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TRAIT ANXIETY AND ITS RELATIONSHIP TO PERIPHERAL CYTOKINE PRODUCTION IN A HEALTHY HUMAN SAMPLE

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ABSTRACT

The aim of the present study was to determine if non-pathological trait anxiety was associated with elevated levels of cortisol and inflammation, gauged in this study as Interluekin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-alpha). The sample included 56 healthy college students from the Penn State University campus made up of twenty males and thirty-six females; the females were divided into those in the luteal and follicular menstrual stage. Patients participated in the same protocol, which consisted of a baseline rest period, a challenge period (13.5 minute speech challenge and 15 minute mental arithmetic test), and a recovery period. Blood and saliva measures were collected at three time points during the study. The first hypothesis stated increased trait anxiety was associated with increased cortisol levels. The second hypothesis posed that increased trait anxiety is associated with increased levels of inflammation. The third hypothesis was that cortisol levels predicted inflammation better than trait anxiety per se. Follicular females showed a relationship between basal cortisol levels and trait anxiety as well as a relationship between basal cortisol levels and inflammation. There was no relationship between trait anxiety and inflammation.

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Chapter 1

Introduction

Anxiety disorders have been diagnosed in people of all ages in varying levels of intensity and have become the focus of an increasing number of research studies. Anxiety can affect an individual's ability to complete daily tasks, increase stress, cause depression, increase risk of illness, and generally reduce his ability to live a societally normal life (Gee, Antony, & Koerner, 2013). According to the National Institute of Mental Health, over forty million American adults suffer from some type of anxiety disorder ("Statistics," 2013). There are many different types of anxiety disorders including generalized anxiety disorder, obsessive-compulsive disorder, panic disorder, post-traumatic stress disorder, and social anxiety disorder ("Statistics," 2013). The many different types of anxiety disorders coupled with the number of Americans that suffer from this disease has caused an increasing public health interest in this area. Officials and researchers around the country are searching for answers to the question of the cause and complexity of anxiety disorders. Despite all of the research that has been done on the varying types of disorders and all of the diagnoses across the continent, there is little sound information behind the cause of these conditions.

Influence of Proinflammatory Cytokines

There is, however, a growing body of literature that suggests mental health processes are influenced by peripheral inflammation, specifically indicating a link between inflammation and depression. Major depression, depressive symptoms, and chronic stress can all be characterized by one type of inflammation in the body: the presence of proinflammatory cytokines, particularly

interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Gee et al., 2013; Robles, Glaser, & Kiecolt-Glaser, 2005). Cytokines are small proteins with a small molecular mass that are made by a cell in response to an external stimulus and influence other cells by binding to a specific receptor on their surface (Parham, 2009). Specifically, proinflammatory cytokine production (i.e. IL-6 and TNF-α) takes place after translocation of nuclear factor κβ (NFκβ) from the cytoplasm to the macrophage nucleus (Parham, 2009).

Elevated levels of proinflammatory cytokines can also induce sickness behavior, marked by decreased activity, fever and decreased appetite in order to conserve energy for the body's immune response (Parham, 2009; Raison, Capuron, & Miller, 2006). While this immunological response is positive during times of infection, chronic stimulation of this pathway due to repeated stressors or exacerbated illness could lead to depressive symptoms in vulnerable individuals (Dantzer, O'Conner, Freund, Johnson, & Kelley, 2008). Depression can also stem from the sedentary lifestyle and lack of energy associated with sickness behavior (Miller, Maletic, & Raison, 2009).

Proinflammatory Cytokines and the Brain

Though the brain is often considered an 'immune-privileged' organ, large proinflammatory cytokines can interact with the brain through several different pathways (Dantzer et al., 2008). The first pathway suggests that overexpressed proinflammatory cytokines in the systemic circulation can gain access to the brain by over-saturating cytokine transporters at the blood-brain-barrier (Dantzer et al., 2008; Miller et al., 2009). The second route involves activation of cytokine receptors on endothelial cells that line the cerebral vasculature, which results in the production of local inflammatory cytokines (Dantzer et al., 2008; Miller et al., 2009). Similarly, circumventricular organs outside of the blood-brain-barrier can be stimulated to

produce proinflammatory cytokines in response to antigen-associated molecular patterns in the cells, thus increasing local production, which causes the cytokines to diffuse passively across the barrier (Dantzer et al., 2008). Finally, locally produced proinflammatory cytokines can bind to cytokine receptors that are associated with peripheral afferent nerve fibers, which relay to the relevant brain regions for further signaling (Miller et al., 2009).

At the experimental level, increases in proinflammatory cytokine levels have been shown to cause alterations in behavior similar to those typical of depression, particularly social withdrawal and cognitive impairment (Capuron & Dantzer, 2003). Similarly, at the clinical level, patients with major depression who are otherwise considered healthy have repeatedly given samples that show activated inflammation pathways upon examination, which follows the previous definition, identifying inflammation through increased proinflammatory cytokine levels and elevated IL-6 plasma concentrations (Capuron & Dantzer, 2003; Raison et al., 2006). The discovered link between increased proinflammatory cytokines and increased depressive symptoms have become progressively more important because depression and anxiety disorders are so commonly comorbid, which suggests a potential link between anxiety and peripheral inflammation.

Anxiety and Inflammation

Though a large number of studies have examined the associations between depression and inflammation, little research has been done to identify the relationship between anxiety and inflammation. That being said, anxiety is similar to depression in that they are both negative behavioral emotions, which could confer increased risk for disorders with an inflammatory etiology (Bohnen, Nicolson, Sulon, & Jolles, 1991). Anxiety that is associated with threat-related information or fear may also play a key role in the relationship between anxiety and

inflammation. For example, there is a growing body of research that indicates that exposure to real or imagined psychological threats activates multiple biological systems, including the hypothalamic-pituitary adrenal (HPA) axis, which is responsible for regulating inflammatory activity and response (O'Donovan et al., 2010). Exaggerated and continual threat perception in anxious individuals could result in chronic activation of the bodily stress response, which could lead to increased inflammatory activity (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002). Negative emotions can also be associated with stress, a factor known to impede the immune response to infectious challenges and to prolong illness duration (Kiecolt-Glaser et al., 2002). This relationship supports the notion that anxiety may directly affect the cells of the immune system and cause up regulation of proinflammatory cytokines.

Cortisol is another important stress-related hormone that has the potential to impact anxiety levels. Similarly to the proinflammatory cytokines, cortisol levels are regulated through the HPA axis, and individual differences in expression can change the hormone's impact on their behavior (Dietrich et al., 2013). Specifically, basal morning cortisol levels and the cortisol awakening response (CAR) prepare the body for action and in dealing with the challenges of the day (Dietrich et al., 2013). Higher basal morning cortisol or a higher CAR reflects higher HPA axis activity, which has been related to symptoms of anxiety in both adolescents and adults (Stetler & Miller, 2011).

Hypotheses

Three hypotheses will be addressed in this experiment in order to further explore the link between trait anxiety and inflammation. The first hypothesis is that increased trait anxiety is associated with increased cortisol levels. The second hypothesis is that increased trait anxiety is associated with increased levels of inflammation (in particular, peripheral proinflammatory

cytokine levels: IL-6 and TNF-alpha). The third hypothesis is that cortisol levels will predict inflammation better than trait anxiety per se.

Chapter 2

Methods and Materials

The data for the following analyses comes from a study conducted by Dr. Laura C. Klein's research lab in the BioBehavioral Health Department at the Pennsylvania State University in 2004. Information on the participants and experimental protocol was taken from Dr. Klein's original methodology. Additional details on the methodology and procedures can be found in Klein et al., 2001.

Participants

Thirty-six women and twenty men (18-30 years old; mean age 21 years), were recruited to participate in a study examining hormonal responses to psychological challenge. Potential participants were recruited through advertisements in the local newspaper and flyers posted in the local community and on Penn State's campus. Each potential participant was interviewed over the phone prior to commitment, to review his or her health history and to determine program eligibility. Specifically, the telephone interviewer asked potential participants questions that document significant health problems and the use of medications or drugs that may affect the interpretation of the neuroendocrine or cardiovascular data. Individuals were excluded if they had a history of smoking, angina, arrhythmia, medications for blood pressure, diagnosed insulin-dependent diabetes, beta-blocker medication use, inhaled beta agonist use, history of stroke or other focal brain lesion, or a history of other neurological disorders. Similarly, all those on oral or parenteral corticosteroids within three months, or with a diagnosed history of depression were excluded. Additionally, no individuals using psychotropic medications within the eight weeks

previous to the interview or with psychiatric hospitalization within the past year were included, and no individuals with severe obesity (greater than 140% of ideal body weight, as determined by body mass index). Women who reported that they may be pregnant, who were attempting to get pregnant, or who were pregnant or lactating within the past twelve months were also excluded due to dramatic neuroendocrine changes associated with pregnancy. Moreover, women with a partial or complete hysterectomy, tubal ligations, history of menstrual irregularities (e.g., non-predictable menstrual cycles), and women using birth control pills were all excluded from the study.

Women were randomly assigned to the luteal or follicular group for their laboratory visit. Specifically, once a potential participant was interviewed by telephone, one of the investigators determined the onset of the next luteal and follicular phases. If eligible, the participant's laboratory visit was scheduled during either phase as determined by the investigator.

Weight and height were measured for each participant at the beginning of each laboratory session and body mass indices calculated; mean body mass indices did not differ across experimental groups. 71 percent of the participants were Caucasian (N=40), 7 percent were African American (N=4), 7 percent were Asian (N=4), 3.5 percent were Hispanic (N=2), and 10.7 percent were self-described as 'other' (N=6). All but one were high school graduates, 78 percent had some college education and 22 percent of participants had education beyond college.

Experimental Protocol

The experimental design is a mixed model with sex (male; female) and menstrual cycle (luteal; follicular) as between subject factors. The within subject factor is stress. All patients participated in the same protocol, which consisted of a baseline rest period, a challenge period (13.5 minute speech challenge and 15 minute mental arithmetic test), and a recovery period.

Blood and saliva measures were collected at three time points during the study: end of the baseline rest period which was immediately prior to the stressor, 15 minutes following completion of the stress protocol, and finally 60 minutes following the second blood draw during the recovery period. Participants were also asked to complete a series of psychological measures that include information about interpersonal relationships and social interactions. See Table 2.1.

Laboratory Protocol

A team of research assistants under the direction of Dr. Laura Klein performed the laboratory procedure in 2004. The study took place at the General Clinical Research Center within in the College of Health and Human Development; eligible participants were scheduled to begin at 1:00 PM. During the procedure, 20cc of blood was taken after each period (rest, stressor, and recovery) and blood pressure was taken every two minutes during the stressor and recovery periods (blood pressure data were not analyzed for this thesis). Table 2.1 provides an experimental timeline for the procedure.

Statistical Analysis

The data obtained from Dr. Klein's study was formatted for and analyzed with SPSS Statistical Software Version 21. The following analyses were used to test the hypotheses: to test hypothesis one (that trait anxiety is related to cortisol production) I used correlational analyses and ANOVAs; to test hypothesis two (that trait anxiety is related to proinflammatory cytokine production) I used correlational analyses; and to test hypothesis three (that cortisol, as compared to trait anxiety, is a better predictor of proinflammatory cytokine production) I used multiple linear regression analyses. For each analysis, I conducted three repeat tests to determine if trait

anxiety was related to rest, stress, and/or recovery levels of cortisol/proinflammatory cytokine levels.

Table 1. An experimental protocol timeline.

Experimental Task	Purpose	Duration	Notes
Study introduction and informed consent	Collect informed consent and ensure participant qualification	15 minutes	None
Questionnaires	Mood assessment, determine baseline levels of mood	30 minutes	POMS-1 and STAI Questionnaires included
Acclimation period	Allow participant to acclimate to equipment	10 minutes	None
Baseline period	Determine resting levels of blood pressure and heart rate	15 minutes	None
Blood and saliva collection #1	Determine resting levels of neuroendocrine hormones	5 minutes	Determine salivary cortisol. Time zero
Laboratory stressors	Evaluate neuroendocrine and cardiovascular reactivity to challenge	30 minutes	Speech preparation, delivery, and mathematics exercises included
Rest period #1	Time allotted to allow hormones to reach maximum levels	15 minutes	None
Blood and saliva collection #2	Determine reactivity levels of neuroendocrine hormones	5 minutes	Determine salivary cortisol. Time 45 minute mark
Rest period #2	Time allotted for hormone levels to return to baseline levels. Post-challenge questionnaires administered	60 minutes	POMS-2 included
Blood and saliva collection #3	Determine recovery levels of neuroendocrine hormones	5 minutes	Determine salivary cortisol. Time 110 minute mark
Study debriefing	Final participant questions, payment	15 minutes	None

Chapter 3

Results

Males and females were analyzed separately for this study because of a sex effect. Males had higher cortisol levels than females at all three time points as shown in Figure 1 (baseline $F_{1,54}$=11.91, P=.001; stress $F_{1,54}$=13.00, P=.001; recovery $F_{1,54}$=4.35, P=.042). Males and females did not differ in IL-6 levels at any time point (baseline $F_{1,52}$=1.53, P=.222; stress $F_{1,51}$=1.15, P=.288; recovery $F_{1,47}$=1.60, P=.212), and there was no notable difference between males and females in TNF-alpha levels (baseline $F_{1,51}$=1.69, P=.200; stress $F_{1,51}$=2.15, P=.148; recovery $F_{1,48}$=1.48, P=.229). Each figure shows the differences between females in the luteal vs. follicular stages.

Figure 1. Mean cortisol values for each time point (rest, stress, recovery) for men and women. Error bars show +/- one standard error.

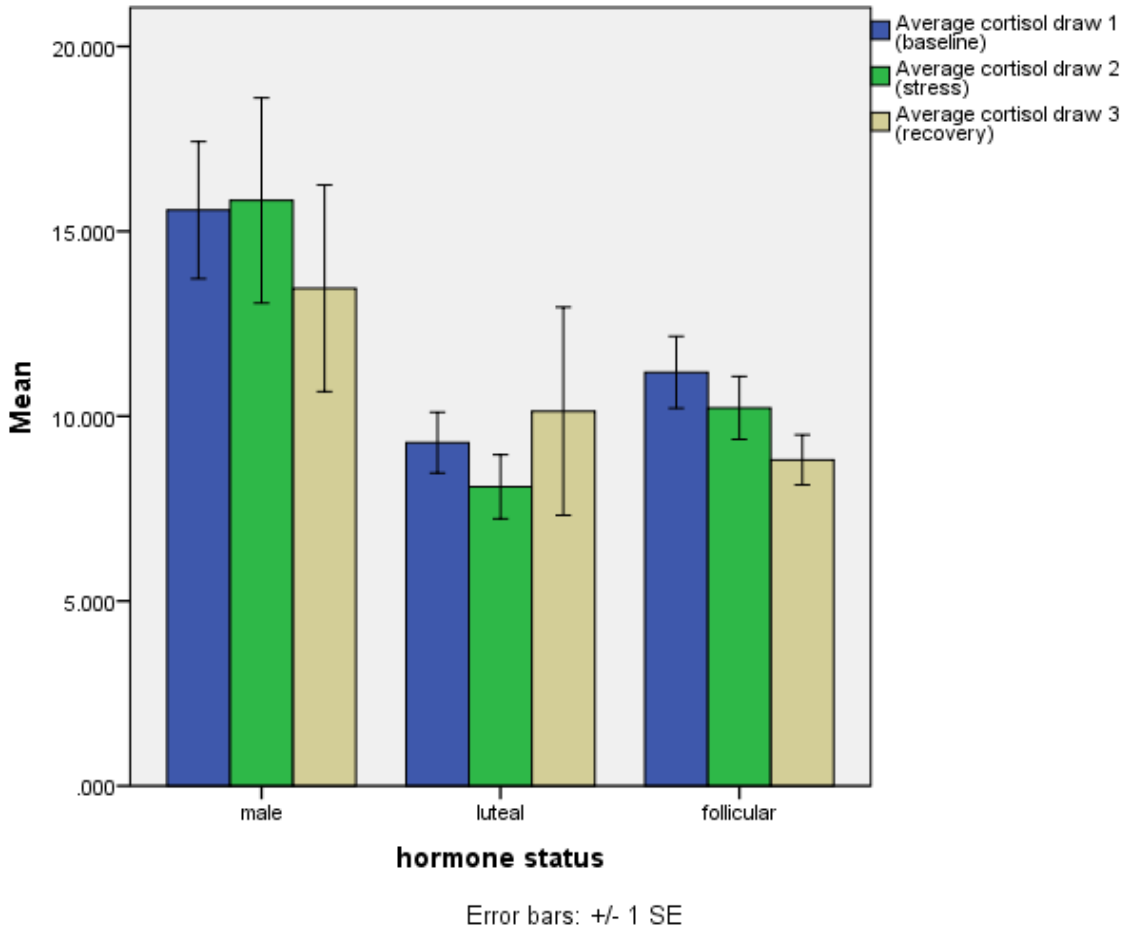


Figure 2. Mean IL-6 values for each time point (rest, stress, recovery) for men and women. Error bars indicate one standard error measure.

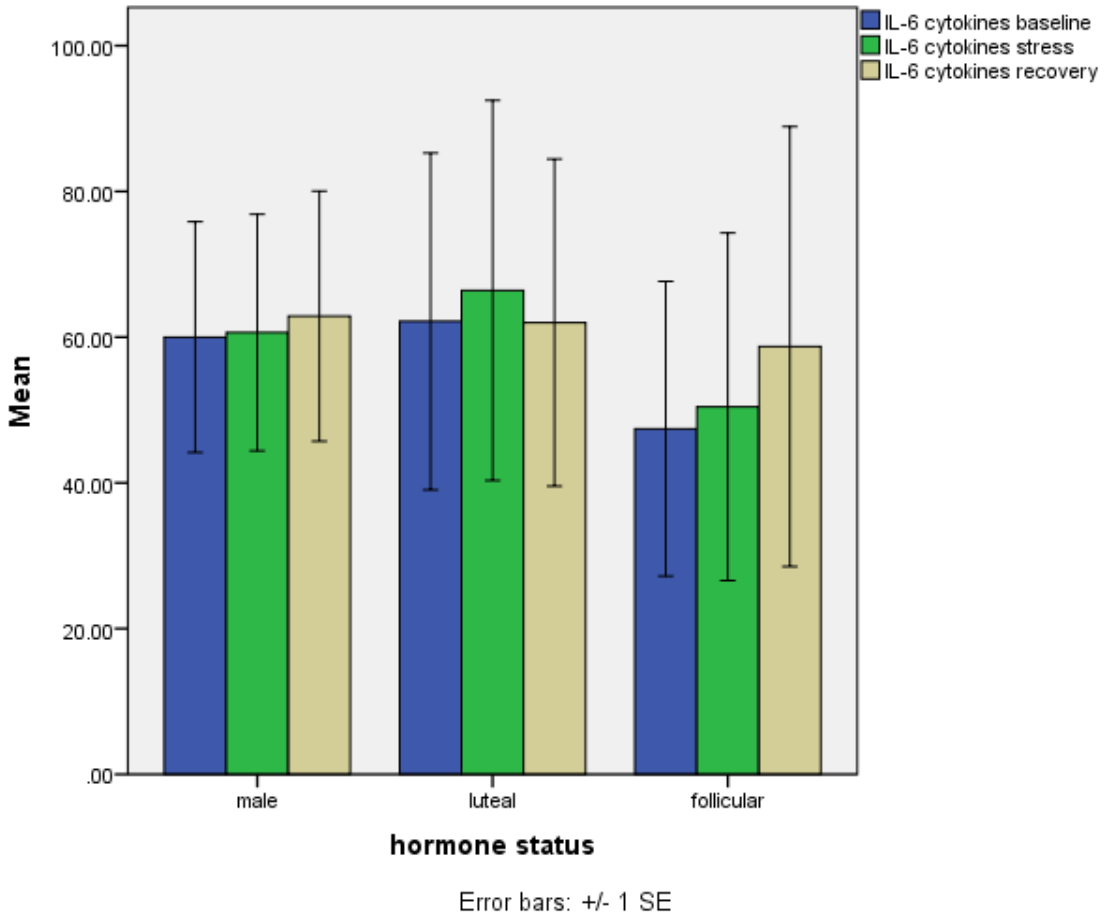
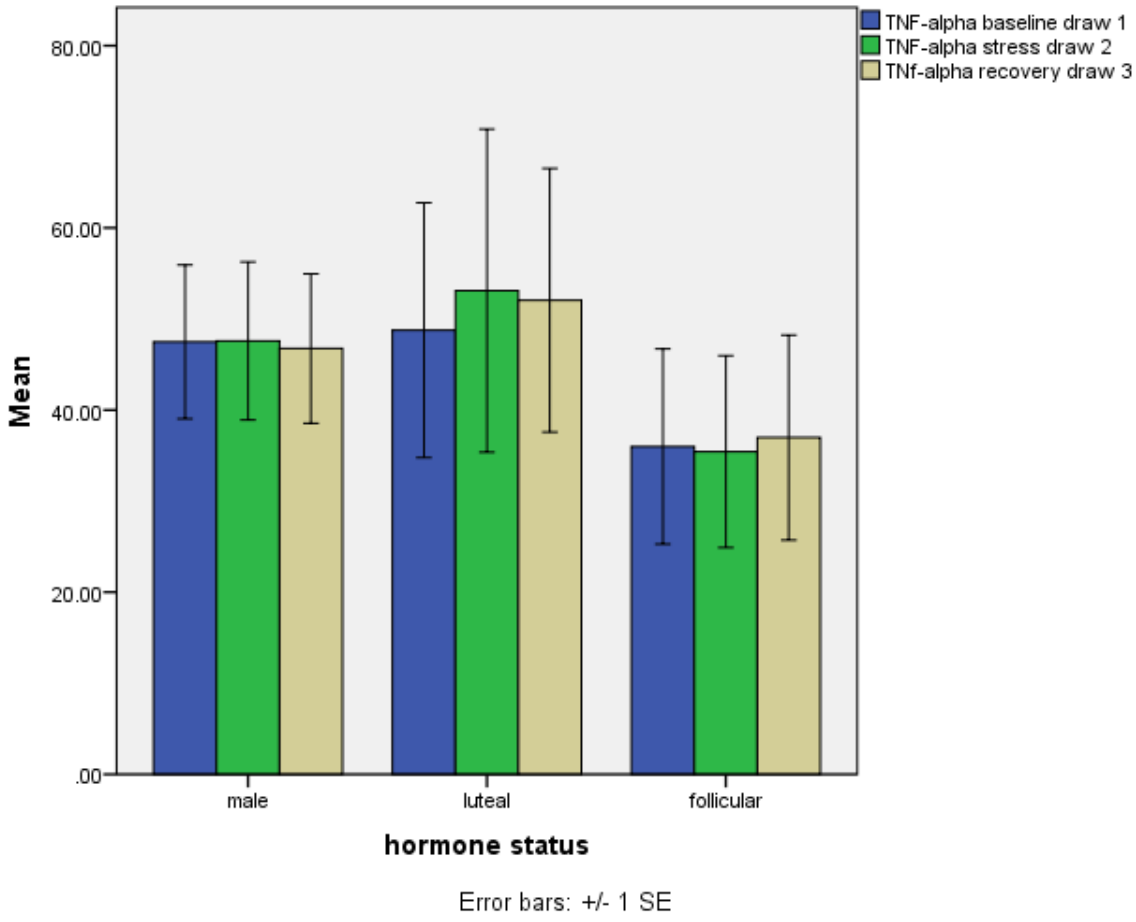


Figure 3. Mean TNF-alpha values for each time point (rest, stress, recovery) for men and women. Error bars indicate one standard error measure.



Hypothesis one: Increased trait anxiety is associated with higher cortisol levels. There was no significant relationship between trait anxiety and cortisol levels for men (n=20; Table 2) at any time point. However, in the female population, there was a trend for increased trait anxiety to be associated with increased baseline cortisol levels (n=36, r=.330, P=.056). This effect was driven by females that were in the follicular phase; specifically, there was a relationship between trait anxiety and baseline cortisol levels for women in the follicular phase (n=17, r=.577, P=.024) but not for women in the luteal phase (n=19, r=.264, P=.275; Table 3). Across both males and females, there were no relationships between trait anxiety and either cortisol response or recovery

levels (i.e. at 15 and 75 minutes after experiencing the arithmetic and social challenge protocol (all P values > .430).

Table 2. Male Correlations: Trait anxiety and cortisol at rest, stress, and recovery periods.

Cortisol	All Males	
	r	P
Rest	-.066	.783
Stress	-.124	.630
Recovery	.187	.430

* P values calculated as 2-tailed.

Table 3. Female Correlations: Trait anxiety and cortisol at rest, stress, and recovery periods.

Cortisol	All Females		Follicular Females		Luteal Females	
	r	P	r	P	r	P
Rest	**.330**	**.056**	**.577**	**.024**	.264	.275
Stress	.085	.632	.155	.582	.132	.589
Recovery	.091	.609	.199	.477	.040	.870

* P values calculated as 2-tailed.

Hypothesis two: Increased trait anxiety is related to increased inflammation. Across males and females, there was no relationship between trait anxiety and the inflammation markers (IL-6 and TNF-alpha levels) at any time point (rest, stress, or recovery; Tables 4 & 5). Additionally, separation of the females into those in the luteal and follicular stages did not yield a significant relationship concerning trait anxiety and inflammation.

Table 4. Male Correlations: Trait anxiety and proinflammatory cytokines at rest, stress, recovery periods.

Inflammatory Cytokine	All Males	
	r	P
IL-6 Rest	.220	.366
IL-6 Stress	.034	.890
IL-6 Recovery	.033	.892
TNF-alpha Rest	.124	.603
TNF-alpha Stress	.061	.809
TNF-alpha Recovery	.144	.569

* P values calculated as 2-tailed.

Table 5. Females Correlations: Trait anxiety and proinflammatory cytokines at rest, stress, recovery periods.

Inflammatory Cytokine	All Females		Follicular Females		Luteal Females	
	r	P	r	P	r	P
IL-6 Rest	.236	.179	.125	.658	.279	.247
IL-6 Stress	.220	.210	.124	.661	.256	.290
IL-6 Recovery	.232	.194	.107	.705	.310	.211
TNF-alpha Rest	.203	.265	-.016	.957	.329	.182
TNF-alpha Stress	.161	.363	-.005	.987	.243	.316
TNF-alpha Recovery	.279	.128	.098	.740	.367	.147

* P values calculated as 2-tailed.

Hypothesis three: Baseline cortisol levels are more closely related to inflammation markers (i.e. IL-6 and TNF-alpha) than trait anxiety. In males, there was no relationship between either trait anxiety or baseline cortisol levels and inflammation at any time point for either marker (all P-values < .375). In females, however, TNF-alpha levels were related to both trait anxiety and baseline cortisol levels. The baseline TNF-alpha measure showed a relationship between both trait anxiety and baseline cortisol (adjusted R^2=.141, trait β=.365, P=.052; cortisol β= -.426, , P=.025; Table 6). Conversely, at the stress TNF-alpha time point only baseline cortisol (and not trait anxiety) was related to inflammation (adjusted R^2= .111, cortisol β= -.395, P=.030; Table 7). Finally, during recovery TNF-alpha levels were related to both trait anxiety and baseline cortisol (adjusted R^2=.179, trait β=.420, P=.024; cortisol β= -.419, P=.024; Table 8).

This effect was driven by women in the follicular phase; specifically, baseline cortisol levels were related to TNF-alpha levels at all three time points: see Tables 9-11. Females in the luteal stage showed no relationship between trait anxiety and inflammation nor baseline cortisol and inflammation at any time point. Additionally, there was no relationship between trait anxiety or baseline cortisol and the IL-6 inflammation marker at any time in the female population as a whole (n=36). This is also true for the luteal and follicular females and IL-6 (all P values > .085)

Table 6. Female Regression: Trait anxiety and baseline cortisol predicting TNF-alpha baseline.

Predictor Variable	Beta	t	P
Trait anxiety	.365	2.029	.052
Baseline cortisol	-.426	-2.368	.025

Regression model: Adjusted R^2=.141, $F_{2,29}$=3.548, P=.042

Table 7. Female Regression: Trait anxiety and baseline cortisol predicting TNF-alpha stress.

Predictor Variable	Beta	t	P
Trait anxiety	.291	1.676	.104
Baseline cortisol	-.395	-2.274	.030

Regression model: Adjusted R^2=.111, $F_{2,31}$=3.066, P=.061

Table 8. Female Regression: Trait anxiety and baseline cortisol predicting TNF-alpha recovery.

Predictor Variable	Beta	t	P
Trait anxiety	.420	2.390	.024
Baseline cortisol	-.419	-2.388	.024

Regression model: Adjusted R^2=.179, $F_{2,28}$=4.276, P=.024

Table 9. Follicular Female Regression: Trait anxiety and baseline cortisol: TNF-alpha baseline.

Predictor Variable	Beta	t	P
Trait anxiety	.468	1.498	.162
Baseline cortisol	-.767	-2.453	.032

Regression model: Adjusted R^2=.236, $F_{2,11}$=3.010, P=.091

Table 10. Follicular Female Regression: Trait anxiety and baseline cortisol: TNF-alpha stress.

Predictor Variable	Beta	t	P
Trait anxiety	.423	1.504	.158
Baseline cortisol	-.741	-2.636	.022

Regression model: Adjusted R^2=.261, $F_{2,12}$=3.474, P=.065

Table 11. Follicular Female Regression: Trait anxiety and baseline cortisol: TNF-alpha recovery.

Predictor Variable	Beta	t	P
Trait anxiety	.461	1.543	.151
Baseline cortisol	-.661	-2.213	.049

Regression model: Adjusted R^2=.190, $F_{2,11}$=2.526, P=.125.

Chapter 4

Discussion

The following discussion is based on the results from the preceding hypothesis testing; the analyses were completed separately for males and females. Hypothesis one, that increased trait anxiety is related to increased cortisol levels, was supported only in follicular females. There was no relationship between trait anxiety and cortisol in men at any time point (baseline, stress, recovery), however, in females, increased trait anxiety was associated with increased baseline cortisol levels, an effect that was specifically driven by females in the follicular phase. There were no relationships between trait anxiety and cortisol levels for females in the luteal phase at any time point. Hypothesis two, that there is a positive relationship between trait anxiety and inflammation, was not supported. Neither males nor females showed any evidence to support this hypothesis at any time point with either inflammation marker (IL-6 or TNF-alpha). Finally, the third hypothesis, that elevated trait anxiety and/or baseline cortisol are related to increased inflammation marker levels, was supported in the female sample by the baseline TNF-alpha measure for both trait anxiety and baseline cortisol. Conversely, only baseline cortisol was related to inflammation at the stress TNF-alpha time point. These relationships were similarly driven by the females in the follicular phase; specifically, baseline cortisol levels negatively correlated with the TNF-alpha inflammation marker at all three time points. Females in the luteal phase and males showed no relationship between trait anxiety and inflammation or baseline cortisol and inflammation at any time point.

Hypothesis one: trait anxiety is positively correlated with cortisol levels. With regard to anxiety, elevated levels have been consistently reported in individuals with panic disorder

(Wedekind, Bandelow, Broocks, & Ruther, 2000), and, to a lesser extent, in individuals with OCD (Gustafsson, Gustafsson, Ivarsson, & Nelson, 2008) and Generalized Anxiety Disorder (Mantella, Butters, & Amico, 2008). Furthermore, research suggests that comorbid anxiety may explain some of the HPA axis hyperactivity effects commonly observed in depression (Young, 1998). Research in the context of social phobia, most likened to trait anxiety, is more limited and findings have not been consistent. However, some studies have reported elevated cortisol levels in response to stress in individuals with social phobia compared to controls (Roelofs, van Peer, Berretty, & Jong, 2009). For example, Roelofs et al. (2009) found that individuals with social phobia displayed significantly elevated stress-induced cortisol levels (i.e. post-stressor samples) following the Trier Social Stress Test compared to those with PTSD and a healthy comparison group (Roelofs et al., 2009).

The literature's inconsistency continues when examining the time of day and variables tested in the study, specifically, our results show increased trait anxiety is correlated with increased basal cortisol levels in follicular females in the afternoon. A study from 2004 indicates that anxious individuals exhibited significantly lower nighttime cortisol levels and an initially sluggish rise in cortisol concentrations during the day, which caused a peak in cortisol activity in the afternoon (Feder, Coplan, Goetz, Mathew, & Pine, 2004). These results are most similar to those from the current study. Conversely, a study from 2007 analyzed the relationship between basal cortisol levels and anxiety in a large population of adolescents with anxiety problems and reported that individuals with persistent anxiety problems had higher morning cortisol levels and a higher cortisol awakening response (Greaves-Lord, Ferdinand, & Oldehinkel, 2007)

Hypothesis two: increased trait anxiety is related to increased levels of inflammation (TNF-alpha and IL-6 makers). There were no results to support this hypothesis. There is limited published information on the relationship between trait anxiety and inflammation, but the literature available suggests that the relationship does not exist. One study, published in 1997, on

the relationship between trait anxiety and inflammatory bowel disease, shows that trait anxiety does not appear to play an important role in the inflammation response (Addolorato, Capristo, & Stefanini, 1997). In a similar study in 1977, cortisol and trait anxiety were assessed after a stressor and there was no relationship between the two factors (Abplanalp, Livingston, Rose, & Sandwisch, 1977).

Hypothesis three: trait anxiety and cortisol levels are related to increased inflammation marker levels. From the results, there is a trend that suggests increased trait anxiety leads to increased baseline TNF-alpha levels, whereas an increase in baseline cortisol leads to a decrease in TNF-alpha baseline levels. These effects were evident only in the follicular female sample.

In the follicular phase of menstruation, before ovulation, estrogen levels are high and progesterone levels are low, while the reverse is true in the subsequent luteal phase (Fox, 1999). Fluctuations in the estrogen and progesterone levels may influence the response and feedback loop of the HPA-axis during stress; specifically, increased estrogen levels coincide with increased cortisol levels (Bouma, Riese, & Ormel, 2009). A study in rats also showed that an increase in estradiol levels suggests more anxiolytic behavior, coded as decreased exploration of the open arms in an elevated plus maze (Mora, Dussaubat, & Diaz-Veliz, 1996). If the same holds true in humans, women in the follicular phase would be more likely to be anxious with high levels of estrogen and cortisol, which was shown in this study.

Limitations of this study include the small male and female sample size, the retrospective analyses of data collected in 2004, and the cross sectional study design. A larger sample size could potentially allow significant relationships to emerge that the small sample size was unable to exhibit. The retrospective aspect of this thesis made some of the analyses challenging due to lack of information for clarification. Finally, the cross sectional design only allowed analyses of the participants at one time point. Retrospective and future studies were not included.

Chapter 5

Conclusion

The link between anxiety and inflammation is still tentative and more research is required to establish a concrete connection. More research is important because anxiety and depression are comorbid and often are diagnosed together, and more recent literature suggests that anxious behavior might precede the diagnosis of depression. If anxiety could be identified earlier, there is a potential for patients to lower their risk of depression (Boyer, 2000). Additionally, having trait anxiety, which is not considered pathological anxiety, may affect other health processes because of the associated elevated baseline cortisol production. This relationship is specifically important in females.

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ACADEMIC VITA

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EDUCATION

The Pennsylvania State University; University Park, PA

The Schreyer Honors College; The College of Agricultural Sciences

B.S. in Toxicology, Honors in BioBehavioral Health

Minor in Global Health

Study Abroad, Tanzania and South Africa Summer 2013

Global Health minor Fieldwork Experience

LEADERSHIP

College of Agricultural Sciences 4/2011 -- Present

Ag Advocate

- Acts as a senior representative for the College
- Gives tours for incoming and prospective students

Undergraduate Admissions 9/2012 – Present

Lion Scout

- Gives tours for prospective students and their families
- Acts as a Penn State representative

Schreyer Honors College Student Council 8/2010 – Present

Academic Chair 5/2011 – 5/2013

- Shell Recruitment Event and THON fundraiser
- Academics, Social Events, Recruitment, THON, Committee member

EXPERIENCE

Behavioral Neuroendocrinology Lab 3/2012 - -Present

Sonia Cavigelli

- Honors Thesis: "State and Trait Anxiety and its Relationship to Peripheral Cytokine Production in a Healthy Human Sample"
- Experience in mice handling, SPSS software, and behavior coding

Center for Health Care and Policy Research 8/2012 – Present

Aligning Forces for Quality

- Undergraduate Research Assistant
- Experience with ATLAS software and computer tasks

Undergraduate Admissions; Summer Tour Guide 5/2012 – 8/2012

Honors and Awards

Dean's List (7 out of 7 semesters)

Schreyer Honors College Academic Excellence Scholarship, 2010-2014

The College of Agricultural Sciences Honors Scholarship, 2010-2014

Bayard D. Kunkle Scholarship, 2013

Schreyer Honors College Ambassador Travel Grant, 2013

Schreyer Honors College Summer Research Grant, 2012, 2013

College of Agricultural Sciences Undergraduate Summer Research Grant, 2012

Association Memberships/Activities

Sharing the Journey: Scholars International, 2012 – Present

Penn State Mortar Board Honors Society, 2013 - Present

Professional Presentations

Undergraduate Research Exposition, 2013 "The influence of allergic asthma lung inflammation on anxiety- and depression-related neurotransmitter function"

Skills

Laboratory: Behavioral testing, animal handling, behavioral coding, animal colony maintenance, mouse anatomy, necropsy

Computer: MS Excel, Word, PowerPoint; SPSS; ATLAS