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Reciprocal Relation Between Psychophysiological Patterns of Stress Responsivity and Sleep

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Reciprocal Relation Between Psychophysiological Patterns of Stress Responsivity and Sleep

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ABSTRACT

Contemporary understanding of the brain indicates that a reciprocal relationship exists between mind and body. Biological functioning adjusts to the consequences of our behavior and our behavior is influenced by our biology. This is the case with the stress responsivity system. The stress hormone cortisol follows a biologically-predetermined daily cycle of secretion (controlled by circadian rhythm) that correlates with expected activity throughout the day, however this cycle can accommodate to different environmental changes that can occur. It has been noticed that individuals who report stress problems also report sleep problems. I hypothesized that sleep quality can predict maladjustments in cortisol's rhythm. All participants provided saliva samples and had to take the Pittsburgh Sleep Quality Index (PSQI). Salivivay cortisol was measured via was enzyme-immuno-assayed for cortisol. I analyzed the data for three independent studies: (1)12 samples were taken for basal and lab days in 65 individuals. People who scored worse in total PSQI showed decreased stress reactivity (γ 21=-.02, t(63)=-2.27, p=0.026) and faster recovery (γ31=-0.102, t(608)=-2.044, p=0.041). (2)6-8 samples per day across 5 days in 120 maltreated or control adolescents. I used a 3-level hierarchical linear model to examine rhythms within each day and within each individual. The cortisol rhythm was flattened on days when adolescents had poor sleep latency (β;=.013, p=.025 for time-since-waking, β=-.0008, p=.039 for quadratic time-since-waking). (3) 10 samples were taken in 44 skydivers for jumping and basal days. Those who scored worse in sleep latency had slower reactivity (γ31=-0.16, t(284)=-3.701, p<.001) and slower recovery (γ31=0.22, t(284)=3.311, p<0.001). Stress and sleep problems are related to cognitive and physiological issues; finding an appropriate connection between them can be elemental in preventing problems.

Keywords: Cortisol, Sleep, HPA, Circadian Rhythm, Stress

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INTRODUCTION

Sleep

In modern society sleep is often disregarded as cumbersome and a waste of time. Our culture praises those who strive to stay awake in the face of slumber; in fact average sleep time has been steadily decreasing throughout the years. Americans received an average of 8 hours of sleep in the 1950s and that went down to 6-7 hours in 2013 (Sleep Foundation, 2013) (Gottlieb, D. 2006). These studies reflect the increasing societal demand on cutting the amount of sleep in daily life as to extend the hours of activity and therefore possible work.

Although the biological purpose of sleep remains an enigma, we can know for sure that sleep is essential for proper functioning of the body. Most animals manifest a period of quiescence of activity that can be described as a form of sleep (Siegel, J. 2008), and we've all heard how sleep occupies one third of our lives (science.education.nih-.gov). Although, does it not seem reasonable to say that evolution would have produced a less dangerous alternative to sleep by now? Maybe one that didn't require the animal to lose consciousness and potentially making it more vulnerable to predators. After millions of years sleep hasn't disappeared so we can assume this specific behavior is essential for the animal's survival. It has been shown that rats die after 2 weeks of sleep deprivation, and in fact they survive longer without food than without sleep (Rechtschaffen, A. 1983), though this same results vary from species to species, and has yet to be observed in primates. In

humans, fatal familial insomnia, an inherited condition where a person is unable to sleep, death occurs between 6-32 months, though it is not known whether the lack of sleep itself is responsible for death or other factors related to the disease are involved (Brande, J. 2004).

Sleep disturbances can be observed along a wide range of psychophysiological disorders. For example, 30-80% of individuals suffering from schizophrenia also suffer from sleep disorders, including reduced sleep efficiency and total sleep time, as well as increased sleep latency (Cohrs, S. 2008). These sleep issues can be seen before the onset of schizophrenia. Insomnia and hypersomnia are common symptoms of depression and have been suggested as predictors of depression (Breslau, N. 1996).

Sleep also has a huge influence in cognition. Fatigue from sleep deprivation can have very detrimental effects in behavior and increase the likelihood of bad decision making. Lack of sleep has been singled out as a major cause of motor vehicle accidents as it is responsible for approximately 40,000 injuries and 1,500 deaths a year in the US alone (Boyle, L. 2010). Poor sleep quality can also have huge negative effects in work performance and has been accused for playing a part in the Challenger disaster, the Exxon Valdez oil spill, and Chernobyl disaster and other major man-made disasters (Mitler, M. 1988).

The two-process model of sleep describes sleep onset as a balance between process S (sleep homeostasis) and process C (circadian rhythms) (Borbely, A. 1982). Process S refers to the drive to sleep which accumulates throughout the day since waking up from previous sleep. A review by Tononi and Cirelli (2003) suggests that slow wave

sleep (SWS) plays a major role in homeostatic synaptic downscaling. Synaptic potentiation during wakefulness increases synaptic weight throughout the day increasing the need for downscaling which is provided by SWS. This helps promote plastic changes in the synaptic connections. Process C is dependent on circadian rhythmicity which controls the internal body clock. Circadian rhythmicity is important in my study so in the next portion I will talk about in detail.

Circadian Rhythms

This mechanism is dependent on the daily interactions with zeitgebers (time givers) which include temperature, sound, and even social interactions, but the most influential of them all is light. Light is received in specialized cells in the retina called the intrinsically photosensitive Retinal Ganglion Cells (ipRGC) which are not known to be involved in sight. Light signals from the ipRGCs are sent to the pineal gland which produces melatonin which helps in synchronizing the sleep-wake cycle by lowering body temperature and causing drowsiness triggering the onset for sleep. Melatonin is mainly produced during the night reaching its peak levels between 11pm and 3am (Wang, G) but it is almost nonexistent during the day. The suprachiasmatic nucleus (SCN) in the hypothalamus regulates all the other aspects of the regulation of the biological clock. The ipRGCs detect the light signals and these are sent to suprachiasmatic nuclei. Humans are not born with entrainment to the light-dark cycle. Synchronization of the circadian rhythm starts early in development but it can vary widely from 2-20 weeks of age (Santiago, L. 2003). Various changes occur in the circadian rhythm throughout life and these will be addressed later.

There is wide debate over what is the exact role of the suprachiasmatic nuclei in sleep regulation including whether it helps to promote wakefulness or sleep. Animal studies of SCN ablation are contradictory, maybe signaling to differences across species. So far evidence supports a bidirectional model where the SCN promotes both wakefulness and sleep throughout different times of the day (Mistlberger, R. 2005).

Circadian Rhythm Disorders

That the circadian rhythm is so heavily dependent on environmental cues has a potential cost if lifestyle does not match the individual's circadian rhythm. These costs can manifest as “extrinsic circadian disorders”. This is also true if internal issues cause dysregulation of the circadian rhythm, making it difficult for the individual to adjust to normal scheduled life. These are called “intrinsic circadian disorders”. Modern extrinsic circadian rhythm disorders can arise from rapid travel across multiple time zones resulting in ‘jet lag’. Extrinsic factors include changes in light exposure and also social or work schedule expectations. Jet lag is characterized by fatigue, irritability and problems with digestion (Waterhouse, J. 2002). Another extrinsic CR disorder is the shift-work CR disorder. The lack of synchronization between activity and day-night schedule can cause fatigue in the short term, but in the long term it has been linked to depression, and heart problems (Costa, G. 1996). The circadian rhythm can also be delayed or advanced causing the individual to sleep and wake up earlier or later than normal, which may prove to be troublesome in daily life and have also been linked to depression. If the environmental cues are absent the individual may suffer from free-running circadian rhythm

disorder. This condition is mainly limited to blind people and nearly half of the blind suffer from it. It is characterized by a lack of entrainment with the light cycle resulting in an inconsistent sleep schedule; many schizophrenics also suffer from this condition. The last CR disorder is the irregular CR disorder, which is characterized by short naps instead of set period of sleep. In this disorder there is daily variation of timing and amount of sleep. Cultural and social pressures can make life difficult to individuals who suffer from desynchronization of their circadian rhythm, but it can also have detrimental effects on one's health. All these disorders carry a risk of depression, cardiovascular issues, stress, digestion problems (Krahn, L. 2007)

Cortisol

In popular science cortisol is usually targeted as dangerous, this sentiment is witnessed by simply making a quick google search of the word "'cortisol". In your search you will find multiple articles pointing out the dangers of the hormone and will offer suggestions on how to lower your levels of it. One particular title of a Psychology Today article reads "Cortisol: Why "The Stress Hormone" Is Public Enemy No.1" (Bergland, C. 2013). This one-sided approach can be misleading, but it's only a reflection of the lack of understanding of how this hormone works. On this portion I will talk about cortisol's form of action, function, and dynamic properties.

Cortisol is a steroid hormone often associated with a physiological response to to stress. Cortisol, as all steroid hormones, is synthesized from cholesterol. The release of cortisol is mediated by the hypothalamic-pituitary-adrenal (HPA) axis. When a stressor is

detected the hypothalamus secretes corticotropin-releasing hormone (CRH), this is detected by the pituitary gland which produces adrenocorticotropin hormone (ACTH) which finally triggers the release of cortisol in the adrenal cortex. Through negative-feedback cortisol stops its own production, sending back signals to the hypothalamus and pituitary gland. In times of stress cortisol serves various regulatory functions such as increasing blood sugar by altering glucose metabolism, and suppressing the inflammatory response in the immune system. The HPA axis is said to be an allostatic system. The allostasis model explains how the different body systems are able to adapt through time to a constantly changing environment (McEwen, B. 1998). Cortisol regulation is adaptive to the environmental context and although high levels of it are commonly associated with negative consequences, a clear-cut approach should not be assumed (Shirtcliff, E. 2014). Studies show that cortisol reacts differently to different stressors and among different individuals. Cortisol reactivity is more sensitive to uncontrollable stress situations and socio-evaluative stress.

Stress does not always result in high cortisol. Holocaust survivors with posttraumatic stress disorder were observed to have low cortisol. Cortisol's levels (Yehuda, R, 1995), low cortisol reactions were also observed in parent-child conflicts (Shirtcliff, E. 2005) and after the death of a child from cancer (Hofer, M. 1972). Either high or low should not be automatically assumed to be good or bad but should be seen as a mere response to a specific context. Within normal ranges high cortisol can make the individual more open to his environment and to his peers, but can also be negative as it can increase our sensitivity to social evaluation and fear of rejection. On the other hand low

cortisol may result in disengagement from our environment, it can also occur when we are faced with an insuperable challenge or familiar stimuli.

Due to its dynamic properties classifying a cortisol pattern as maladjustment can be difficult. For the purpose of this paper I will describe maladjustments as a loss in malleability in cortisol's regulation. With lack of malleability the individual will have more problems adjusting to the ever-changing environment, and he will not be able to appropriately respond to the wide variety of stressors that he might face. Particular maladjustments that result in long term exposure to cortisol have been linked to a wide variety of health issues including cardiovascular diseases (Whitworth, J. 2005), depression (Sherwood, E. 2003), digestive problems, weight changes (Putignano, P. 2001), etc. Chronically elevated cortisol levels may also cause reductions in neuronal plasticity and neurogenesis (mainly in the hippocampus), which are considered as potential physiological mechanisms of several mood disorders (Sapolsky, R. 2000).

Cortisol Diurnal Rhythm

Cortisol secretion throughout the day follows a pattern guided by circadian rhythmicity. Normally it is expected to see the zenith of cortisol secretion in the morning approximately 30 minutes after waking up (Edwards, S. 2001), this is called the "cortisol awakening response" (CAR). After the reaching peak CAR, cortisol levels sharply drop until 3 hours upon awakening only to have a steadier decline throughout the day and evening until reaching nadir around 12:00 am on average. The purpose of the CAR is yet to be discovered. Some studies suggest that the CAR serves as a preparation for upcoming

events, this may explain why CAR is higher on workdays than in weekends (Schlotz, W. 2007), or higher in competitive ball-room dancers in the morning of a competition as opposed to a normal day (Rohleder, N. 2007). CAR has also been suggested to have an intrinsic connection to the hippocampus. Ablation to the hippocampus has been shown to eliminate cortisol's response to awakening (Buchanan, T. 2004), and individuals with larger hippocampus tend to have larger CAR (Pruessner, M. 2007). The CAR connection to the hippocampus might suggest that it plays a role in helping in activating the sense of orientation. The CAR and associated metabolic processes may be involved in reactivating the sense of self in time, and space, and well as one's relationship to other people and the environment.

Regardless of its true function, the CAR has recently garnered attention as it may prove to be an important biomarker in the evaluation of HPA axis functioning. The CAR is easy to measure as it does not need any external stressors or stimuli to activate as it is just a response to awakening, and its variability has been associated with psychophysiological aspects and health related issues. A blunted CAR has been observed in individuals with post-traumatic stress disorder (PTSD) (Neylan, T. 2005; Wessa, M. 2006) as well as chronic fatigue syndrome (Roberts, A. 2004), and sleep which we will talk later. An elevated CAR was seen in individuals with obesity (Therrien, F. 2007) and respiratory issues among others. Studies relating depression to CAR show inconsistent findings, as increased (Bhagwagar, Z. 2005) and decreased (Stetler, C., 2005) CAR has been observed in depressed individuals. The ambiguity of these observations may be a result of

individual differences and type of depression. The study of the CAR might give us an insight on the diagnosis, prevention and even treatment of several of these conditions.

In a meta-analysis comparing chronic stress and diurnal rhythm, Miller (2007) pointed out that morning cortisol is high after recently becoming exposed to the stressor, as time passes CAR decreases to a level below normal. This observation might explain the low morning cortisol in PTSD subjects. This reduction in cortisol in chronic stress might be beneficial as it can diminish cortisol's inhibition of the immune system. Alternatively, it can also be detrimental as it can result in an over activity of the immune system that could result in autoimmune disorders. This low cortisol may also be a result of allostatic load. The allostatic load, proposed by McEwen (1998), describes the "wear and tear" of the body and brain. A prolonged overactivity of the HPA axis may result in it not being able to respond properly to different stressors, affecting its malleability and reactivity.

Another abnormality in cortisol diurnal rhythm that I want to touch in this paper is that of elevated evening cortisol or a flattening of cortisol rhythm. A flatter diurnal rhythm has been associated multiple times to depression and anxiety. Early adolescents who were followed from age 11-13 showed a propensity for mental health symptoms (i.e. depression, anxiety, etc…) when a flatter slope was observed (for a review see Shirtcliff, E. 2008). Depressed individuals with family history of mental health symptoms also showed a flatten rhythm throughout the day (Hsiao, F. 2010). In their meta-analysis, Miller et al (2010) found that had been exposed to acute physical and/or social stressors tend to have high evening cortisol and flatter rhythms.

Sleep and Cortisol Diurnal Rhythm

Popular belief commonly refers to stress as a causal factor contributing to poor sleep quality, but studies show that the connection between stress and sleep is not well understood. Sleep and stress have a correlational relationship in that each affects the other. Lack of sleep is often attributed in part to stress and stress is often attributed to lack of sleep. The bi-directional nature of the stress-sleep relationship may create difficulties in finding a causal factor and fully elucidating the relationship between these factors. I will investigate the association between stress and sleep as bidirectional, rather than one factor being causal. Many studies have found connections between sleep and autonomic responses by measuring catecholamine secretion and heart rate (Irwin M, 1999. Lusardi P, 1996) hinting of an activation of the sympathetic system after sleep deprivation. This study is relevant because autonomic nervous system activity is a critical piece of allostatic load and operates frequently in conjunction with the HPA axis. The role of cortisol in regards to sleep is less understood. Some studies have a found a mild increase in cortisol secretion after sleep deprivation (Chapotot, F. 2001; Leproult, R. 1997) while others find no changes at all (Akerstedt, T. 1980; Follenius, M. 1992).

I believe results can be clarified with a study design with several strengths. First, I believe it is important to study the changes of cortisol secretion throughout the day because this study design focuses on the rhythms of cortisol release and sleep patterns. In support, elevated evening cortisol (but not other times of day) has been observed after a night of sleep deprivation compared to a control day with normal sleep (Leproult, R. 1997). Second, studying the overall sleep patterns, not just one night of deprivation, might

eliminate the possibility that stress is increased because of the unique events related to sleep deprivation and not sleep loss itself. Allostatic load is conceptualized as a wear and tear on the body, and a single night of sleep loss may not be sufficient time to dysregulate diurnal rhythms. Instead, the body may quickly recover from this “allostatic state” in which the body deviates temporarily from established set points. Third, I want to see if the cognitive deficiencies caused by poor sleep affect in any way the HPA axis' ability to respond to stressors, which very few studies have addressed. Measuring the cortisol response in poor sleepers who participated in stress test such as the Trier Social Stress Test (TSST) may help me answer this question.

To test my hypotheses I will use data from three independent studies:

(1) *Magnetic resonance imaging (MRI) study*, (2) *Trier social stress test (TSST) study*, (3) *Skydiving study*.

The first study collects cortisol data throughout the day across 2-5 days for a complete diurnal rhythm between waking and bedtime. This permits me to see if there are any changes to the daily cortisol rhythm. The latter two studies measure hormone response to a specific environmental challenge which helped in determining whether stress reactivity is affected by sleep. While the overarching hypotheses are that the relationship is bidirectional, our measures of sleep refer to prior sleep, so cortisol will be computed (for statistical purposes) as the outcome. Each study uses identical data collection strategies that include the PSQI (Pittsburgh Sleep Quality Index) and saliva samples

In sum, the association between cortisol and sleep quality has not been sufficiently well-validated because extant studies have largely investigated cortisol levels as being too low or too high, rather than focusing on cortisol's intrinsic circadian rhythm. I hypothesize that a relationship can be found between sleep patterns and diurnal cortisol rhythm. Specifically I believe that poor sleep is correlated to a flatter cortisol slope throughout the day. The stress-sleep relationship is an example of how our behavior and biological functioning affect each other.

METHODS

Data Sources

The hypotheses were tested from four existing data sets collected at the Stress Psychology in Teens (SPIT) lab at the University of New Orleans (UNO). All procedures were approved by the UNO Institutional Review Board. Data from these projects hint that rhythms may be dysregulated in participants with greatest stress or psychopathology risk. My hypothesis is that some of this enhanced risk may stem from sleep problems. Data from the following three independently conducted studies was used:

(1) *The Magnetic resonance imaging (MRI) study of maltreated youth.* This study measured hormonal reactivity to a MRI, as well neurological differences in youth with history of physical abuse.

(2) *The (Trier social stress test) TSST study of stress.* Measured hormonal reactivity to a socio-evaluative stressor.

(3) *The Skydiving study of Sensation Seeking.* Tested hormonal reactivity to skydiving.

Participants

Participants were healthy young adult men (n =153) and women (n =132) with a mean age of 21.2 (range 9-49). Participant demographics are described in Table 1.

Overall Sample

N	285
Males	153 (54%)
Females	132 (46%)
Mean Age	21.2 years
Age Range	9-49 years

MRI Study

N	160
Males	82 (51%)
Females	78 (49%)
Mean Age	11.16 years
Age Range	9-14 years

Skydiving Study

N	44
Males	32 (73%)
Females	12 (27%)
Mean Age	29.6 years
Age Range	18-49 years

TSST Study

N	81
Males	39 (48%)
Females	42 (52%)
Mean Age	22.38± 4.34
Age Range	18-47 years

Table 1*. Participant demographics*

MEASURES

The PSQI is a measure for subjective sleep quality; it has shown good correlation with objective measures such as the polysomnographic test (Backhaus, J.2002). It measures seven different component of sleep: sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction for the last week. It has a scale ranging from 0-3 where 3 is the extremely poor sleep (Smyth, C. 2000). The PSQI was measured on the morning of each day of saliva collection for all three studies.

Within each study, repeated measures of saliva were collected via passive drool, frozen immediately and remained frozen at -80oC. Saliva was later measured for cortisol using a commercially available enzyme- immunoassay (www.salimetrics.com). All samples were assayed in duplicate; samples that varied by greater than 7% were repeat tested on a separate run. Samples from the same individual were run on the same plate. Saliva collection is a preferable method of obtaining cortisol as it is non-invasive, reducing the chances of a stress response and allowing for repeated cortisol measures.

For the MRI study, up to 32 saliva samples were collected on each participant across 5 days, including a lab-day, two school-days and two-home days. Six saliva samples were collected by the youth on each day (eight for the lab-day) between waking and bedtime. On basal days (at home and at school) participants collected their own saliva in the same way as it was collected in the laboratory as participants were given

instructions on the collection and storing of the samples. All laboratory visits began around the same time of day (mean=0928h, SD=14 min).

For the TSST study, six samples were collected in the afternoon of an acute challenge (TSST) where participants were exposed to a social evaluative context. The participants arrived in the afternoon around 2pm. The participants were given 10 minutes to prepare a speech for a hypothetical job interview. The participant gave a speech for five minute followed by another five minutes of mental math challenge. These tasks were performed in front of a panel of three judges whose intent was to provide as little emotional support to the participant as possible. Six additional samples were collected in a subset on a non-stressful day at matched times.

For the skydiving study, five samples were collected in the afternoon of an acute challenge where participants jumped out of an airplane; five additional samples were collected in a subset on a non-stressful day at matched times.

After participants arrived at the location for skydiving, and after informed consents were signed, participants received ten minutes of instruction provided by the skydiving company. After this the participants boarded the plane, ascended to 14,000ft and jumped. The mean time of jumps was 2:12pm. In addition to the skydiving day, participants collected saliva on similar times of day on a basal day.

Statistical Analyses

Each study was analyzed separately to accommodate the differences in timing of sample collection. For data analysis I used a two or three level hierarchical-linear-model to examine rhythms within each day and individual. Hierarchical linear modeling is advantageous because it allows multiple levels of analysis to be simultaneously modeled without violating the assumption of independence of observations. HLM is advantageous over a repeated measures ANOVA in that it does not require all the samples to be collected in parallel and can accommodate missing data. For the present studies, cortisol samples within each individual are modeled at Level 1 (within individual). Predictors of cortisol levels include time-varying measures such as time since waking (TSW); finding a significant effect of TSW indicates that cortisol levels change across the day between waking and bedtime and indicates that cortisol has a diurnal rhythm. The effect of TSW is simultaneously modeled with cortisol levels (the intercept). Level 2 captures the between-individual effects, including the PSQI associations with cortisol level and diurnal rhythm. Given the extensive number of days of collection for the MRI SPIT data, I used a 3-level model to differentiate day-level variance at level 2 and between-individual effects at level 3. This three-level model is not possible with only two days of collection as in the other two studies.

RESULTS

Changes in Diurnal Rhythm

MRI Study Results

HLM data analyses are set up with three levels predicting cortisol reactivity showing intercept main effects, slopes, and variations with level 1 capturing moment to moment ($Y_0 = P_0 + \ldots + e_0$), level 2 capturing day-specific differences or stabilities ($P_0 = \beta_{00} + \ldots + r_0$), and level 3 capturing individual differences ($\beta_{00} = \gamma_{000} + \ldots + \mu_{00}$).

Overall cortisol levels were significantly higher in lab day than in basal day ($_{400}$= .08527, p<.0001)

On average, individuals' cortisol level significantly slopes down (γ_{100}= -.173, p<.0001) from the group average, significantly swoops back up (γ_{200}= .019, p<.0001), and significantly swoops back down (γ_{300}= -.0007, p<.0001) when considering individuals' diurnal rhythms by including time since waking, quadratic time since waking and cubic time since waking as predictors of cortisol.

As shown in **figure 1** the PSQI subscale for sleep latency was related to cortisol's diurnal rhythm ($\gamma 110$=.013, t(117)=2.28, p=.025 for linear time since waking and $\gamma 210$=-.001, t(482)=-2.07, p=.039 for quadratic time since waking effect). It was observed that individuals that took longer to fall asleep had flatter diurnal slopes across the day whereas good sleepers had steep diurnal slopes. No significant effect was found among the other subscales of the PSQI. Results suggest that poor sleep quality, measured as sleep

latency, is related to a flattened diurnal rhythm across several days within a stressed population: maltreated youth.

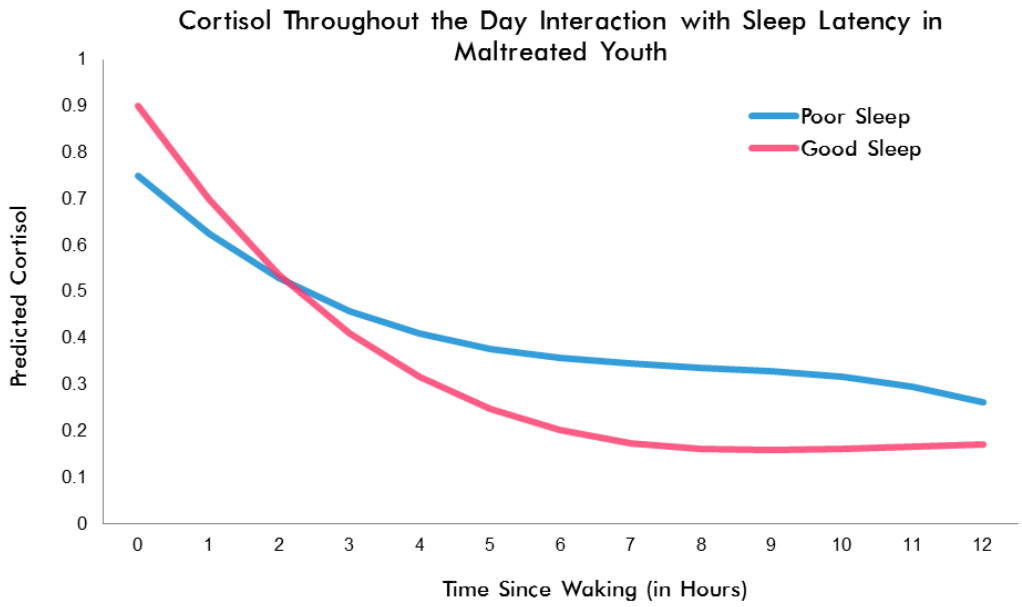

Figure 1. *A flatter curve is observed in worse sleep latency.*

Cortisol Reactivity and Recovery

TSST Study

On average the sample showed a rising cortisol before the cortisol peak signaling a reactivity effect ($\gamma 20$=0.137, p= 0.003). After the peak a decline of cortisol followed ($\gamma 30$=-0.365, p= <0.001) showing the recovery effect.

For the TSST total PSQI score was found to be related to lower peak cortisol levels ($\gamma 01$=-0.04, t(63)= -2.58, p<.01), such that poor sleepers had lower cortisol levels. Cortisol reactivity to stress was related to sleep ($\gamma 21$= -.02, t(63)=-2.27, p=0.026) such that poor sleepers had smaller cortisol reactivity to stress (see figure 2).

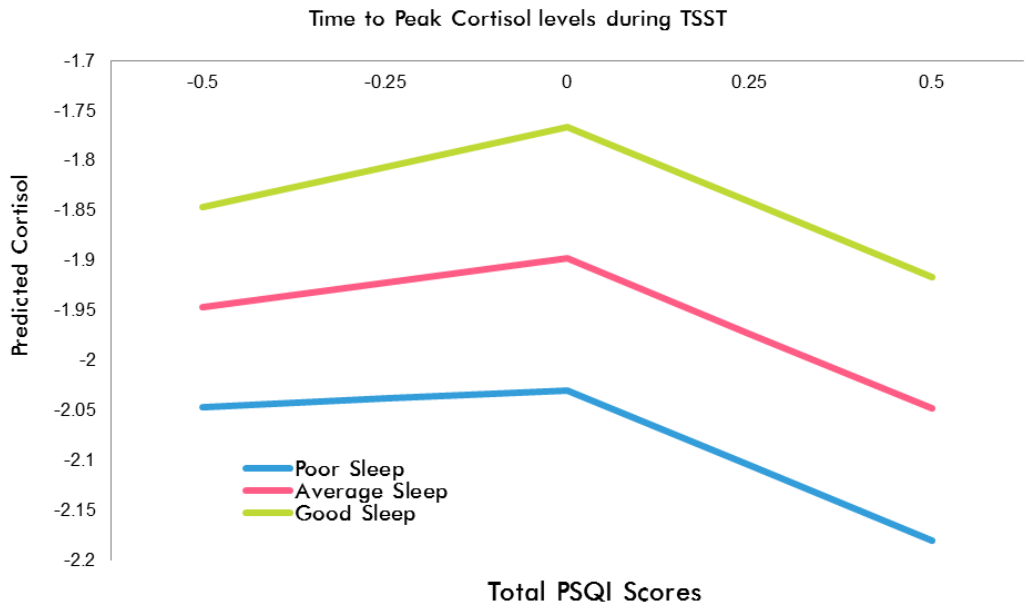

***Figure 2**. Blunted reactivity in poor PSQI scores*

Within the PSQI subscales, it found that individuals who scored high in sleep disturbance had faster recovery from stress ($\gamma 31$=-0.102, t(608)=-2.044, p=0.041) as seen in figure 3. Poor sleepers in terms of sleep disturbance recovered faster from exposure to the stressor than those who have less sleep disturbance.

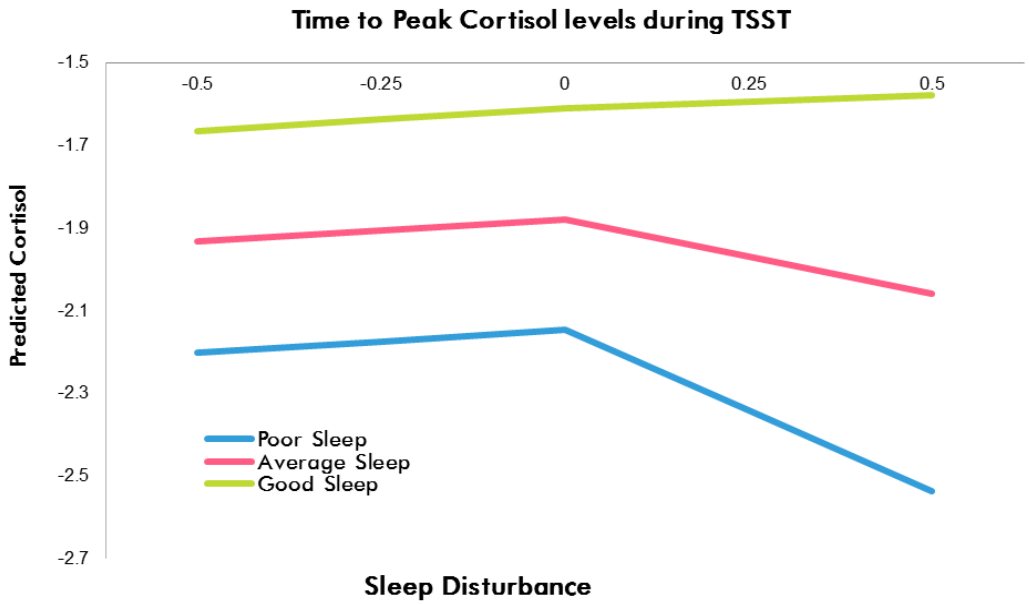

Figure 3*. Slower recovery in high sleep disturbance*

In the daytime dysfunction subscale high daytime dysfunction was related to faster recovery ($\gamma 31$=-0.14, t(608)=-2.229, p<0.026). Those who reported poor functioning, allegedly due to poor sleep, recovered faster after exposure to stressor.

Within habitual sleep efficiency (HSE) subscale people who reported bad HSE showed a decrease in cortisol levels before peak ($\gamma 31$=-0.073, t(63)= 0.0345, p=0.039) meaning it showed a smaller reactivity.

Within the overall sleep quality subscale, the effects of sleep were on the difference in cortisol on the lab day versus basal day ($\gamma 11$=0.28, t(63)=3.268, p=0.002), such that poor sleep quality was linked with a greater difference between the two days. Poor sleep quality was found to be related to elevated cortisol on basal days whereas good sleep quality was related to very low cortisol on basal days.

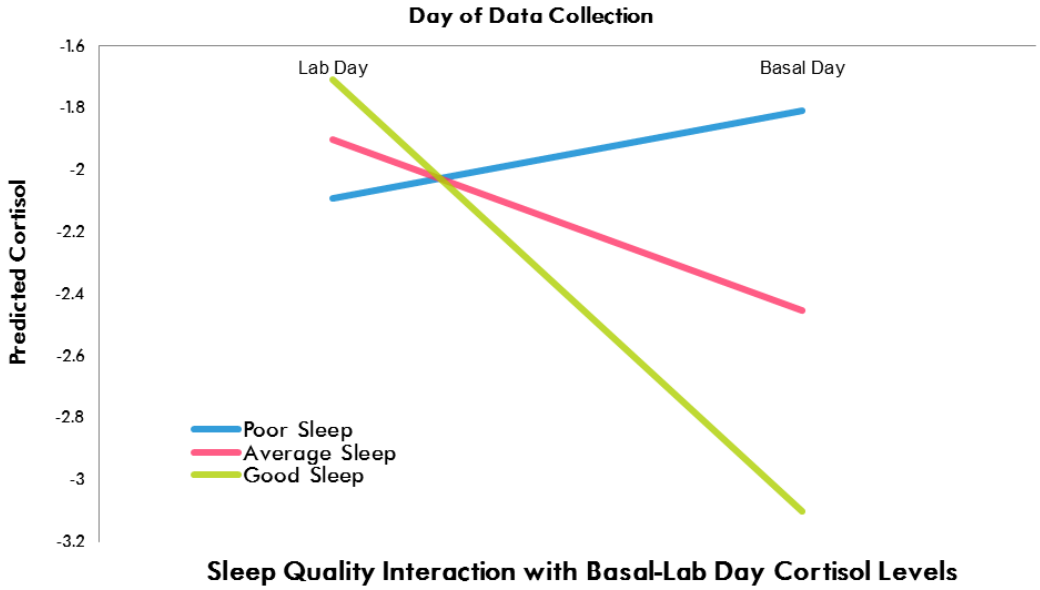

Figure 4. *Reporters of poor sleep quality have higher cortisol in basal day.*

In sum, within young adults in the TSST study, individuals who were poor sleepers according to several scales on the PSQI appear to show a blunted response to stress as indicated by lower reactivity, low peak cortisol levels and further declines after the TSST. Moreover, this blunting is apparent specifically in the stress context as indicated by low cortisol in the lab-context but elevated cortisol on a basal day.

Skydiving Study

Cortisol levels in jumping day were significantly higher than those in basal day ($\gamma 10$=0.75, p<0.001)

An overall reactivity effect found ($\gamma 20$=0.36, p<0.001) where cortisol was rising before the peak. After the peak cortisol levels started decreasing ($\gamma 30$=-0.31, p<0.001) showing the recovery effect.

For the skydiving study slower reactivity was found in individuals who scored high in sleep latency ($\gamma 31$=-0.16, t(284)=-3.701, p<.001). Those who take longer to fall asleep had smaller stress reactivity. People with high sleep latency scores also had more prolonged recovery after their cortisol peak (γ31=0.22, t(284)=3.311, p<0.001).

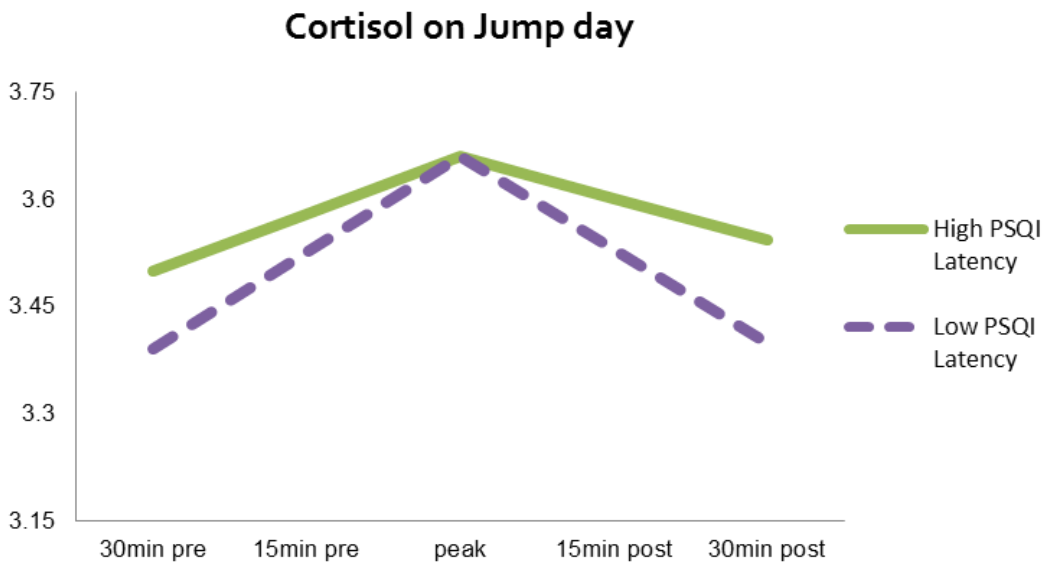

Figure 5. *A slower reactivity and recovery were observed in high sleep latency*

Somewhat divergent from the findings with the TSST study, within the skydiving study I found that cortisol had faster reactivity in time before peak in those who scored high in PSQI total ($\gamma 21$=0.036, t(286)=2.05, p<0.041). Poor sleepers in PSQI total had steeper cortisol response to stress. There was no changed observed for recovery.

In Habitual sleep efficiency (HSE) cortisol showed higher levels of cortisol ($\gamma 11$=0.137, t(286)=2.601, p<0.010). Cortisol was also higher after the peak showing a delayed recovery ($\gamma 31$=0.091, t(286)=2.052, p=0.041).

DISCUSSION

In the MRI study of maltreated youth, I found a significant effect in the diurnal rhythm in relation to sleep latency. The diurnal rhythm was flatter throughout the day, with lower cortisol in the morning and higher cortisol in the evening in individuals who took longer to fall asleep. This result is in accordance with my original predictions as well as other studies who found higher cortisol in the evening in poor sleepers (Leproult. 1997; Backhaus, J.). This result also reflects studies that found flatter rhythms in people with chronic stress and depression hinting at a dysregulation of cortisol's rhythm. This might suggest a link between sleep and allostatic load of the HPA axis. Despite this result no significant effect was found in any other component of the PSQI in the MRI study population.

Studies show that cortisol levels increase up to 50% between ages 20-80 and that the amplitude of the diurnal rhythm is shown to flatten with age (Van Cauter, 1996). These age related changes hint at the effects of allostatic load that may come with the wearing of the HPA axis throughout a long life of dealing with every day challenges. These effects may be worsened by poor sleep as demonstrated by Vgontzas et al (2003). They found a markedly increased evening cortisol in an older population after being deprived of sleep. This may be due to these inherent changes of cortisol patterns and sleep that come with age. This age-related deterioration points out to the bidirectional relation of stress and cortisols diurnal rhythm. The young age of my sample is inadequate to test this, but it

would be important to take in consideration for future studies as these natural decay may help shine a light for these type of dysregulations and their health impacts.

When testing for reactivity and recovery for an acute stressor I analyzed two separate studies. In the TSST study I found a significant effect in the PSQI Total variable, which is a sum of all the PSQI subscales. Those who scored worse for total PSQI had lower cortisol levels and slower reactivity to the task. Poor sleepers in terms of Habitual Sleep Efficiency (HSE) also had blunted reactivity before the cortisol peak. A slow reactivity was also seen in people who reported worse sleep latency in skydivers. These results might hint that sleep has certain influence or relation in our ability to react to stressors, particularly poor sleep may lead to delayed stress responses. A discrepancy is shown when we see that the opposite effect happens in skydivers who scored poorly in PSQI total. These skydivers show a steeper incline of cortisol before the peak.

In my analyses for recovery or the level of cortisol after the peak I found that sleep disturbance and daytime dysfunction showed faster recoveries or lower levels of cortisol after the peak in TSST subjects. Completely the opposite effect is seen in skydivers who reported poor HSE and sleep latency. These discrepancies in results of cortisol reactivity and recovery between the TSST study and the Skydiving study might be due to the different nature of both stressors. While TSST relays on the individuals preoccupation of social evaluation to cause a cortisol stress reaction, the stress response from skydiving is triggered by a need for sensation seeking and an inherent fear of death. A next step for this study should be doing a more in depth analysis of the different effects that sleep can have on different types of stressors.

Participants in TSST who reported poor sleep quality had elevated cortisol during basal day as opposed to good sleepers who had much lower cortisol this day. This might also be an evidence of allostatic load of the HPA axis in connection to sleep, as it shows an inability in these individuals to lower their cortisol to a normal level.

An important limitation in my study was the lack of an objective sleep measure, the validity of the PSQI as a sleep measure has been widely debated and studies testing its correlation to objective measures are ambiguous. I also believe that an effect of sleep and cortisol patterns can be better tested in longitudinal studies as effects of cortisol dysregulation can be better seen in the long term.

Although some results seemed contradictory in this study, they do point out at a possible dysregulation of the HPA axis in connection to sleep problems, and it should not be ignored as an important influence in stress regulation. Future studies might want to explore the effect of sleep on the negative-feedback sensitivity of the HPA axis as it is a major component in glucocorticoid regulation.

Sleep, without doubt, plays an immensely important role as a homeostatic regulator for many body functions. The dysfunction of sleep might contribute to the “wear and tear” of the body which may result in the allostatic load of the HPA axis. As reflected in my results, lack of proper sleep might also interfere in the body’s ability to respond properly to everyday challenges, interfering with our interaction with our environment, our relationships, and goals. On the other hand, cortisol dysregultion caused by constant

stress might affect our ability to sleep properly therefore furthering the damage on the body.

There is still much left to the puzzle. Sleep has an intricate interconnection with many other hormones as insulin, ghrelin, leptin as well as cytokines and glucose among countless other biomarkers, all of which might also share a relationship with cortisol and among each other. Maybe after further exploration of each of this relationships one day a model can be formed about the body's interaction with sleep.

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APPROVAL SHEET

This is to certify that Miguel A. Velasquez has successfully completed his Senior Honors Thesis, entitled:

Reciprocal Relation between Psychophysiological Patterns of Stress Responsivity and Sleep

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