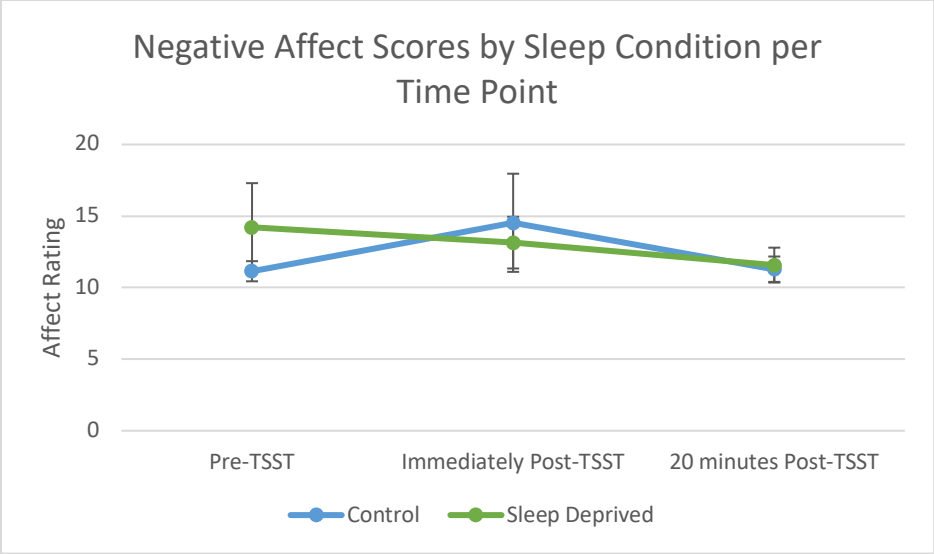

Figure 2
Negative Affect Scores by Sleep Condition per Time Point

Mean scores of negative affect as measured by PANAS, grouped by sleep condition and time point. Error bars represent standard deviations.

There was also a significant main effect of time, $F(2,52)=5.314$, $p=0.021$, indicating that regardless of the type of affect and condition, the lowest negative affect scores occurred 20 minutes after the TSST ended. There was also a significant main effect of affect, $F(1,26)=38.751$, $p<0.001$, regardless of condition or time point, with positive affect having higher mean scores than negative affect.

DHEA

Twenty-three participants with three saliva samples each (n=69) were used to analyze the DHEA results. One participant was excluded due to taking micronaps during sleep deprivation session, while the other four were excluded due to their saliva samples being of insufficient volume. A 2x3 mixed model ANOVA was performed with conditions as a between subjects factor and DHEA at the three time points (pre-TSST, immediately post-TSST 20 minutes post-TSST) as repeated measures. After correcting

for sphericity, there was not a significant interaction between time and condition $F(1.286,27.012)=0.252$, $p=0.680$, indicating that regardless of DHEA levels, time and conditions were not significantly different. After correcting for sphericity, there was no significant main effect for time $F(1.286,27.012)=0.223$, $p=0.693$, indicating that regardless of condition and DHEA levels, the time of collection was not significant. There was also no main effect for condition $F(1,21)=0.644$, $p=0.431$, indicating that regardless of time and DHEA levels, conditions were not significantly different (see Figure 3 and 4).

Cortisol

A total of 25 participants with three saliva samples each (n=75) were used to run the cortisol analyses. One participant was excluded due to taking micronaps during sleep deprivation session and the other 2 were excluded due to their saliva samples being of insufficient volume. A 2x3 mixed model ANOVA was performed with conditions as a between subjects factor and cortisol at the three time points (pre-TSST, immediately post-TSST 20 minutes post-TSST) as repeated measures. After correcting for sphericity, there was not a significant interaction between time and condition, $F(1.504,34.581)=1.734$, $p=0.196$, indicating that there was no significance difference in cortisol levels between time of collection and conditions. After correcting for sphericity, there was no main effect for time, $F(1.504,34.581)=2.107$, $p=0.147$, indicating that regardless of condition, the time of collection was not significantly different in cortisol levels. There was also no main effect for condition $F(1,23)=0.005$, $p=.943$, indicating that regardless of time and cortisol levels, conditions were not significantly different (see Figure 3 and 4).

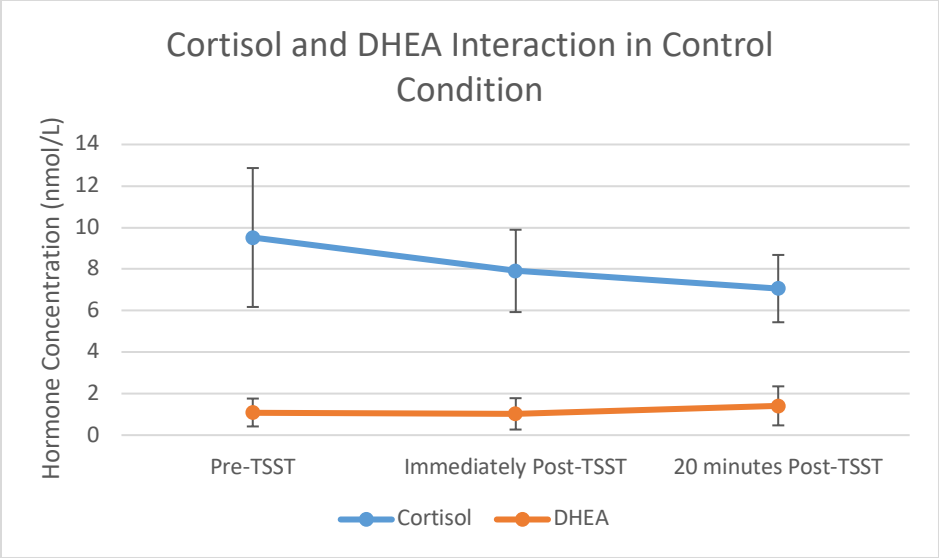

Figure 3
Cortisol and DHEA in the Control Condition per Time Point

Mean Cortisol and DHEA concentrations in the control condition (n=12) per time point. Error bars represent standard deviations.

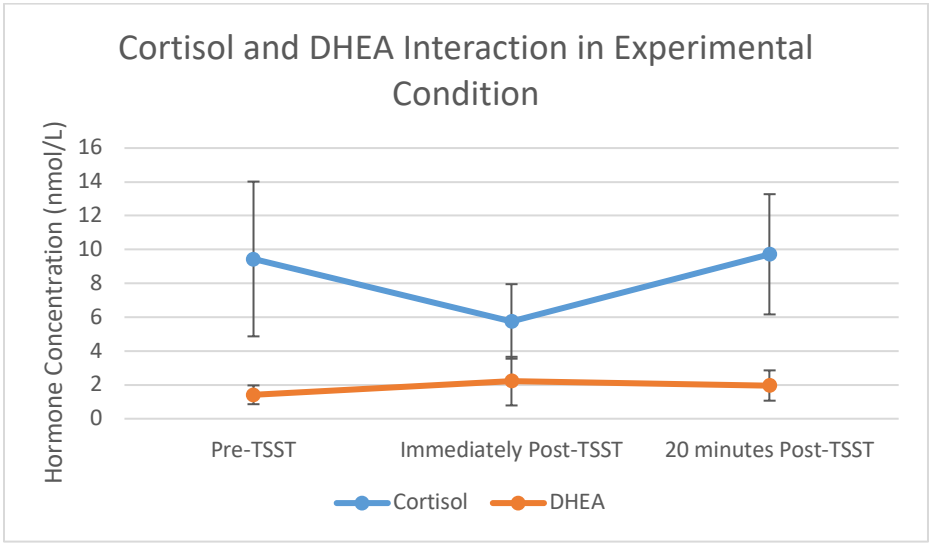

Figure 4
Cortisol and DHEA in the Experimental Condition per Time Point

Mean Cortisol and DHEA concentrations in the experimental condition (n=11) per time point. Error bars represent standard deviations.

Cortisol to DHEA Ratio

A total of 21 participants with 3 saliva samples each (n=63) were used to analyze the ratio between cortisol and DHEA to test the hypothesis that there would be a difference in the cortisol to DHEA ratio between sleep deprived and control participants. One participant was excluded due to micronapping while the other 6 were excluded due to their saliva samples being of insufficient volume. Following Morgan and colleagues (2004), the ratio was created by dividing cortisol levels by DHEA levels. A 2x3 mixed model ANOVA was performed with condition as a between subject factor and the cortisol to DHEA ratio at the three time points (pre-TSST, immediately post-TSST 20 minutes post-TSST) as repeated measures. There was no significant interaction between the time points and the condition, $F(2,38)=0.701$, $p=0.503$, indicating that the relationship between time of collection and conditions was not significantly different in their cortisol to DHEA ratios. There was no main effect of time $F(2,38)=0.953$, $p=0.395$, indicating that the ratio between cortisol to DHEA and condition did not significantly differ between time points. There was no main effect of conditions, $F(1,19)=0.236$, $p=0.633$, indicating that the ratio between cortisol to DHEA and time point did not significantly differ between conditions (see Figure 5).

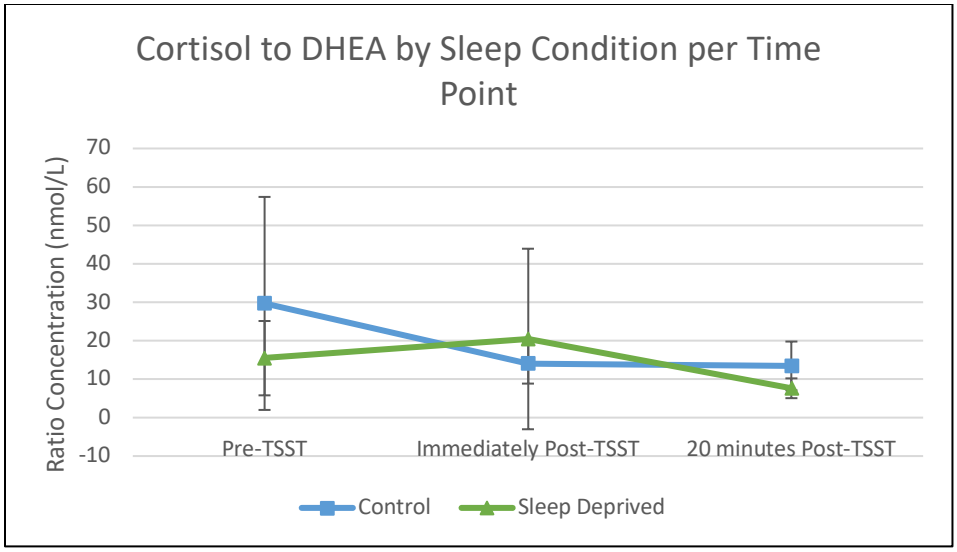

Figure 5
Cortisol to DHEA by Sleep Condition per Time Point

Mean cortisol to DHEA ratios, grouped by Control (n=11) and Sleep Deprived (n=10) condition per time point. Error bars represent standard deviations.

Cortisol to DHEA Ratio and Affect

Twenty-one participants were included in the current analyses. Two mixed model ANOVAs were performed to test the hypothesis that the cortisol to DHEA ratio would predict changes in affect. The first 2x3x3 ANOVA used condition as the between subjects factor and the cortisol to DHEA ratio and positive affect at the three time points as the repeated measures. There was no significant interaction between the cortisol to DHEA ratio and positive affect, $F(1,19)=0.534$, $p=0.474$, indicating that regardless of condition, the ratio of cortisol to DHEA did not significantly relate to positive affect. Nor was there a significant interaction between the time of collection (pre-TSST, immediately post-TSST 20 minutes post-TSST), the cortisol to DHEA ratio and positive affect, $F(2,38)=0.592$, $p=0.534$ (see Figure 6), indicating that the relationship between the cortisol to DHEA ratio and negative affect did not significantly differ across time points. There was also no significant interaction between condition, the cortisol to DHEA ratio

and positive affect, $F(2,38)=0.483$, $p=0.621$, indicating that the relationship between positive affect and the cortisol to DHEA ratio was not significantly different between conditions.

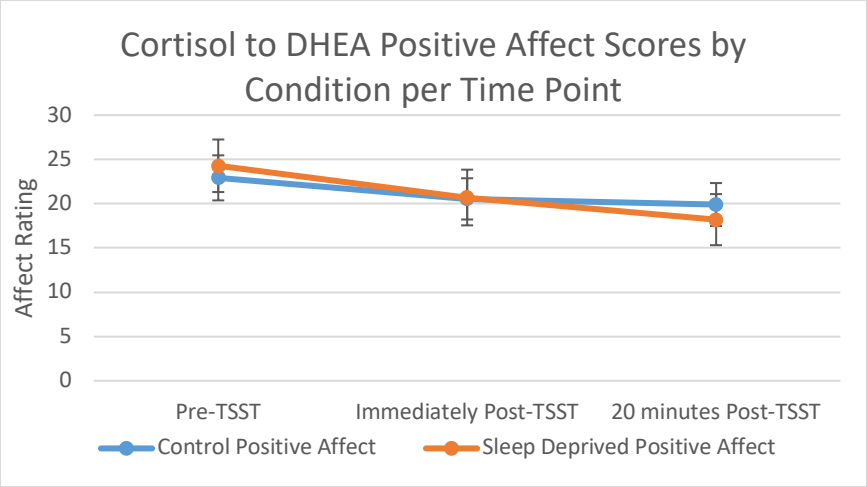

Figure 6
Positive Affect Scores for Cortisol to DHEA by Condition per Time Point

Mean scores on the positive affect section of the PANAS for participants with cortisol to DHEA ratio only (n=21), grouped by Control (n=11) and Sleep Deprived (n=10) conditions and time point. For Cortisol to DHEA ratio, see Figure 5. Error bars represent standard deviations.

For the second 2x3x3 ANOVA, condition was the between subjects factor and the Cortisol to DHEA Ratio and negative affect at the three time points as the repeated measures. There was not a significant interaction between the cortisol to DHEA ratio and negative affect $F(1,19)=0.863$, $p=0.365$, indicating that regardless of condition, the ratio of cortisol to DHEA did not significantly interact with negative affect. Nor was there a significant interaction between time of collection (pre-TSST, immediately post-TSST 20 minutes post-TSST), the cortisol to DHEA ratio and negative affect $F(2,38)=1.009$, $p=0.363$ (see Figure 7), indicating that the relationship between the cortisol to DHEA

ratio and negative affect did not significantly differ across time points. There was also no significant interaction between the conditions and the cortisol to DHEA ratio on negative affect at the different time points and the ratio, $F(2,38)=0.374$, $p=0.638$, indicating that the relationship between negative affect and the cortisol to DHEA ratio was not significantly different between conditions.

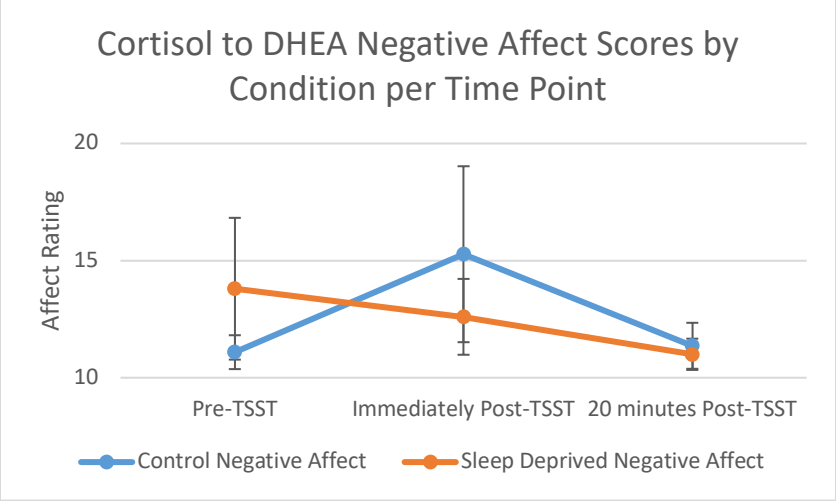

Figure 7
Negative Affect Scores for Cortisol to DHEA by Condition per Time Point

Mean scores on the negative affect section of the PANAS for participants with cortisol to DHEA ratio only (n=21), grouped by Control (n=11) and Sleep Deprived (n=10) Conditions and time point. For Cortisol to DHEA ratio, see Figure 5. Error bars represent standard deviations.

CHAPTER V:

DISCUSSION

Overall, sleep deprivation was found to have minimal, but notable, effects on stress. The control condition had significantly higher positive affect scores than the sleep deprived condition throughout the duration of the experiment, consistent with previous research. Much of the research supports that sleep deprivation decreases the amount of positive affect an individual reports (Killgore, 2010; Talbot et al., 2010; Vandekerckhove & Cluydts, 2010). While sleep deprivation did lead to a significant decrease in positive affect, the acute stressor did not significantly change affect in sleep deprived participants in the typical way. These results suggest that the combination of sleep deprivation and an acute stressor may be complicated.

Secondly, positive affect scores were significantly higher than negative affect scores among all participants. These results are consistent with previous findings when positive affect scores are high, negative affect scores are significantly lower (Schmukle et al., 2002) so the results are consistent with previous research. Control participants showed similar patterns in affect as most participants who complete the TSST, with increases in negative affect (Feldman et al., 1999) and decreases in positive affect immediately after the TSST (Childs & Wits, 2009) that return back to baseline affect 20 minutes after the TSST (Childs & Wits, 2009). However, sleep deprived participants did not display these trajectories. One possibility as to why this study deviated from previous findings is that the TSST did not act as a powerful enough stressor in our sleep deprived participants. Schwarz and colleagues (2018) found that one night of sleep deprivation was not enough to significantly change the response to the TSST. Another possibility is that our participants may have a more adaptive response to stress (Eisenmann et al.,

2016). One study found that recalling positive memories during acute stress can dampen cortisol increase while decreasing negative affect (Speer & Delgado, 2017).

Contrary to the hypothesis, the current study suggests that one night of total sleep deprivation does not significantly impact the cortisol to DHEA ratio. No significant differences were found in the cortisol to DHEA ratio between sleep deprived and control participants across the three time points. Salin-Pascual and collegues (1988) also that found that one night of total sleep deprivation did not significantly change cortisol levels in healthy participants. Given these findings, one night of sleep deprivation may not be as impactful on hormone levels as previously hypothesized.

The lack of change in the hormone levels could potentially be due to the circadian trends they tend to follow, which caused samples to be collected in a time frame that could have masked a cortisol response. Since cortisol is known to be elevated in the morning and peak 40 minutes after awakening, then decrease rapidly (Hasegawa-Ohira et al., 2016), it is plausible that any stress reactivity could have been obscured by naturally occurring changes in cortisol. Participants had to live within a 30-minute radius and arrive to the laboratory at 7:00 am. The first saliva sample was taken 15 minutes after arriving at the laboratory, possibly putting the first collection within the cortisol peak. The next saliva sample was collected 30 minutes after arriving to the lab and the last saliva sample was collected 50 minutes after arriving to the lab. Given that participants had a variety of wake times, two to three of the saliva samples could have been collected during the naturally declining cortisol level period. In the sleep deprived condition, cortisol is known to be significantly elevated in the morning and the decline is much slower (Leproult et al., 1997; Wright et al., 2015). These findings, coupled with the fact that salivary cortisol peaks 10 minutes post-TSST (Kirschbaum et al., 1993), could result in any increase in cortisol due to the stress response, being obscured due to the increase

matching earlier cortisol concentrations. This timing could account for any stress reactivity being obscured. While previous research has found that cortisol levels increase due to the TSST (Kirschbaum et al., 1993; Schoofs & Wolf, 2011), testosterone and estradiol, sex hormones that are converted from DHEA, are not significantly affected by the TSST (Schoofs et al., 2011). The cortisol diurnal rhythm and lack of DHEA reactivity could account for the lack of change in the ratio between the two hormones. Furthermore, it is well documented that in the TSST, not all individuals exhibit a robust cortisol response (Miller et al., 2013). Work by Miller and colleagues (2013) recommends using classification criteria of a 15.5% increase in cortisol in order to identify participants as "responders" and "non-responders." Using this classification criteria for responders (Miller et al., 2013), the current study had a 30% of participants classified as non-responders. This percentage is on the higher end of the 20-30% typical range of non-responders (Miller et al., 2013).

Also contrary to what was hypothesized, the cortisol to DHEA ratio did not have any buffering effects on affect. These findings suggest that sleep deprivation does not significantly impact the stress response in the cortisol to DHEA ratio. Due to the insignificant cortisol to DHEA ratio in the two conditions, there may not have been enough participants with either high or low ratios to indicate a buffering effect. If no participants had a high cortisol to DHEA ratio, a comparison to the low cortisol to DHEA ratio could not occur. Thus, a comparison of how significantly different cortisol to DHEA ratios changed affect would be unavailable. However, given the novelty of this study, it is difficult to speculate why this occurred.

Study Limitations

While this study was able to control for many factors associated with sleep, stress, and hormone levels, there were many limitations. Factors that are known to affect

sleepiness and alertness such as motivational factors and boredom (Goel et al., 2013) and distractions by environmental stimuli and noise (Landström, Englund, Nordström, & Åström, 1998) were not accounted for. In addition, since the control group went to their own home to sleep, we had to rely on self-reported sleep quantity and quality by the participants as equipment failure led to the fitbit technology not recording sleep.

In terms of methodology, all of the sleepiness scales were only measured the first day of the experiment, before anyone was sleep deprived or stressed. Any interpretations about subjective sleepiness and hormone levels are not interpretable, as only baseline data about sleepiness were taken. Also, no subjective levels of stress in addition to the PANAS were taken before or after the TSST to gather further information regarding the effectiveness of the TSST. Other data recordings (e.g., heart rate) were gathered but are beyond the scope of this thesis. Given the change in affect levels before and after the TSST, it can be assumed that the TSST was a successful stress manipulation. However, given how difficult it is to quantify acute stress, other physiological and behavioral measures would have elucidated the effectiveness of the TSST.

Suggestions for Future Research

Future studies should further investigate the effects of sleep deprivation on the cortisol to DHEA ratio. Given that the current study showed no significant effect on 24-hours of sleep deprivation, longer periods of sleep deprivation should be considered. Sleep deprivation of 36-hours would avoid any interaction with the cortisol awakening response, increasing the likelihood that any changes in cortisol were due to the stressor. Chronic sleep deprivation (e.g., 48 hours) could also provide more insight to the cortisol to DHEA ratio.

To gather the effectiveness of the 24-hour sleep deprivation, the sleepiness scales should be taken after participants are sleep deprived and more physiological data should

be recorded for sleep condition participants while they are asleep. Monitoring sleep condition participants' sleep-wake pattern with an EEG would also be useful in determining the quality and quantity of sleep. Furthermore, given that regions such as the prefrontal cortex and medial temporal lobe are impacted by both sleep deprivation and stress, neuroimaging studies should be done to investigate if there are changes in connectivity of these regions.

To understand the effects cortisol to DHEA ratio levels have on subjective stress after a stressor, subjective stress should be measured at multiple time points in the experiment. Other physiological and behavioral measures should also be taken to determine the effectiveness of the stressor, given that acute stress is difficult to quantify and there are individual differences in the stress response. Given that the TSST did not significantly affect physiological stress in the current study, different forms of stressors should be considered. Other psychological stressors or physiological stressors can add to the body of knowledge about the hormone ratio and stress levels. Future studies should also look at the differences physiological stressors and psychological stressors have on cortisol to DHEA ratios. Moreover, more participants that are considered responders to stressors should be included in future studies.

Differences in results due to age should be further explored as well, as age has been found to have effects on both sleep and cortisol (Vgontzas et al., 1998) and DHEA (Maninger et al., 2009). Lastly, future studies should include a larger sample size to more accurately understand the effects of sleep deprivation, stress and cortisol to DHEA ratios.

REFERENCES

Åkerstedt, T., & Gillberg, M. (1990). Subjective and objective sleepiness in the active individual. *International Journal of Neuroscience*, *52*(1-2), 29-37.

Alhaj, H. A., Massey, A. E., & McAllister-Williams, R. H. (2006). Effects of DHEA administration on episodic memory, cortisol and mood in healthy young men: a double-blind, placebo-controlled study. *Psychopharmacology*, *188*(4), 541-551.

American Psychological Association (2017). Stress in America: The State of Our Nation. Stress in America Survey.

Bauducco, S. V., Flink, I. K., Jansson-Fröjmark, M., & Linton, S. J. (2016). Sleep duration and patterns in adolescents: correlates and the role of daily stressors. *Sleep health*, *2*(3), 211-218.

Bear, M. F., Connors, B. W., & Paradiso, M. A. (2016). *Neuroscience: Exploring the brain* (Fourth edition.). Philadelphia: Wolters Kluwer.

Benedict, C., Hallschmid, M., Lassen, A., Mahnke, C., Schultes, B., Schiöth, H. B., Born, J. & Lange, T. (2011). Acute sleep deprivation reduces energy expenditure in healthy men. *The American journal of clinical nutrition*, *93*(6), 1229-1236.

Benedict, C., Brooks, S. J., O'Daly, O. G., Almen, M. S., Morell, A., Åberg, K., Gingnell, M., Schultes, B., Hallschmid, M., Broman, J.E & Larsson, E. M. (2012). Acute sleep deprivation enhances the brain's response to hedonic food stimuli: an fMRI study. *The Journal of Clinical Endocrinology & Metabolism*, *97*(3), E443-E447.

Brondel, L., Romer, M. A., Nougues, P. M., Touyarou, P., & Davenne, D. (2010). Acute partial sleep deprivation increases food intake in healthy men. *The American journal of clinical nutrition*, *91*(6), 1550-1559.

Buchanan, T. W., Tranel, D., & Kirschbaum, C. (2009). Hippocampal damage abolishes the cortisol response to psychosocial stress in humans. *Hormones and Behavior*, *56*(1), 44-50.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry research*, *28*(2), 193-213.

Charney, D. S. (2004). Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. *American journal of Psychiatry*, *161*(2), 195-216.

Childs, E., & de Wit, H. (2009). Hormonal, cardiovascular, and subjective responses to acute stress in smokers. *Psychopharmacology*, *203*(1), 1.

Cohen, S., Kamarck, T., & Mermelstein, R. (1983). A global measure of perceived stress. *Journal of Health and Social Behavior*, *24*(4), 385-396.

Dahlgren, A., Kecklund, G., Theorell, T., & Åkerstedt, T. (2009). Day-to-day variation in saliva cortisol—relation with sleep, stress and self-rated health. *Biological Psychology*, *82*(2), 149-155.

Davidson, R. J. (2000). Affective style, psychopathology, and resilience: brain mechanisms and plasticity. *American Psychologist*, *55*(11), 1196.

Dettoni, J. L., Consolim-Colombo, F. M., Drager, L. F., Rubira, M. C., Cavasin de Souza, S. B. P., Irigoyen, M. C., Mostarda,C., Borile, S., Krieger, E.M., Moreno Jr., H. & Lorenzi-Filho, G. (2012). Cardiovascular effects of partial sleep deprivation in healthy volunteers. *Journal of Applied Physiology*, *113*(2), 232-236.

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychological bulletin*, *130*(3), 355.

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews Neuroscience*, *11*(2), 114.

Doan, S., Deyoung, G., Fuller-Rowell, T., Liu, C., Meyer, J., & Doan, S. (2018). Investigating relations among stress, sleep and nail cortisol and DHEA. S*tress (Amsterdam, Netherlands), 21(*2), 188–193. https://doi.org/10.1080/10253890.2018.1429398

Drummond, S. P., Brown, G. G., Stricker, J. L., Buxton, R. B., Wong, E. C., & Gillin, J. C. (1999). Sleep deprivation-induced reduction in cortical functional response to serial subtraction. *Neuroreport, 10*(18), 3745-3748.

Echouffo-Tcheugui, J. B., Conner, S. C., Himali, J. J., Maillard, P., DeCarli, C. S., Beiser, A. S., Vasan, R.S. & Seshadri, S. (2018). Circulating cortisol and cognitive and structural brain measures: The Framingham Heart Study. *Neurology*, *91*(21), e1961-e1970.

Eisenmann, E. D., Rorabaugh, B. R., & Zoladz, P. R. (2016). Acute stress decreases but chronic stress increases myocardial sensitivity to ischemic injury in rodents. *Frontiers in psychiatry*, *7*, 71.

Feldman, P. J., Cohen, S., Lepore, S. J., Matthews, K. A., Kamarck, T. W., & Marsland, A. L. (1999). Negative emotions and acute physiological responses to stress. *Annals of Behavioral Medicine*, *21*(3), 216-222.

Friedmann, J., Globus, G., Huntley, A., Mullaney, D., Naitoh, P., & Johnson, L. (1977). Performance and mood during and after gradual sleep reduction. *Psychophysiology*, *14*(3), 245-250.

Friess, E., Trachsel, L., Guldner,J., Schier, T., Steiger, A., & Holsboer, F. (1995). DHEA administration increases rapid eye movement sleep and EEG power in the sigma frequency range. *American Journal of Physiology-Endocrinology And Metabolism*, *268*(1), E107-E113.

Goel, N., Rao, H., Durmer, J. S., & Dinges, D. F. (2009). Neurocognitive consequences of sleep deprivation. *Seminars in neurology*, *29*(4), 320–339. https://doi.org/10.1055/s-0029-1237117

Goel, N., Basner, M., Rao, H., & Dinges, D. F. (2013). Circadian rhythms, sleep deprivation, and human performance. *Progress in molecular biology and translational science*, *119*, 155-190.

Goodarzi, M. O., Carmina, E., & Azziz, R. (2015). Dhea, dheas and pcos. The Journal of steroid biochemistry and molecular biology, 145, 213-225.

Greenberg, R., Pillard, R., & Pearlman, C. (1972). Effect of dream (stage rem) deprivation on adaptation to stress. *Psychosomatic Medicine, 34*(3), 257-262.

Grossman, E. S., Hoffman, Y. S. G., & Shrira, A. (2017). Trauma-related context increases sleep disturbances in people with acute stress disorder symptoms: Sleep disturbances, ASD and context. *Stress and Health, 33*(2), 153-157. doi:10.1002/smi.2679

Hajszan, T., MacLusky, N. J., & Leranth, C. (2004). Dehydroepiandrosterone increases hippocampal spine synapse density in ovariectomized female rats. *Endocrinology*, *145*(3), 1042-1045.

Hamidovic, A., Childs, E., Conrad, M., King, A., & de Wit, H. (2010). Stress-induced changes in mood and cortisol release predict mood effects of amphetamine. *Drug and alcohol dependence*, *109*(1-3), 175-180.

Hansen, Å. M., Thomsen, J. F., Kaergaard, A., Kolstad, H. A., Kaerlev, L., Mors, O., Rugulies, R., Bonde, J.P., Anderson, J.H., & Mikkelsen, S. (2012). Salivary cortisol and sleep problems among civil servants. *Psychoneuroendocrinology*, *37*(7), 1086-1095.

Hasegawa-Ohira, M., Suguri, K., & Nomura, S. (2016). The dehydroepiandrosterone awakening response as a possible index of subjective sleep quality. *Advanced Biomedical Engineering*, *5*, 132-136.

Het, S., & Wolf, O. T. (2007). Mood changes in response to psychosocial stress in healthy young women: effects of pretreatment with cortisol. *Behavioral neuroscience*, *121*(1), 11.

Hoddes, E., Zarcone, V., Smythe, H., Phillips, R., & Dement, W. C. (1973). Quantification of sleepiness: a new approach. *Psychophysiology*, *10*(4), 431-436.

Holman, E. A., Silver, R. C., Poulin, M., Andersen, J., Gil-Rivas, V., & McIntosh, D. N. (2008). Terrorism, acute stress, and cardiovascular health: A 3-year national study following the September 11th attacks. *Archives of general psychiatry*, *65*(1), 73-80.

Horne, J. (2011). The end of sleep: 'Sleep debt' versus biological adaptation of human sleep to waking needs. *Biological Psychology, 87*(1), 1-14. doi:10.1016/j.biopsycho.2010.10.004

Huang, T., Poole, E. M., Vetter, C., Rexrode, K. M., Kubzansky, L. D., Schernhammer, E., Rohleder, N., Hu, F.B., Redline, S., & Tworoger, S. S. (2017). Habitual sleep quality and diurnal rhythms of salivary cortisol and dehydroepiandrosterone in postmenopausal women. *Psychoneuroendocrinology*, *84*, 172-180.

Izawa, S., Sugaya, N., Shirotsuki, K., Yamada, K. C., Ogawa, N., Ouchi, Y., Nagano, Y.,& Nomura, S. (2008). Salivary dehydroepiandrosterone secretion in response to acute psychosocial stress and its correlations with biological and psychological changes. *Biological Psychology*, *79*(3), 294–298. https://doi.org/10.1016/j.biopsycho.2008.07.003

Jeckel, C. M. M., Lopes, R. P., Berleze, M. C. C., Luz, C. M., Feix, L. da F., Argimon, I. I. L., Stewin, L.M., & Bauer, M. E. (2010). Neuroendocrine and immunological correlates of chronic stress in "strictly healthy" populations. *Neuroimmunomodulation*, *17*(1), 9–18. https://doi.org/10.1159/000243080

Johns, M. W. (1991). A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep*, *14*(6), 540-545.

Joo, E. Y., Yoon, C. W., Koo, D. L., Kim, D., & Hong, S. B. (2012). Adverse Effects of 24 Hours of Sleep Deprivation on Cognition and Stress Hormones. *Journal of Clinical Neurology (Seoul, Korea)*, *8*(2), 146–150. https://doi.org/10.3988/jcn.2012.8.2.146

Kalimi, M., Shafagoj, Y., Loria, R., Padgett, D., & Regelson, W. (1994). Anti-glucocorticoid effects of dehydroepiandrosterone (DHEA). *Molecular and cellular biochemistry*, *131*(2), 99-104.

Kamin, H. S., & Kertes, D. A. (2017). Cortisol and DHEA in development and psychopathology. *Hormones and Behavior*, *89*, 69–85. https://doi.org/10.1016/j.yhbeh.2016.11.018

Ketai, R. (1975). Affect, mood, emotion, and feeling: semantic considerations. *The American journal of psychiatry*.

Killgore, W. D. (2010). Effects of sleep deprivation on cognition. In *Progress in brain research* (Vol. 185, pp. 105-129). Elsevier.

Kirschbaum, C., Pirke, K., & Hellhammer, D.H. (1993). The "Trier Social Stress Test" - a tool for investigating psychobiological stress response in a laboratory setting. *Neuropsychobiology*. *28*(1-2), 76–81.

Ko, S. B. (2013). Night shift work, sleep quality, and obesity. *Journal of lifestyle medicine*, *3*(2), 110.

Landolt, Hans-Peter; Holst, Sebastian C; Sousek, Alexandra (2014). *Effects of acute and chronic sleep deprivation.* In: Bassetti, C; Dogas, Zoran; Peigneux, Philippe. Sleep Medicine Textbook. Regensburg: European Sleep Research Society, 49-61.

Laudat, M. H., Cerdas, S., Fournier, C., Guiban, D., Guilhaume, B., & Luton, J. P. (1988). Salivary cortisol measurement: a practical approach to assess pituitary-adrenal function. *The Journal of Clinical Endocrinology & Metabolism*, *66*(2), 343-348.

LeBlanc, V. R. (2009). The effects of acute stress on performance: implications for health professions education. *Academic Medicine*, *84*(10), S25-S33.

Lennartsson, A.-K., Kushnir, M. M., Bergquist, J., & Jonsdottir, I. H. (2012). DHEA and DHEA-S response to acute psychosocial stress in healthy men and women. *Biological Psychology*, *90*(2), 143–149. https://doi.org/10.1016/j.biopsycho.2012.03.003

Leor, J., Poole, W. K., & Kloner, R. A. (1996). Sudden cardiac death triggered by an earthquake. *New England Journal of Medicine*, *334*(7), 413-419.

Leproult, R., Copinschi, G., Buxton, O., & Van Cauter, E. (1997). Sleep loss results in an elevation of cortisol levels the next evening. Sleep, 20(10), 865-870.

Louca, M., & Short, M. A. (2014). The effect of one night's sleep deprivation on adolescent neurobehavioral performance. *Sleep*, *37*(11), 1799–1807. http://doi.org/10.5665/sleep.4174

Liu, Y. (2016). Prevalence of Healthy Sleep Duration among Adults — United States, 2014. *MMWR. Morbidity and Mortality Weekly Report*, *65*. https://doi.org/10.15585/mmwr.mm6506a1

Lupien, S. J., Maheu, F., Tu, M., Fiocco, A., & Schramek, T. E. (2007). The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. *Brain and cognition*, *65*(3), 209-237.

Ma, N., Dinges, D. F., Basner, M., & Rao, H. (2015). How acute total sleep loss affects the attending brain: A meta-analysis of neuroimaging studies. Sleep, 38(2), 233–240. https://doi.org/10.5665/sleep.4404

Maninger, N., Wolkowitz, O. M., Reus, V. I., Epel, E. S., & Mellon, S. H. (2009). Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). *Frontiers in neuroendocrinology*, *30*(1), 65-91.

Maquet, P., Péters, J. M., Aerts, J., Delfiore, G., Degueldre, C., Luxen, A., & Franck, G. (1996). Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. *Nature*, *383*(6596), 163-166.

McEwen, B. S., & Gianaros, P. J. (2010). Central role of the brain in stress and adaptation: links to socioeconomic status, health, and disease. *Annals of the New York Academy of Sciences*, *1186*, 190.

McKlveen, J. M., Myers, B., Flak, J. N., Bundzikova, J., Solomon, M. B., Seroogy, K. B., & Herman, J. P. (2013). Role of prefrontal cortex glucocorticoid receptors in stress and emotion. *Biological psychiatry*, *74*(9), 672-679.

Miller, R., Plessow, F., Kirschbaum, C., Stalder, T. (2013). Classification criteria for distinguishing cortisol responders from nonresponders to psychosocial stress: Evaluation of salivary cortisol pulse detection in panel designs. *Psychosomatic Medicine, (75)*, 832-840.

Minkel, J., Moreta, M., Muto, J., Htaik, O., Jones, C., Basner, M., & Dinges, D. (2014). Sleep deprivation potentiates HPA axis stress reactivity in healthy adults. *Health Psychology, 33*(11), 1430-1434. doi:10.1037/a0034219

Morgan, C. A., Southwick, S., Hazlett, G., Rasmusson, A., Hoyt, G., Zimolo, Z., & Charney, D. (2004). Relationships Among Plasma Dehydroepiandrosterone Sulfate and CortisolLevels, Symptoms of Dissociation, and Objective Performance in Humans Exposed to Acute Stress. *Archives of General Psychiatry*, *61*(8), 819-825.

Motomura, Y., Kitamura, S., Oba, K., Terasawa, Y., Enomoto, M., Katayose, Y., Hida, A., Moriguchi, Y., Higuchi, S., & Mishima, K. (2013). Sleep debt elicits negative emotional reaction through diminished amygdala-anterior cingulate functional connectivity. *PloS one*, *8*(2).

Motomura, Y., Katsunuma, R., Yoshimura, M., & Mishima, K. (2017). Two days' sleep debt causes mood decline during resting state via diminished amygdala-prefrontal connectivity. *Sleep*, *40*(10).

Nguyen, T. V., McCracken, J. T., Ducharme, S., Cropp, B. F., Botteron, K. N., Evans, A. C., & Karama, S. (2013). Interactive effects of dehydroepiandrosterone and

testosterone on cortical thickness during early brain development. *Journal of Neuroscience*, *33*(26), 10840-10848.

Nussey, S. S., & Whitehead, S. A. (2001). *Endocrinology: an integrated approach*. CRC Press.

O'Brien, M. J., O'Toole, R. V., Newell, M. Z., Lydecker, A. D., Nascone, J., Sciadini, M., Pollak, A., Turen, C., & Eglseder, W. A. (2012). Does sleep deprivation impair orthopaedic surgeons' cognitive and psychomotor performance?. *JBJS*, *94*(21), 1975-1981.

Ohayon, M. M., Carskadon, M. A., Guilleminault, C., & Vitiello, M. V. (2004). Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. *Sleep*, *27*(7), 1255-1273.

Payne, J. D., & Nadel, L. (2004). Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol. *Learning & Memory*, *11*(6), 671-678.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI. United States: Elsevier Inc. doi:10.1006/nimg.2002.1087

Philip, P., Sagaspe, P., Prague, M., Tassi, P., Capelli, A., Bioulac, B., Commenges, D. & Taillard, J. (2012). Acute versus chronic partial sleep deprivation in middle-aged people: differential effect on performance and sleepiness. *Sleep*, 35(7), 997-1002.

Pluchino, N., Drakopoulos, P., Bianchi-Demicheli, F., Wenger, J. M., Petignat, P., & Genazzani, A. R. (2015). Neurobiology of DHEA and effects on sexuality, mood and cognition. *The Journal of steroid biochemistry and molecular biology*, *145*, 273-280.

Prall, S. P., Larson, E. E., & Muehlenbein, M. P. (2017). The role of dehydroepiandrosterone on functional innate immune responses to acute stress. *Stress and Health*, *33*(5), 656-664.

Prough, R. A., Clark, B. J., & Klinge, C. M. (2016). Novel mechanisms for DHEA action. *Journal of molecular endocrinology*, *56*(3), R139-R155.

Pruessner, J. C., Dedovic, K., Khalili-Mahani, N., Engert, V., Pruessner, M., Buss, C., Renwick, R., Dagher, A., Meaney, M.J., & Lupien, S. (2008). Deactivation of the limbic system during acute psychosocial stress: evidence from positron emission tomography and functional magnetic resonance imaging studies. *Biological psychiatry*, *63*(2), 234-240.

Qiao, S., Li, X., Zilioli, S., Chen, Z., Deng, H., Pan, J., & Guo, W. (2017). Hair Measurements of Cortisol, DHEA, and DHEA to Cortisol Ratio as Biomarkers of Chronic Stress among People Living with HIV in China: Known-Group Validation. *PLoS ONE*, *12*(1), e0169827. Retrieved from Opposing Viewpoints in Context.

Qin, S., Hermans, E. J., van Marle, H. J., Luo, J., & Fernández, G. (2009). Acute psychological stress reduces working memory-related activity in the dorsolateral prefrontal cortex. *Biological psychiatry*, *66*(1), 25-32.

Randler, C., & Vollmer, C. (2013). Aggression in Young Adults — A Matter of Short Sleep and Social Jetlag? Psychological Reports, 113(3), 754–765. https://doi.org/10.2466/16.02.PR0.113x31z7

Rasch, B., & Born, J. (2013). About sleep's role in memory. *Physiological reviews*, *93*(2), 681-766.

Russell, G., & Lightman, S. (2019). The human stress response. *Nature Reviews Endocrinology*, *15*(9), 525–534. https://doi.org/10.1038/s41574-019-0228-0

Salin-Pascual, R. J., Ortega-Soto, H., Huerto-Delgadillo, L., Camacho-Arroyo, I., Roldán-Roldán, G., & Tamarkin, L. (1988). The effect of total sleep deprivation on plasma melatonin and cortisol in healthy human volunteers. *Sleep*, *11*(4), 362-369.

Sanches, I., Teixeira, F., dos Santos, J. M., & Ferreira, A. J. (2015). Effects of acute sleep deprivation resulting from night shift work on young doctors. *Acta medica portuguesa*, *28*(4), 457-462.

Schmukle, S. C., Egloff, B., & Burns, L. R. (2002). The relationship between positive and negative affect in the Positive and Negative Affect Schedule. *Journal of Research in Personality*, *36*(5), 463-475.

Schoofs, D., & Wolf, O. T. (2011). Are salivary gonadal steroid concentrations influenced by acute psychosocial stress? A study using the Trier Social Stress Test (TSST). *International Journal of Psychophysiology*, *80*(1), 36-43.

Scullin, M. K. (2013). Sleep, memory, and aging: The link between slow-wave sleep and episodic memory changes from younger to older adults. *Psychology and Aging*, *28*(1), 105–114. https://doi.org/10.1037/a0028830

Shekleton, J. A., Flynn-Evans, E. E., Miller, B., Epstein, L. J., Kirsch, D., Brogna, L. A., Burke, L.M., Bremer, E., Murray, J.M., Gehrman, P., & Lockley, S.W. (2014). Neurobehavioral performance impairment in insomnia: Relationships with self-reported sleep and daytime functioning. *Sleep*, *37*(1), 107–116. http://doi.org/10.5665/sleep.3318

Shields, G., Lam, J., Trainor, B., & Yonelinas, A. (2016). Exposure to acute stress enhances decision-making competence: Evidence for the role of DHEA. *Psychoneuroendocrinology*, *67*, 51–60. https://doi.org/10.1016/j.psyneuen.2016.01.031

Shirotsuki, K., Izawa, S., Sugaya, N., Yamada, K. C., Ogawa, N., Ouchi, Y., Nagano, Y., & Nomura, S. (2009). Salivary cortisol and DHEA reactivity to psychosocial stress in socially anxious males. *International Journal of Psychophysiology*, *72*(2), 198-203.

Slovic, P., Finucane, M. L., Peters, E., & MacGregor, D. G. (2007). The affect heuristic. *European journal of operational research*, *177*(3), 1333-1352.

Speer, M. E., & Delgado, M. R. (2017). Reminiscing about positive memories buffers acute stress responses. *Nature human behaviour*, *1*(5), 0093.

Sripada, R. K., Marx, C. E., King, A. P., Rajaram, N., Garfinkel, S. N., Abelson, J. L., & Liberzon, I. (2013). DHEA enhances emotion regulation neurocircuits and modulates memory for emotional stimuli. *Neuropsychopharmacology*, *38*(9), 1798-1807.

Steiger, A. (2003). Sleep and endocrinology. *Journal of internal medicine, 254*(1), 13-22.

Stephens, M. A., & Wand, G. (2012). Stress and the HPA axis: role of glucocorticoids in alcohol dependence. *Alcohol research : current reviews*, *34*(4), 468–483.

Talbot, L. S., McGlinchey, E. L., Kaplan, K. A., Dahl, R. E., & Harvey, A. G. (2010). Sleep deprivation in adolescents and adults: Changes in affect. *Emotion*, *10*(6), 831.

Taylor, M. K., Padilla, G. A., Stanfill, K. E., Markham, A. E., Khosravi, J. Y., Dial Ward, M. D., & Koehler, M. M. (2012). Effects of dehydroepiandrosterone supplementation during stressful military training: a randomized, controlled, double-blind field study. *Stress*, *15*(1), 85-96.

Tononi, G., & Cirelli, C. (2003). Sleep and synaptic homeostasis: a hypothesis. *Brain research bulletin*, *62*(2), 143-150.

Tsigos, C., Kyrou, I., Kassi, E., & Chrousos, G. P. (2016). Stress, endocrine physiology and pathophysiology. In *Endotext [Internet]*. MDText. com, Inc..

Van Dongen, H. P., Caldwell, J. A., & Caldwell, J. L. (2006). Investigating systematic individual differences in sleep-deprived performance on a high-fidelity flight simulator. *Behavior research methods*, *38*(2), 333-343.

Van Eck, M., Berkhof, H., Nicolson, N., & Sulon, J. (1996). The effects of perceived stress, traits, mood states, and stressful daily events on salivary cortisol. *Psychosomatic medicine*, *58*(5), 447-458.

Van Reeth, O., Weibel, L., Spiegel, K., Leproult, R., Dugovic, C., & Maccari, S. (2000). Interactions between stress and sleep: from basic research to clinical situations. *Sleep Medicine Reviews*, *4*(2), 201-220.

Vandekerckhove, M., & Cluydts, R. (2010). The emotional brain and sleep: an intimate relationship. *Sleep medicine reviews*, *14*(4), 219-226.

Vgontzas, A. N., Pejovic, S., Zoumakis, E., Lin, H. M., Bixler, E. O., Basta, M., Fang, J., Sarrigiannidis, A., & Chrousos, G. P. (2007). Daytime napping after a night of sleep loss decreases sleepiness, improves performance, and causes beneficial changes in cortisol and interleukin-6 secretion. *American Journal of Physiology-Endocrinology and Metabolism*, *292*(1), E253-E261.

Vollert, C., Zagaar, M., Hovatta, I., Taneja, M., Vu, A., Dao, A., Levine, A., Alkadhi, K., & Salim, S. (2011). Exercise prevents sleep deprivation-associated anxiety-like behavior in rats: Potential role of oxidative stress mechanisms. *Behavioural Brain Research*, *224*(2), 233–240.

Wali, S. O., Qutah, K., Abushanab, L., Basamh, R. A., Abushanab, J., & Krayem, A. (2013). Effect of on-call-related sleep deprivation on physicians' mood and alertness. *Annals of thoracic medicine*, *8*(1), 22.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of personality and social psychology*, *54*(6), 1063.

Wright Jr, K. P., Drake, A. L., Frey, D. J., Fleshner, M., Desouza, C. A., Gronfier, C., & Czeisler, C. A. (2015). Influence of sleep deprivation and circadian misalignment on cortisol, inflammatory markers, and cytokine balance. *Brain, behavior, and immunity*, *47*, 24-34.

Wu, J. C., Gillin, J. C., Buchsbaum, M. S., Hershey, T., Hazlett, E., & Sicotte, N. Bunney, Jr., WE (1991). The effect of sleep deprivation on cerebral glucose metabolic rate in normal humans assessed with positron emission tomography. *Sleep*, *14*(2), 155-162.

Wu, J. C., Gillin, J. C., Buchsbaum, M. S., Chen, P., Keator, D. B., Wu, N. K., Darnall, L.A., Fallon, J.H., & Bunney, W. E. (2006). Frontal lobe metabolic decreases with sleep deprivation not totally reversed by recovery sleep. *Neuropsychopharmacology*, *31*(12), 2783-2792.

Yeung, M. K., Lee, T. L., Cheung, W. K., & Chan, A. S. (2018). Frontal underactivation during working memory processing in adults with acute partial sleep deprivation: A near-infrared spectroscopy study. Frontiers in Psychology, 9, 742. doi:10.3389/fpsyg.2018.00742

Zambotti, M. d., Sugarbaker, D., Trinder, J., Colrain, I. M., & Baker, F. C. (2016). Acute stress alters autonomic modulation during sleep in women approaching menopause. *Psychoneuroendocrinology, 66*, 1-10. doi:10.1016/j.psyneuen.2015.12.017

Zhong, X., Hilton, H. J., Gates, G. J., Jelic, S., Stern, Y., Bartels, M. N., DeMeersman, R. E., & Basner, R. C. (2005). Increased sympathetic and decreased parasympathetic cardiovascular modulation in normal humans with acute sleep deprivation. *Journal of applied physiology*, *98*(6), 2024-2032.

Zohar, D., Tzischinsky, O., Epstein, R., & Lavie, P. (2005). The effects of sleep loss on medical residents' emotional reactions to work events: a cognitive-energy model. Sleep, 28(1), 47-54.