Award Number: W81XWH-07-1-0269

TITLE: Biomarkers of Risk for Post-Traumatic Stress Disorder (PTSD)

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REPORT DATE: April 2011

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release; distribution unlimited

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**Biomarkers of Risk for Post-Traumatic Stress Disorder (PTSD)**

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**Performing Organization:** Butler Hospital
**Address:** Providence, RI 02905

**U.S. Army Medical Research and Materiel Command**
**Fort Detrick, Maryland 21702-5012**

**Abstract:**
The objective of this project was to study genetic and neuroendocrine biomarkers of risk in a carefully assessed population of military personnel who recently returned from war zones. Baseline and 12-month follow-up assessment data were collected on behavioral and psychosocial measures. Major findings were that the COMT Val/Met polymorphism, interacted with combat exposure to predict diagnoses of PTSD. Specifically individuals with the Met allele appeared more sensitive to higher levels of combat trauma exposure. In the sample as a whole, cortisol concentrations did not differ between participants with a current diagnosis of PTSD and those without PTSD. However, among those who had a past significant trauma, there was a significant between groups effect of current PTSD (p<.05) after controlling for significant effects of past PTSD symptoms, those with current PTSD had blunted diurnal cortisol concentrations. In addition, after controlling for covariates, there was a main effect of COMT (p<.005), such that individuals homozygous for the Met allele had higher overall cortisol concentrations, particularly morning and nighttime concentrations. There was also a significant effect of a polymorphism in FKBP5, a glucocorticoid regulating gene, such that those homozygous for the C allele had elevated evening cortisol concentrations (p<.05).

**Subject Terms:**
PTSD, trauma, genetics, cortisol, biological marker, risk factors
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Introduction

Experience from prior military conflicts and early data from Iraq and Afghanistan suggest that a significant percentage of troops on hazardous deployments will develop posttraumatic stress disorder (PTSD). This is one of the most common, debilitating, and chronic psychological disorders diagnosed among veterans. A large body of evidence in PTSD now documents dysfunction of the hormone system that coordinates the biological response to stress (the hypothalamic-pituitary-adrenal [HPA] axis). However, existing studies typically involve participants who have suffered from the disorder for many years, and information on biological processes occurring early in the disorder is lacking. In addition, specific genes that regulate HPA axis function have recently been identified in humans. Genes that are involved in the processing of emotions and cognition may also be involved in the pathogenesis of PTSD. In recent years investigators have begun to identify some of the relevant genes, and a few recent studies have identified specific gene-environment interactions that appear to confer risk for mood and anxiety disorders. The objective of this proposal is to study these biomarkers of risk in a carefully assessed population of military personnel who have recently returned from war zones. This study will enroll a target sample of 300 men and women who have recently returned from hazardous deployment in a war zone and are undergoing a comprehensive assessment of symptoms and stressors in a related 12-month longitudinal study. Samples of saliva will be obtained for analysis of DNA and candidate genes as well as hormone concentrations (cortisol). Hormone and genetic data will be used to predict the development of PTSD and chronic PTSD. In addition, interactions of trauma severity and other stressors as well as social supports with the biological factors will be examined. Findings of this study will contribute to knowledge about the biomarkers of risk for PTSD and will therefore increase our knowledge of the disease process and may help us to identify individuals who are at highest risk for PTSD.

Body

Task 1. To recruit subjects from a recently funded parent study of military personnel following warzone deployment who will provide biological specimens for hormone assay and genotyping for this study.

a. Conduct screenings of potential participants who provided informed consent to the parent study
   We consented 209 participants of the 238 who participated in the parent study.

b. Collect biological specimens from participants
We collected 209 saliva samples for genetic analysis. One subject was excluded from data analysis due to inadequate data collection. We collected 1600 cortisol samples from 160 individuals who were eligible and consented to participate in the neuroendocrine component of the study. Three subjects were excluded from the analyses due to inadequate data collection (n=2) and meeting an exclusion criterion (working night shifts, n=1).

c. Process and store biological specimens
All of the above genetic and cortisol specimens were catalogued and carefully processed.

Task 2. To assess neuroendocrine function and candidate genes and test these potential biomarkers for their association with the development and maintenance of PTSD.

a. Hormone assays, University of Cincinnati, Dr. Thomas Geracioti
All cortisol assays (1600 samples) were performed in duplicate and data received from Dr. Geracioti’s laboratory.

b. DNA extraction and genotyping, VAMC Providence, Dr. John McGeary
Dr. McGeary’s laboratory extracted DNA and genotyped 208 samples.

c. Data management Butler Hospital, Dr. Audrey Tyrka
All biological data has been tracked, processed, sent for assay, results received and cleaned.

d. Data analyses of initial assessment and follow-up data Butler Hospital, Dr. Audrey Tyrka. We have completed data analyses for the initial assessment and 12-month follow-up data.

We requested a no-cost extension because we did not have complete assessment data from initial or 12-month follow-up assessments in the parent study. We now have complete data on diagnoses, measures of stress and social support, and psychotropic medication use and the initial assessment. In addition, we have 12-month follow-up data for PTSD diagnoses as well as data on past diagnoses. This is especially important for the genetic analyses because risk genes confer risk for past, current, and future diagnoses, relative to when the genetic material was collected.

In addition, we have matched the assessment data to the cortisol assessment time period. Because our study started later than the parent study, and in addition, some participants had a lag between their first assessment visit and when the collected their saliva for cortisol, the cortisol data did not always match up temporally with the initial baseline visit. Therefore, we constructed the dataset so that cortisol matched the assessment data by substituting data from a later assessment when that was a better fit, and controlled for time since return from deployment in the analyses.
The data using this more complete and better-matched dataset are described in the following sections.

**Genetics Sample**

The following table presents the demographic characteristics and summaries of the measures for the genetic sample.

**Characteristics of Subjects with Genetics Data, N = 208**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean (SD)</td>
<td>33.41 (9.7)</td>
</tr>
<tr>
<td>Range</td>
<td>20-61</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>190 (91.35%)</td>
</tr>
<tr>
<td>Female</td>
<td>18 (8.65%)</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>154 (74.04%)</td>
</tr>
<tr>
<td>African American</td>
<td>16 (7.69%)</td>
</tr>
<tr>
<td>Asian</td>
<td>6 (2.88%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>28 (13.46%)</td>
</tr>
<tr>
<td>American Indian</td>
<td>1 (0.48%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (1.44%)</td>
</tr>
<tr>
<td>Most Recent Deployment Location, n (%)</td>
<td></td>
</tr>
<tr>
<td>Iraq</td>
<td>200 (96.15%)</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>8 (3.84%)</td>
</tr>
<tr>
<td>SCID Axis I Diagnoses Other than PTSD, n (%)</td>
<td></td>
</tr>
<tr>
<td>Current mood disorder</td>
<td>47 (22.59%)</td>
</tr>
<tr>
<td>Past mood disorder</td>
<td>27 (12.98%)</td>
</tr>
<tr>
<td>Current anxiety disorder</td>
<td>14 (6.73%)</td>
</tr>
<tr>
<td>Past anxiety disorder</td>
<td>5 (2.40%)</td>
</tr>
<tr>
<td>Current substance use disorder</td>
<td>23 (11.06%)</td>
</tr>
<tr>
<td>Past substance use disorder</td>
<td>67 (32.21%)</td>
</tr>
<tr>
<td>CAPS PTSD Diagnoses, n (%)</td>
<td></td>
</tr>
<tr>
<td>Current diagnosis at baseline</td>
<td>19 (9.13%)</td>
</tr>
<tr>
<td>PTSD diagnosis at any time point</td>
<td>40 (19.23%)</td>
</tr>
<tr>
<td>Cortisol Concentration (ug/dL), Mean (SD)</td>
<td></td>
</tr>
<tr>
<td>Awakening</td>
<td>0.48 (0.30)</td>
</tr>
<tr>
<td>30 minutes after awakening</td>
<td>0.57 (0.30)</td>
</tr>
<tr>
<td>1pm</td>
<td>0.22 (0.23)</td>
</tr>
<tr>
<td>5pm</td>
<td>0.14 (0.13)</td>
</tr>
<tr>
<td>9pm</td>
<td>0.12 (0.22)</td>
</tr>
<tr>
<td>CTQ Total 28 item self-report, Mean (SD)</td>
<td>8.15 (2.90)</td>
</tr>
<tr>
<td>Subjects reporting abuse or neglect on CTQ, n (%)</td>
<td>78 (37.50%)</td>
</tr>
<tr>
<td>Hoge Combat Experience Scale Total, Mean (SD)</td>
<td>8.93 (8.80)</td>
</tr>
<tr>
<td>DDRI Life and Family Concerns Total, Mean (SD)</td>
<td>27.02 (6.97)</td>
</tr>
</tbody>
</table>
In our last summary, we reported that we did not identify genetic predictors of PTSD in 18 participants who had trauma-related PTSD. We noted that this may have been due to insufficient power, and the lack of inclusion of subsequent diagnoses as well as lifetime diagnoses in these analyses.

Over the course of this last period, we have received complete assessment data from Dr. Shea in the parent study, including lifetime PTSD diagnoses, as well as the 12 month follow-up data. As seen in the table, we now have 40 participants with lifetime diagnoses of PTSD. In addition, we now have complete data for environmental effects including the Childhood Trauma Questionnaire which assesses five types of childhood abuse and neglect, the Hoge scale which measures exposure to combat trauma, and the DDRI which assesses several types of social stressors and sources of support.

We conducted logistic regression analyses predicting 1) lifetime diagnosis of PTSD (current, follow-up or retrospectively reported past PTSD), and 2) PTSD diagnoses only at one of the assessments (since, although this category is less inclusive, these diagnoses may be more reliable). These analyzed controlled for age and sex. All genes were in Hardy-Weinberg equilibrium. We tested for effects of the following genes: the serotonin transporter (5-HTTLPR), dopamine type 2 receptor (DRD2), dopamine transporter (DAT), catechol-o-methyltransferase (COMT Val66Met), brain-derived neurotrophic factor (BDNF), and polymorphisms in the gene for neuropeptide Y (NPY). None of these genes predicted PTSD diagnoses in this sample.

Next, because there was variability in the degree of combat exposure as well as exposure to other stressors and supports, we conducted a series of analyses to test gene x environment interactions in the prediction of PTSD. We conducted similar logistic regressions, but included the three measures of environmental stress/trauma or support listed above, in individual logistic regression models that tested for the interaction of each gene with the environmental factor in the prediction of PTSD diagnoses. The environmental factors predicted PTSD in several models (We are currently working with Dr. Shea on publications of these effects in the parent risk factor study which has a larger number of participants and explores these effects more systematically), only one gene, again the COMT Val/Met polymorphism, interacted with the environmental factors to predict PTSD. In a logistic regression model predicting lifetime PTSD diagnoses with this gene and relatively high or low exposure to combat on the Hoge scale (median split), there was an effect of COMT (B=4.8, p<.01), an effect of combat exposure (B=1.2, p=.001), and an interaction of COMT by combat (B=0.9, p <.05). Specifically, individuals with the Val allele were more likely to have PTSD with lower levels of combat exposure, while those with the Met allele appeared more sensitive to higher levels of combat trauma exposure in terms of risk for PTSD (see Figures below).
These findings are consistent with some data indicating that the Met allele may confer sensitivity to stress (Kolassa et al., 2010). However, because the numbers of affected individuals is small, and this is one gene among many tested, this finding should be considered preliminary.

Cortisol Sample

As mentioned above, the final cortisol dataset (n=157) has been modified substantially in order to have a good temporal match to the assessment data because not all participants collected saliva samples at the time of the baseline assessment. Now that we have the later assessment data available, we have been able to pull measures from the appropriate assessment when this was not done at the baseline assessment. As mentioned above, we have controlled for time since return from deployment as a covariate in the analyses. All analyses of cortisol also accounted for age and sex. In addition, we now have data on psychotropic medication use and other psychiatric diagnoses, so we have incorporated this into the analyses. Use of psychotropic medication (n=20) was significantly related to cortisol concentration throughout the day, so this variable was controlled in subsequent analyses. Current major depression, which has been linked to altered HPA axis function, was not associated with diurnal cortisol concentrations in this sample. Ethnicity was also not linked to cortisol.
concentration. The following table shows the characteristics of the sample with cortisol data. As shown, 13 participants met the criteria for PTSD and 11 did not have current PTSD but met the criteria for the diagnosis in the past.

**Characteristics of Subjects with Cortisol Concentration Data, N = 157**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong>, Mean (SD)</td>
<td>34.63 (9.7)</td>
</tr>
<tr>
<td>Range</td>
<td>20-61</td>
</tr>
<tr>
<td><strong>Gender</strong>, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>147 (93.63%)</td>
</tr>
<tr>
<td>Female</td>
<td>10 (6.37%)</td>
</tr>
<tr>
<td><strong>Race/Ethnicity</strong>, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>121 (77.07%)</td>
</tr>
<tr>
<td>African American</td>
<td>11 (7.01%)</td>
</tr>
<tr>
<td>Asian</td>
<td>3 (1.91%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>15 (9.55%)</td>
</tr>
<tr>
<td>American Indian</td>
<td>1 (0.64%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (3.82%)</td>
</tr>
<tr>
<td><strong>Most Recent Deployment Location</strong>, n (%)</td>
<td></td>
</tr>
<tr>
<td>Iraq</td>
<td>150 (95.54%)</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>7 (4.46%)</td>
</tr>
<tr>
<td><strong>SCID Axis I Diagnoses Other than PTSD</strong>, n (%)</td>
<td></td>
</tr>
<tr>
<td>Current mood disorder</td>
<td>32 (20.38%)</td>
</tr>
<tr>
<td>Past mood disorder</td>
<td>17 (10.82%)</td>
</tr>
<tr>
<td>Current anxiety disorder</td>
<td>9 (5.73%)</td>
</tr>
<tr>
<td>Past anxiety disorder</td>
<td>4 (2.55%)</td>
</tr>
<tr>
<td>Current substance use disorder</td>
<td>18 (11.47%)</td>
</tr>
<tr>
<td>Past substance use disorder</td>
<td>52 (33.12%)</td>
</tr>
<tr>
<td><strong>CAPS PTSD Diagnoses</strong>, n (%)</td>
<td></td>
</tr>
<tr>
<td>Current diagnosis at cortisol assessment</td>
<td>13 (8.28%)</td>
</tr>
<tr>
<td>Past diagnosis prior to cortisol assessment</td>
<td>11 (7.01%)</td>
</tr>
<tr>
<td><strong>Cortisol Concentration (ug/dL), Mean (SD)</strong></td>
<td></td>
</tr>
<tr>
<td>Awakening</td>
<td>0.48 (0.30)</td>
</tr>
<tr>
<td>30 minutes after awakening</td>
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</tr>
<tr>
<td>1pm</td>
<td>0.22 (0.23)</td>
</tr>
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<td>5pm</td>
<td>0.14 (0.13)</td>
</tr>
<tr>
<td>9pm</td>
<td>0.12 (0.22)</td>
</tr>
<tr>
<td><strong>CTQ Total 28 item self-report, Mean (SD)</strong></td>
<td>7.99 (2.78)</td>
</tr>
<tr>
<td>Subjects reporting abuse or neglect on CTQ, n (%)</td>
<td>61 (38.85%)</td>
</tr>
<tr>
<td><strong>Hoge Combat Experience Scale Total, Mean (SD)</strong></td>
<td>8.47 (8.25)</td>
</tr>
<tr>
<td><strong>DDRI Life and Family Concerns Total, Mean (SD)</strong></td>
<td>27.06 (7.18)</td>
</tr>
</tbody>
</table>
PTSD in Relation to Diurnal Cortisol Concentrations

In the whole sample, cortisol concentrations did not differ between participants with a current diagnosis of PTSD and those without PTSD. However, in those who had a past significant trauma, there was a significant between groups effect of current PTSD symptoms (F(1,102)=5.6, p=.02), after controlling for age and significant effects of past PTSD symptoms (See figure to left).

Although we previously reported a significant effects of warzone trauma exposure (Hoge scale) and childhood maltreatment (Childhood Trauma Questionnaire) on diurnal cortisol concentrations, with the updated dataset, this analysis was no longer significant, and trauma exposure and childhood maltreatment showed only trend-level associations (p=.09 and p=.08, respectively).

Genetic Predictors of Diurnal Cortisol Concentrations

Similarly, while previously we found a significant interaction of 5-HTTLPR and childhood maltreatment (F (4,114)=4.59, p=.002) in a model that controlled for age, sex, and PTSD symptoms, this effect was no longer significant in the updated dataset, which also controlled for psychotropic medication use and the number of days since return from deployment and collection of saliva samples for cortisol (p=.06).

As with our prior report, we did find an effect of the COMT Val/Met polymorphism. In the repeated measures general linear model controlling for age, sex, PTSD symptoms, time since return, and psychotropic drug use, there was a main effect of COMT (F1,116)=9.34, p=.003), such that individuals homozygous for the Met allele had higher overall cortisol concentrations, particularly morning and nighttime concentrations (see Figure to the left). The interaction effect that we previously reported did not reach significance with the new dataset however (p=.08).
There was also a significant effect of a polymorphism in FKBP5, a glucocorticoid regulating gene, on diurnal cortisol concentrations \( F(4,129)=3.6, p=.008 \). Individuals homozygous for the C allele of this gene had elevated 9pm cortisol concentrations \( F(2, 133)=4.0, p=.02 \), see Figure). The C allele of this SNP has been linked to risk for PTSD, and is associated with greater induction of FKBP5 mRNA by cortisol, which results in decreased glucocorticoid receptor (GR) sensitivity (Binder et al., 2009). Reduced GR negative feedback may result in prolonged cortisol increases following stressors (Binder et al., 2009), and could therefore lead to vulnerability to psychiatric disorders such as PTSD. However, this result is preliminary as we had a small number of affected participants homozygous for the allele.

Data analyses of 12 month assessments (months 33-35) Butler Hospital Completed as discussed above.

- **Key Research Accomplishments**
  - Total consented subjects: 209
  - Total genetic samples used in analyses: 208 subjects
  - Total salivary cortisol used in analyses: 157 subjects
  - Processed and stored all specimens
  - Conducted analyses with key findings described above.

- **Reportable Outcomes**

Shea, MT, Tyrka, AR, Reddy, M, & Sevin, E. Psychosocial Risk Factors for PTSD in National Guard and Reserve Veterans Following War-Zone Deployment


Conclusions

We found limited support for attenuated cortisol concentrations throughout the day among Veterans with symptoms of PTSD, but only among those with past trauma exposures. These findings are consistent with previous suggestions that chronic or repeated stress exposure may lead first to excessive cortisol activation, and then over time to counter-regulatory blunting of HPA axis function as the system seeks equilibrium in a state of stress.

We did not find main effects or stress interaction effects of the serotonin transporter (5-HTTLPR), dopamine type 2 receptor (DRD2), dopamine transporter (DAT), brain-derived neurotrophic factor (BDNF), or neuropeptide Y genes on risk for PTSD in this sample. We did identify a gene x environment interaction of the COMT Val/Met polymorphism and combat trauma exposure suggesting that the Met allele conferred greater sensitivity to combat stress. Analysis of the cortisol data also showed an effect of this gene such that those with the Met allele had higher diurnal cortisol concentrations. Taken together, these findings for the COMT Val/Met gene suggest the possibility that the Met allele confers greater sensitivity to stress. However, as the number of affected participants was small and this was one gene among many tested, we must consider these findings preliminary.

Variation in FKBP5 was linked to altered HPA axis function, in particular, evening cortisol concentrations. The C allele of this SNP has been linked to risk for PTSD, and is associated with greater induction of FKBP5 mRNA by cortisol, which results in decreased glucocorticoid receptor (GR) sensitivity (Binder, 2009). Reduced GR negative feedback may result in prolonged cortisol increases following stressors (Binder, 2009), and could therefore lead to vulnerability to psychiatric disorders such as PTSD. However, this result is preliminary as we had a small number of affected participants homozygous for the allele.

These findings point to possible genetic and environmental modifiers of diurnal cortisol rhythm and risk for PTSD in this sample of trauma-exposed combat veterans. Alterations in stress hormone concentrations have been linked to changes in neurotransmitters and brain regions involved in depression and anxiety disorders including PTSD, and may be involved in the development of this disorder.
References


Title: Psychosocial Risk Factors for PTSD in National Guard and Reserve Veterans Following War-Zone Deployment

Authors: M. Tracie Shea, Audrey Tyrka, Madhavi Reddy, & Elizabeth Sevin

The continuing return of veterans from wars in Iraq and Afghanistan increases the urgency of early identification of longer term problems. Despite increased knowledge of risk factors for PTSD (Brewin et al., 2000; Ozer et al., 2003), for military samples most research has been conducted many years after the trauma. Furthermore, meta-analysis has shown important difference between military and civilian samples in the relative importance of specific variables (Brewin et al., 2000). This presentation will report findings from a study designed to identify risk factors for PTSD symptoms and diagnosis in National Guard and Reserve veterans following deployment in Iraq or Afghanistan. The sample consists of 238 participants with post-deployment assessments, including structured interviews for PTSD (CAPS) and additional Axis I disorders (SCID-I), and a combination of interview and self report measures of hypothesized psychosocial risk factors. The latter includes pre-deployment variables (prior trauma, history of psychiatric disorder), deployment variables (severity of combat exposure, perceived threat, peritraumatic stress and dissociation, unit relationships and life / family concerns), and post-deployment variables (social support, life stressors, and negative affectivity). At the initial assessment, 24 (10.1%) of the sample met current criteria for PTSD. Findings from tests of hypothesized main, mediating, and moderating effects will be presented.
War-Zone Deployment: Stress, Neurobiology, and PTSD Outcomes
Audrey R. Tyrka, MD, PhD (Faculty), Madhavi K. Reddy, PhD (Post-Doctoral Fellow), Darcy E. Burgers, BA (Staff), John McGearry, PhD (Faculty), Elizabeth Sevin, BS (Staff), Linda L. Carpenter, MD (Faculty), Lawrence H. Price, MD (Faculty), M. Tracie Shea, PhD (Faculty)
Mood Disorders Research Program and Laboratory of Molecular Psychiatry, Butler Hospital Department of Psychiatry and Human Behavior, Warren Alpert Medical School of Brown University

Background: Military personnel on hazardous deployments are at risk of developing significant behavioral and emotional problems, including posttraumatic stress disorder (PTSD). Exposure to traumatic events and the development of PTSD may lead to disruptions in the hormone system that coordinates the biological response to stress (the hypothalamic-pituitary-adrenal [HPA] axis). Further, investigators have recently identified specific genes that may be involved in the pathogenesis of PTSD, as well as gene-environment interactions that increase risk for mood and anxiety disorders.

Methods: Members of National Guard and Reserve units were recruited for a parent study examining the psychosocial determinants of PTSD and chronic PTSD following their return from deployment to Iraq or Afghanistan. One hundred forty seven male participants provided saliva for DNA extraction and genotyping and also collected saliva samples at home for assay of diurnal cortisol concentration. Participants were assessed for lifetime and current PTSD using the Clinician-Administered PTSD Scale (CAPS) and other diagnoses using the SCID. History of trauma exposure and severity, early life stress, and social support were also recorded. Repeated measures general linear models were conducted to test effects of PTSD symptoms and a diagnosis of PTSD on salivary cortisol concentrations over the course of the day. Age and past PTSD symptoms were controlled in these models. Additional models tested effects of putative risk genes on diurnal cortisol concentrations.

Results: The repeated measures general linear models showed a significant between groups effect of current PTSD symptoms (p=.02), after controlling for age and significant effects of past symptoms. A current diagnosis of PTSD was associated with nonsignificantly lower diurnal cortisol concentrations. Variation in FKBP5, a gene involved in HPA axis function, was linked to elevated evening cortisol concentrations (p<.05).

Conclusions: Understanding the biomarkers of risk for PTSD and the neurobiological consequences of PTSD may increase our knowledge of the etiology of the disorder and help us to identify individuals who are at highest risk for developing PTSD.
CURRICULUM VITAE
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E-mail: Audrey_Tyrka@Brown.edu

EDUCATION
Undergraduate: State University of New York College at Purchase, Purchase, NY, B.A. Psychology, 1988, Summa Cum Laude.

Columbia University, School of General Studies, New York, NY, Pre-Medical Certificate, 1992
Medical School: University of Pennsylvania School of Medicine, Philadelphia, PA, M.D., 1999, (combined M.D.-Ph.D. program, 1992-1999)

PREDOCTORAL FELLOWSHIPS
1993-1994 National Institute of General Medical Sciences, Medical Scientist Training Program
1994-1999 National Institute of Mental Health, F30 National Research Service Award

POSTGRADUATE TRAINING
Residency: Resident in Psychiatry, Brown University School of Medicine, Providence, RI, 1999-2003.

Research Track, Psychiatry Residency and the Mood Disorders Research Program and Laboratory for Clinical Neuroscience, Butler Hospital and Brown University, 2001-2003.

PREDOCTORAL HONORS AND AWARDS
1988 B.A., Summa Cum Laude, State University of New York College at Purchase
1988 Award for Outstanding Undergraduate Research, State University of New York
1994  Robert M. Toll Psychiatry Research Prize, University of Pennsylvania
1999  AMA Rock Sleyster Memorial Scholarship
1999  Kenneth E. Appel Psychiatry Award, University of Pennsylvania School of Medicine

POSTGRADUATE HONORS AND AWARDS
2002  The American College of Psychiatrists 2002 Laughlin Fellowship Recipient.
2002  First Prize, Resident Research, Sixth Annual Research Symposium, Brown University School of Medicine Department of Psychiatry and Human Behavior
2003  American Psychiatric Association Research Colloquium for Junior Investigators, Participant and Travel Award Recipient
2003  NIMH Mentored Patient-Oriented Research Career Development Award
2003  Janssen Psychiatry Resident Award of Excellence
2003  NARSAD Young Investigator Award
2003  Janssen Pharmaceutica Faculty Development Award in Psychopharmacology
2003  NIH Clinical Research Loan Repayment Program
2004  American College of Neuropsychopharmacology Young Investigator Travel Award
2005  Future Leaders in Psychiatry Symposium Travel Award
2007, 2008, 2009  Citation, Best Doctors in America (Best Doctors, Inc)
2011  Outstanding Teaching Award in General Psychiatry, Warren Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior
2009  The DBSA 2009 Gerald L. Klerman Young Investigator Award

PROFESSIONAL LICENSES AND BOARD CERTIFICATION

Diplomate, National Board of Medical Examiners, 2000.

Licensed Medical Doctor, Board of Medical Licensure and Discipline, State of Rhode Island and Providence Plantations, 2003.

ACADEMIC APPOINTMENTS
Assistant Professor of Psychiatry and Human Behavior, Brown Medical School, Providence, RI, 7/03-
Associate Chief, Mood Disorders Program, Butler Hospital, 7/03-

HOSPITAL APPOINTMENTS
Attending Psychiatrist, Butler Hospital, 2003-
Attending Psychiatrist, Kent County Memorial Hospital, Providence, RI 2003-
Assistant Unit Chief, General Treatment Unit Delmonico 4, Butler Hospital, 2005-2007

OTHER APPOINTMENTS
Editorial Boards:
Editorial Board Member, Acta Psychiatrica Scandinavica, 2007-
Director, Trainee Editorial Board, Acta Psychiatrica Scandinavica, 2007-
Editorial Board Member, Development and Psychopathology, 2011-

Ad Hoc Journal Reviewer:
American Journal of Psychiatry
Archives of General Psychiatry
Biological Psychiatry
Bipolar Disorders
Developmental Psychobiology
European Neuropsychopharmacology
Hormones and Behavior
Journal of Abnormal Psychology
Journal of Adolescent Health
Journal of Affective Disorders
Molecular Psychiatry
Neuropsychopharmacology
Pediatrics
PLoS ONE
Psychiatry Research
Psychological Medicine
Psychoneuroendocrinology
Psychopharmacology
Psychophysiology
Psychosomatic Medicine

National Scientific Committees:
Scientific Advisory Board Member, Depression Bipolar Support Alliance, 2009-
American College of Neuropsychopharmacology, Program Committee Member, 2011-

Grant Reviewer:
Grant Reviewer, Special Emphasis Panel “NIMH Centers for Pediatric Mental Health.” ZMH1-ERB-A-05, 6/07
Grant Reviewer, Special Emphasis Panel Department of Defense PTSD/TBI Post Traumatic Stress Disorder Intramural #2, 11/07
Grant Reviewer, USAMRMC, Scientific Peer Advisory and Review Services, Panel on PTSD, 1/09
Grant Reviewer, USAMRMC, Scientific Peer Advisory and Review Services, Biomarkers of PTSD, 3/09
Grant Reviewer, USAMRMC, Scientific Peer Advisory and Review Services, Post-Traumatic Stress Disorder, 7/09

HOSPITAL COMMITTEES
Butler Hospital Unit Leadership 2003-2006
Butler Hospital Physician’s Subcommittee: Improvement of Organizational Performance 2004-
Butler Hospital President’s Leadership Work Group 2007-
Butler Hospital Committee on Ethnic Diversity in Research Participation, 2006-2007
Butler Hospital Committee on Staff Wellness Programs 2008-2009
Butler Hospital Physician Satisfaction Committee 2010-

UNIVERSITY COMMITTEES
The Warren Alpert Medical School of Brown University: Medical Curriculum Committee, Subcommittee on Years 3 and 4, 2004-6
The Warren Alpert Medical School of Brown University, Office of Women in Medicine, MomDocFamily Advisory Board Member, 2011-
MEMBERSHIPS IN SOCIETIES

American Psychiatric Association 1989-
Rhode Island Psychiatric Society, 2004-
Society of Biological Psychiatry, 2005-
American College of Neuropsychopharmacology, Associate Member, 2007-
The New York Academy of Sciences, 2010-

ORIGINAL PUBLICATIONS IN PEER-REVIEWED JOURNALS


**OTHER PEER-REVIEWED PUBLICATIONS**


**BOOKS AND BOOK CHAPTERS**


**OTHER NON-PEER-REVIEWED PUBLICATIONS**


PUBLICATIONS IN PREPARATION OR IN REVISION


ABSTRACTS


A74. Marsella, SA, Carpenter, LL, **Tyrka, AR,** Wilkinson, CW, and Price, LH. Eszopiclone treatment and decreased cortisol levels in adults with primary insomnia. 17th Annual Research Celebration, Rhode Island Hospital, Providence, RI. October, 2009.


INVITED PRESENTATIONS

1. “New Views on Women and Depression.” Women and Infants Hospital Annual Women’s Health Conference, 1/15/05, Regional Presentation.

2. “Risk for Depression: It’s Nature and Nurture.” Academic Meeting of the Butler Hospital Board of Trustees, 3/22/05, Regional Presentation.

3. “Psychotic Depression.” Butler Hospital Case Conference Series, 4/26/05, Regional Presentation.

4. “Sensitivity to Stress and Risk for Depression.” Academic Presentation to the Butler Hospital Staff Association, 4/7/05, Regional Presentation.


GRANTS

1. National Institute of General Medical Sciences Medical Scientist Training Program, role: Training Grant Recipient, 8/93-8/94.

2. 5 F30 MH10819 Predoctoral National Research Service Award, “Neuropsychological Indicators of Risk for Schizophrenia,” role: Principal Investigator, 9/94-5/00.

3. NARSAD (Young Investigator Award), “Hypothalamic-Pituitary-Adrenal Function in Adults with a History of Childhood Parental Loss,” role: Principal Investigator; 6/03-5/05, $60,000.

4. Janssen Pharmaceutica Faculty Development Award in Psychopharmacology, role: Principal Investigator, 5/18/03, $25,000.

5. RSGPB PBP-103382 American Cancer Society, “Improving Smoking Cessation in Smokers with Depressive Symptoms”, role: Study Physician, 7/02-6/04


7. 1K23MH067947 Mentored Patient-Oriented Research Career Development Award, “Risk for Depression, Stress, and Neuroendocrine Function,” role: Principal Investigator; 12/03-11/08, $905,000.


9. United States Department of the Interior, “Perceived Early Life Stress and DEX/CRH Test Response as Predictors of Psychological Sequelae following Exposure of Healthy Adults to War Stress,” role: Co-Investigator, 7/04-6/05, $40,000.


13. Cyberonics, Inc. “Randomized Comparison of Outcomes in Patients with Treatment-Resistant Depression Who Receive VNS Therapy Administered at Different Amounts of Electrical Charge” role: **Co-Investigator**; 11/1/07-12/1/10; $230,000.

14. Medtronic, Inc. “RECLAIM Deep Brain Stimulation (DBS) Clinical Study for Treatment-Resistant Depression.” Multi-Site; role: **Sub-Investigator** 4/16/2009-


17. R01 NR012005 “RCT of Hatha Yoga for Persistent Depression,” role: **Co-Investigator**, 2/11-01/15, $1,718,041


**UNIVERSITY TEACHING ROLES**

Psychiatric Interviewing, PGY 1 Residents, 2003-present.

Introduction to Psychiatric Literature, PGY 1 Residents, 2003-2004

Mood Disorders Psychopharmacology lectures, PGY 1-4 Residents, 2003-present.

Mood Disorders Psychopathology lectures, PGY 1-4 Residents 2003-present .

Grant Reviewer, Post-doctoral fellows grantsmanship workshop 2004-2006

Research Supervisor, Post-Doctoral Psychology Fellows (K. Rikhye, PsyD; M.Kelly, PhD), 2004-2007

Dissertation Committee Member for Ryan Haggerty, PhD, Pre-Doctoral Psychology Student at Suffolk University, 2005-2007

Course Director/Instructor, Principles of Biostatistics, T32 Post-Doctoral Fellows, 2006-2008

Morbidity and Mortality Conference Preceptor, PGY 1-4, 2007

Supervisor, Brown University Psychology Department senior student Independent Research Project (L. Khoury, BS) 2007-2008

HOSPITAL TEACHING ROLES


Supervisor, Brown psychiatry residents (Inpatient; PGY-1 - PGY-4), 2003-2007


Supervisor, Brown psychiatry residents (Outpatient, PG-3), 2003-present.