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Fort Detrick, Maryland 21702-5012

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14. 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 ($p < .05$).					
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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 Geraciotti
All cortisol assays (1600 samples) were performed in duplicate and data received from Dr. Geraciotti'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 they 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

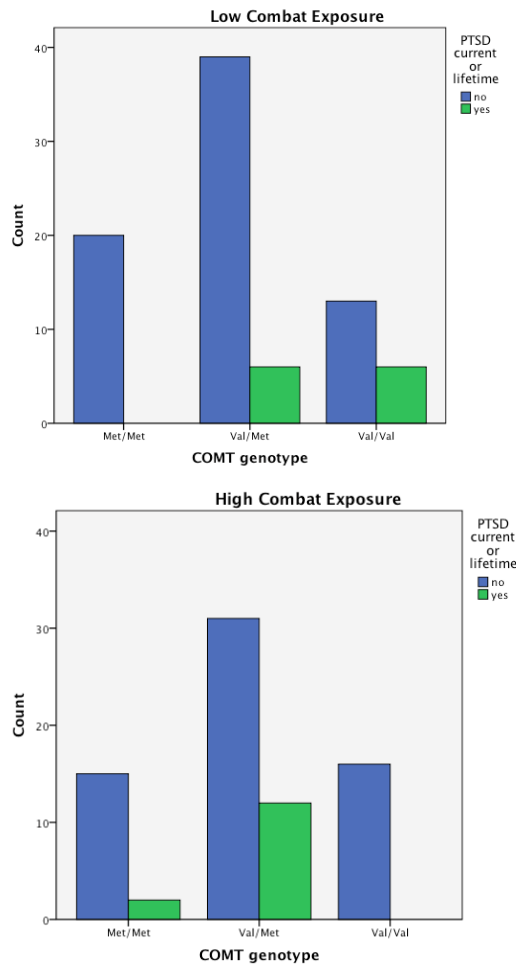
Age, Mean (SD)	33.41 (9.7)
Range	20-61
Gender, n (%)	
Male	190 (91.35%)
Female	18 (8.65%)
Race/Ethnicity, n (%)	
Caucasian	154 (74.04%)
African American	16 (7.69%)
Asian	6 (2.88%)
Hispanic	28 (13.46%)
American Indian	1 (0.48%)
Other	3 (1.44%)
Most Recent Deployment Location, n (%)	
Iraq	200 (96.15%)
Afghanistan	8 (3.84%)
SCID Axis I Diagnoses Other than PTSD, n (%)	
Current mood disorder	47 (22.59%)
Past mood disorder	27 (12.98%)
Current anxiety disorder	14 (6.73%)
Past anxiety disorder	5 (2.40%)
Current substance use disorder	23 (11.06%)
Past substance use disorder	67 (32.21%)
CAPS PTSD Diagnoses, n (%)	
Current diagnosis at baseline	19 (9.13%)
PTSD diagnosis at any time point	40 (19.23%)
Cortisol Concentration (ug/dL), Mean (SD)	
Awakening	0.48 (0.30)
30 minutes after awakening	0.57 (0.30)
1pm	0.22 (0.23)
5pm	0.14 (0.13)
9pm	0.12 (0.22)
CTQ Total 28 item self-report, Mean (SD)	8.15 (2.90)
Subjects reporting abuse or neglect on CTQ, n (%)	78 (37.50%)
Hoge Combat Experience Scale Total, Mean (SD)	8.93 (8.80)
DDRI Life and Family Concerns Total, Mean (SD)	27.02 (6.97)

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 analyses 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

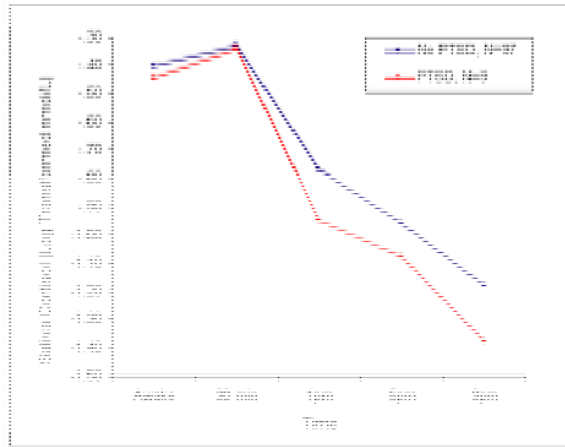
As mentioned above, the final cortisol dataset (n=157) has been modified substantially in order to have a good temporal match to the assessment data because not all participants collected saliva samples at the time of the baseline assessment. Now that we have the later assessment data available, we have 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

Age, Mean (SD)	34.63 (9.7)
Range	20-61
Gender, n (%)	
Male	147 (93.63%)
Female	10 (6.37%)
Race/Ethnicity, n (%)	
Caucasian	121 (77.07%)
African American	11 (7.01%)
Asian	3 (1.91%)
Hispanic	15 (9.55%)
American Indian	1 (0.64%)
Other	6 (3.82%)
Most Recent Deployment Location, n (%)	
Iraq	150 (95.54%)
Afghanistan	7 (4.46%)
SCID Axis I Diagnoses Other than PTSD, n (%)	
Current mood disorder	32 (20.38%)
Past mood disorder	17 (10.82%)
Current anxiety disorder	9 (5.73%)
Past anxiety disorder	4 (2.55%)
Current substance use disorder	18 (11.47%)
Past substance use disorder	52 (33.12%)
CAPS PTSD Diagnoses, n (%)	
Current diagnosis at cortisol assessment	13 (8.28%)
Past diagnosis prior to cortisol assessment	11 (7.01%)
Cortisol Concentration (ug/dL), Mean (SD)	
Awakening	0.48 (0.30)
30 minutes after awakening	0.57 (0.30)
1pm	0.22 (0.23)
5pm	0.14 (0.13)
9pm	0.12 (0.22)
CTQ Total 28 item self-report, Mean (SD)	7.99 (2.78)
Subjects reporting abuse or neglect on CTQ, n (%)	61 (38.85%)
Hoge Combat Experience Scale Total, Mean (SD)	8.47 (8.25)
DDRI Life and Family Concerns Total, Mean (SD)	27.06 (7.18)

PTSD in Relation to Diurnal Cortisol Concentrations



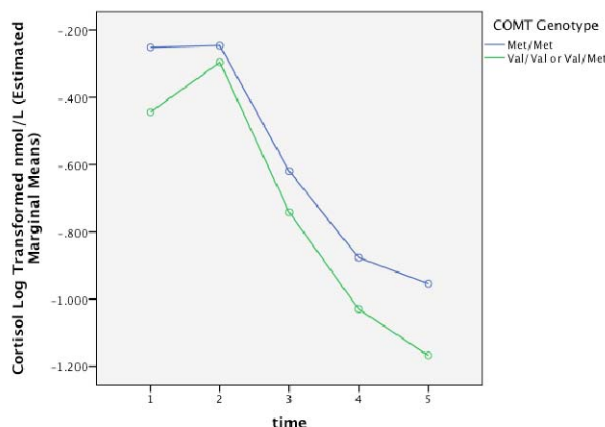
In the whole sample, cortisol concentrations did not differ between participants with a current *diagnosis* of PTSD and those without PTSD. However, in those who had a past significant trauma, there was a significant between groups effect of current PTSD *symptoms* ($F(1,102)=5.6$, $p=.02$), after controlling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

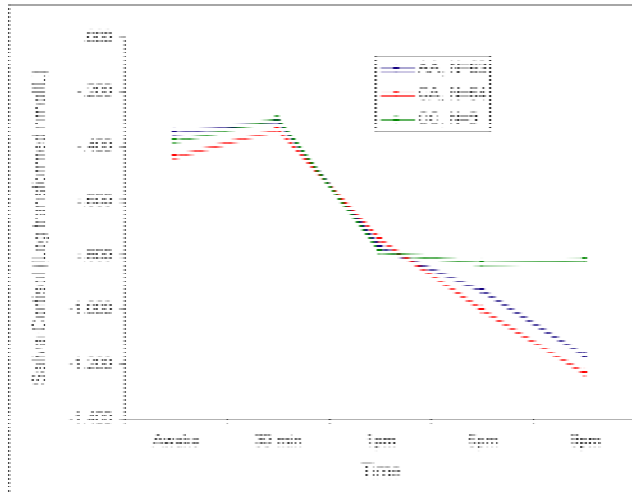
Genetic Predictors of Diurnal Cortisol Concentrations

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 ($F(1,116)=9.34$, $p=.003$), 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.

- e. Prepare manuscripts for publication Butler Hospital, Dr. Audrey Tyrka
We are currently working on manuscripts for publication from this study.
- g. 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
Title of symposium: Marshall, E. C. & Vujanovic, A. A. (Chairs). (2010). *Trauma Exposure: Transdiagnostic Risk and Resilience Factors*. Symposium submitted for presentation at the 44th annual conference of the Association for Behavioral and Cognitive Therapies, San Francisco, CA.

Tyrka, AR, Reddy, MK, Burgers, DE, Lee, JK, McGeary, J, Sevin, E, Carpenter, LL, Price, LH, and Shea, MT. War-Zone Deployment: Stress, Neurobiology, and PTSD Outcomes. Fourteenth Annual Research Symposium on Mental Health Sciences, Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, March, 2011.

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

Binder, E. (2009). The role of FKBP5, a co-chaperone of the glucocorticoid receptor in the pathogenesis and therapy of affective and anxiety disorders. *Psychoneuroendocrinology* 34: 186-195.

Kolassa, IT., Kolassa, S., Ertl, V., Papassotiropoulos, A., De Quervain, D.J.-F. (2010). The risk of posttraumatic stress disorder after trauma depends on traumatic load and the catechol-O-methyltransferase Val158Met Polymorphism. *Biological Psychiatry* 67: 304-308.

(Title of symposium: Marshall, E. C. & Vujanovic, A. A. (Chairs). (2010). *Trauma Exposure: Transdiagnostic Risk and Resilience Factors*. Symposium submitted for presentation at the 44th annual conference of the Association for Behavioral and Cognitive Therapies, San Francisco, CA.)

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 McGeary, 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 non-significantly 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.

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EDUCATION

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

Pre-Medical: State University of New York College at Purchase, Purchase, NY, pre-medical coursework, 1989-1991.

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)

Graduate School: University of Pennsylvania, Department of Psychology, Philadelphia, PA, Ph.D., Psychology, 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 2011	Citation, Best Doctors in America (Best Doctors, Inc)
2007	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.

Diplomate, American Board of Psychiatry and Neurology, 2004.

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

Grant Reviewer, Special Emphasis Panel, NIMH, "Dissertations," ZMH1 ERB-E (04) S, 11/10.

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

1. **Tyrka, A.** and Smith, G.P. Potency of SCH 23390 for decreasing sucrose intake in rat pups depends on mode of ingestion. Pharmacology Biochemistry & Behavior, 39(4):955-961, 1991.
2. Smith, G.P., **Tyrka, A.** and Gibbs, J. Type-A CCK receptors mediate the inhibition of food intake and activity by CCK-8 in 9- to 12-day-old rat pups. Pharmacology Biochemistry & Behavior, 38(1):207-210, 1991.
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6. **Tyrka, A.** and Smith, G. P. SCH 23390, but not raclopride, decreases intake of intraorally infused 10% sucrose in adult rats. Pharmacology Biochemistry & Behavior, 45(1):243-246,1993.
7. **Tyrka, A.R.**, Cannon, T. D., Haslam, N., Mednick, S.A., Schulsinger, F., and Schulsinger, H. The Latent Structure of Schizotypy I: Premorbid indicators of a taxon of individuals at-risk for schizophrenia spectrum disorders. Journal of Abnormal Psychology, 104: 173-183, 1995.
8. Carpenter, L.L., Heninger, G.R., McDougle, C.J., **Tyrka, A.R.**, Epperson, C.N., Price, L.H. Cerebrospinal fluid interleukin (IL)-6 in obsessive-compulsive disorder and trichotillomania. Psychiatry Research, 112 (3) 257-262, 2002.

9. **Tyrka, A.R.**, Waldron, I., Graber, J.A., and Brooks-Gunn, J. Prospective predictors of the development of eating disorders in adolescent girls. International Journal of Eating Disorders, 32 (3) 282-290, 2002.
10. Graber, J.A., **Tyrka, A.R.**, and Brooks-Gunn, J. How similar are different subclinical eating problems and bulimia nervosa? Journal of Child Psychology and Psychiatry, 44 (2) 262-273, 2003.
11. Carpenter, L.L., Heninger, G.R., Malison, R.T., **Tyrka, A.R.**, and Price, L.H. Cerebrospinal fluid interleukin (IL)-6 in unipolar major depression. Journal of Affective Disorders, 79 285-289, 2004.
12. Carpenter, L.L., **Tyrka, A.R.**, McDougale, C.J., Malison, R.T., Owens, M.J., Nemeroff, C.B., and Price, L.H. Cerebrospinal fluid corticotropin releasing factor and perceived early life stress in depressed patients and healthy control subjects. Neuropsychopharmacology, 29 (4) 777-784, 2004.
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14. Carpenter, L.L., Schechter, J.M., Underwood, J.A., **Tyrka, A.R.**, and Price, L.H. Service expectations and clinical characteristics of patients receiving psychiatric emergency services. Psychiatric Services, 56: 743-745, 2005.
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19. Grover, K.E., Carpenter, L.L., Gagne, G.G., Mello, A.A.F., Mello, M.F., Price, L.H., and **Tyrka, A.R.** The relationship between childhood abuse and adult personality disorder symptoms, Journal of Personality Disorders, 21, 442-447, 2007.

20. Carpenter, L.L., Carvalho, J.P., **Tyrka, A.R.**, Wier, L.M., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Decreased adrenocorticotrophic hormone and cortisol responses to stress in healthy adults with a history of significant childhood maltreatment. Biological Psychiatry, 62, 1080-7, 2007.
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29. Price, L.H., Carpenter, L.L., **Tyrka, A.R.** Lithium augmentation for refractory depression: A critical reappraisal. Primary Psychiatry, 15(11), 35-42, 2008.
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2. Philip, N.S., Carpenter, L.L., **Tyrka, A.R.**, Price, L.H. Nicotinic acetylcholine receptors and depression: A review of the preclinical and clinical literature. Psychopharmacology, 212(1), 1-12, 2010.
3. Nugent, N.R., **Tyrka, A.R.**, Carpenter, L.L., Price, L.H. Gene-environment interactions: Early life stress and risk for depressive and anxiety disorders. Psychopharmacology, 214(1), 175-196, 2011.

BOOKS AND BOOK CHAPTERS

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2. **Tyrka, A.R.**, Graber, J.A., and Brooks-Gunn, J. The development of disordered eating: Correlates and predictors of eating problems in the context of adolescence. In M Lewis, AJ Sameroff, and SM Miller (Eds), *Handbook of Developmental Psychopathology, 2nd Ed.*, New York: Kluwer Academic/ Plenum Publishers, 2000.
3. **Tyrka, A.R.**, Wier, L.M. Eating disorders. In K.A. McGarry and I.L. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 96-96, 2007.

4. **Tyrka, A.R.**, Carvalho, J.P.. Depression. In K.A. McGarry and I.L. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 82-84, 2007.
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7. **Tyrka, A.R.**, Philip, N.S. Depression. In K.A. McGarry and I.L. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, in press.
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OTHER NON-PEER-REVIEWED PUBLICATIONS

1. **Tyrka, A.R.**, Carpenter, L.L., Carvalho, J.P., and Price, L.H. Biomarkers in the human stress system: Do they signal risk for depression? Medicine and Health Rhode Island, 89 (5), 180-182, 2006.
2. Carpenter, L.L., Friehs, G.M., **Tyrka, A.R.**, Rasmussen, S., Price, L., and Greenberg, B.D. Vagus nerve stimulation and deep brain stimulation for treatment resistant depression, Medicine and Health Rhode Island, 89 (4), 137-141, 2006.
3. Wier, L.M., Tavares, S.B., **Tyrka, A.R.**, Price, L.H., and Carpenter, L.L. Levetiracetam-Induced Depression in a Healthy Adult. Journal of Clinical Psychiatry, 67, 1159-60, 2006.
4. Feijo Mello, A., Francisco Jurruena, M., Pariente C.M., **Tyrka, A.R.**, Price, L.H., Carpenter, L.L., Alberto Del Porto, J. Depression and stress: is there an endophenotype? Revista Brasileira de Psiquiatria, 29 (Supl 1), S13-8, 2007.
5. Price, L.H., **Tyrka, A.R.** Letter to the Editor Re: Adjunctive antidepressant treatment for bipolar depression. New England Journal of Medicine, 357, p 614, 2007.
6. Mello, M.F., Faria, A.A., Mello, A.F., Carpenter, L.L., **Tyrka, A.R.**, Price, L.H. Childhood maltreatment and adult psychopathology: pathways to hypothalamic-pituitary-adrenal axis dysfunction, Rev Bras Psiquiatr. Suppl 2:S41-8, 2009.
7. Philip N.S., Carpenter L.L., **Tyrka A.R.**, Price L.H.. Using atypical antipsychotics to augment treatment of nonpsychotic unipolar depression. Directions in Psychiatry 29(1):51-59, 2009.
8. Philip, N.S., Carpenter, L.L., **Tyrka, A.R.**, Price, L.H. Pharmacologic approaches to treatment resistant depression: a re-examination for the modern era, Expert Opin Pharmacother, 11, 709-22, 2010.

9. Khoury L.M., Carpenter L.L., Price L.H., **Tyrka A.R.** Early-life stress and altered neuroendocrine function: Risk for mood and anxiety disorders. Directions in Psychiatry, 30 (2): 63-75, 2010.
10. **Tyrka, A.R.**, Price, L.H., Anderson, G.M., Carpenter, L.L. In reply to "Childhood maltreatment and HPA axis reactivity" [Ltr to the Ed]. Biological Psychiatry, 67, e61-e62, 2010.
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1. **Tyrka, A.R.**, Price, L.H., Marsit, C., Walters, C., Wilkinson, C.W., Carpenter, L.L. Epigenetic modulation of leukocyte glucocorticoid receptor in healthy adults: Effects of childhood parenting experiences. In revision for the American Journal of Psychiatry.
2. Carpenter, L.L., Tyrka, A.R., Marsella, S.A., Wilkinson, C.W., Geraciotti, T.D., Price, L.L. Eszopiclone treatment and cortisol response in adults with primary insomnia. In preparation.
3. **Tyrka, A.R.**, Kelly, M.M., Graber, J.A., Warren, M.P. and Brooks-Gunn, J. Neuroendocrine predictors of behavioral adjustment in boys: A prospective longitudinal study of a community sample. In preparation.
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5. **Tyrka, A.R.**, Philip, N.S., Price, L.H., Marsella, S.A., Gelernter, J., Geraciotti, T. Carpenter, L.L. COMT Genetic Variation: Gene-environment interactions predicting depression and HPA axis function. In preparation.
6. **Tyrka, A.R.**, Price, L.H., Walters, C., Gelernter, J., Carpenter, L.L. BDNF Val/Met polymorphism interacts with childhood maltreatment to predict HPA axis function. In preparation.

ABSTRACTS

- A1. **Tyrka, A.**, Smith, G.P., and Gibbs, J. SCH 23390 inhibits intake of sucrose more during independent ingestion than during intraoral infusion in rats as early as postnatal day 7. Society for Neuroscience, 1990.
- A2. Broder, L., Smith, G.P., **Tyrka, A.**, and Gibbs, J. Independent ingestion and intraoral infusion of 10% sucrose produce different patterns of central dopamine metabolism in 14-day-old rats. Society for Neuroscience, 1990.

- A3. **Tyrka, A.**, and Smith, G.P. Is density of reinforcement responsible for the differential effect of DA antagonists on rat pups during two ingestion tests? Society for Neuroscience, 1991.
- A4. **Tyrka, A.R.**, Gibbs, J., and Smith, G.P. SCH 23390, but not raclopride, decreases intake of intraorally infused 10% sucrose in adult rats. Society for the Study of Ingestive Behavior, 1991.
- A5. **Tyrka, A.R.**, Waldron, I., Graber, J.A. and Brooks-Gunn, J. Prospective predictors of the development of eating disorders in a community sample of young women. University of Pennsylvania Annual Research Symposium, April, 1999.
- A6. Carpenter L. L., **Tyrka A.R.**, Price L. H. Cerebrospinal Fluid (CSF) Interleukin-6 in depressed patients and healthy controls. Sixth Annual Brown University Research Symposium, March 2002.
- A7. **Tyrka A. R.**, Carpenter L. L., Anderson G. A., Brown R., Price L. H. Relationship between early life stress and pituitary-adrenal function as measured by the dexamethasone/corticotrophin releasing hormone test. Sixth Annual Brown University Research Symposium, March 2002.
- A8. **Tyrka, A. R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., Price, L.H. Early-Life Stress and Response to the Dexamethasone/Corticotropin-Releasing Hormone Test in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2002.
- A9. Carpenter L. L., **Tyrka A. R.**, Schechter J., Haggarty R., and Price L. H. Tiagabine (gabitril) for major depressive disorder with anxiety. Seventh Annual Brown University Research Symposium, March 2003.
- A10. Carpenter, L. L., **Tyrka A. R.**, Stout, S. C., Owens, M. J., Nemeroff, C. B., and Price, L. H. Elevated cerebrospinal fluid (CSF) concentrations of substance p in major depression. Seventh Annual Brown University Research Symposium, March 2003.
- A11. **Tyrka A. R.**, Price L. H., Owens M. J., Nemeroff C. B., and Carpenter L. L. Cerebrospinal fluid corticotropin-releasing factor following oral paroxetine in adults with depression and perceived early-life stress. Seventh Annual Brown University Research Symposium, March 2003.
- A12. Carpenter LL, **Tyrka AR**, Schechter J, Haggerty R, Lawrence Price MD. An open-label trial of tiagabine for major depressive disorder with anxiety. Society for Biological Psychiatry Annual Meeting, #107, May, 2003.
- A13. Carpenter. L.L., **Tyrka, A.R.**, Schechter, J., Haggarty, R., and Price, L.H. Tiagabine for MDD with anxiety. American Psychiatric Association Ann Mtg, #NR501, May 2003.
- A14. **Tyrka, A.R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., and Price, L.H. Early-Life Stress And Response To The Dexamethasone/Corticotropin-Releasing Hormone Test In Healthy Adults. Society for Biological Psychiatry Annual Meeting, #145, May, 2003.

- A15. **Tyrka, A.R.**, Carpenter, L.L., Brown, R.A., Strong, D.R., Kahler, C.W., Anderson, G.M., and Price, L.H. Early-Life Stress and Pituitary-Adrenal Function in Healthy Adults. American Psychiatric Association Annual Meeting, #NR61, May, 2003.
- A16. Carpenter LL, **Tyrka AR**, Schecter J, Haggerty R, Lawrence Price MD. An open-label trial of tiagabine for major depressive disorder with anxiety. Institute on Psychiatric Services, 2003.
- A17. **Tyrka, A.R.**, Carpenter, L.L., McDougale, C.J., Kirwin, P.D., Owens, M.J., Nemeroff, C.B., and Price, L.H. CSF Corticotropin-releasing factor increases during tryptophan depletion. Eighth Annual Brown University Research Symposium, March 2004.
- A18. **Tyrka, A.R.**, Carpenter, L.L., McDougale, C.J., Kirwin, P.D., Owens, M.J., Nemeroff, C.B., and Price, L.H. CSF Corticotropin-releasing factor increases during tryptophan depletion. American Psychiatric Association Annual Meeting, #NR78, May 2004.
- A19. Greenberg, B.D., Price, L.H., Friehs, G., Malone, D., Rezai, A.R., Shapira, N.A., Foote, K.D., Okun, M.A., Rauch, S.L., Dougherty, D., Noren, G., Malloy, P.F., Salloway, S., Marsland, R., **Tyrka, A.**, Carpenter, L., Goodman, W., and Rasmussen, S.A. Deep Brain Stimulation in Intractable OCD, and Preliminary Results in Intractable Depression. 44th Annual Meeting of the New Clinical Drug Evaluation Unit (NCDEU), June, 2004.
- A20. Grover, K.E., **Tyrka, A.R.**, Carpenter, L.L., Mello, A.A.F., Mello, M.F., Gagne, G.G., and Price, L.H. Personality and hypothalamic-pituitary-adrenal function in healthy adults. Rhode Island Hospital 12th Annual Hospital Research Celebration, October, 2004.
- A21. Greenberg BD, Friehs G, Carpenter L, **Tyrka A**, Malone D, Rezai A, Shapira N, Foote K, Okun M, Goodman W, Rasmussen S, **Price LH**. Deep brain stimulation: Clinical findings in intractable depression and OCD. Abstr Amer Coll Neuropsychopharm #468, December, 2004.A21.
- A22. **Tyrka, A.R.**, Carpenter, L.L., Feijo do Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., and Price, L.H. Temperament and Pituitary-Adrenal Response to the DEX/CRH Test in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2004.
- A23. Carpenter L.L., **Tyrka, A.R.**, Carvalho, J., Wier, L. Gagne, G., Mello, A.F., Mello, M.F., and Price, L.H. Decreased cortisol response to the trier social stress test in healthy adults with significant childhood adversity. Ninth Annual Brown University Research Symposium, March 2005.
- A24. Rikhye, K. Carpenter, L.L, **Tyrka, A.R.**, Gagne, G, Feijo de Mello, A.A., Feijo de Mello, M., Price, L.H. Interplay between childhood adversity, parental bonding, and sex effects: Impact on quality of life. Ninth Annual Brown University Research Symposium, March 2005.
- A25. **Tyrka, A.R.**, Carpenter, L.L., Feijo de Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Pituitary-Adrenal Response to the

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- A26. Grover, K.E., **Tyrka, A.R.**, Carpenter, L.L., Gagne, G.G., Feijo de Mello, A.A., Feijo de Mello, M., and Price, L.H. The Relationship between Childhood Abuse and Adult Personality Disorder Symptoms. Ninth Annual Brown University Research Symposium, March 2005.
- A27. **Tyrka, A.R.**, Carpenter, L.L., Feijo de Mello, A.A., Feijo de Mello, M., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Pituitary-Adrenal Response to the DEX/CRH Test in Healthy Adults. Annual Meeting of the Society of Biological Psychiatry, May, 2005.
- A28. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Mello, A.F., Mello, M.F., Gagne, G.G., Grover, K.E., Anderson, G.M., and Price, L.H. Temperament and Response to the Dex/CRH Test in Healthy Adults. 36th Annual Conference of the International Society of Psychoneuroendocrinology, September, 2005.
- A29. Carpenter, L.L., **Tyrka, A.R.**, Carvalho, J.P., Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., and Price, L.H. Decreased Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. 36th Annual Conference of the International Society of Psychoneuroendocrinology, September, 2005.
- A30. Wier, L.M., **Tyrka, A.R.**, Carpenter, L.L., Carvalho, J., Rikhye, K., Anderson, G.M., and Price, L.H. Stress-Reactive Temperaments and Cortisol Response to the Dex/CRH Test in Healthy Adults. Rhode Island Hospital Thirteenth Annual Research Celebration, Providence, RI, September, 2005.
- A31. Carvalho, John P., **Tyrka, A.R.**, Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Price, L.H., and Carpenter, L.L. The Relationship Between Childhood Adversity and Stress Responsivity. Rhode Island Hospital Thirteenth Annual Research Celebration, Providence, RI, September, 2005.
- A32. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Wilkinson, C.W., Anderson, G.M., and Price, L.H. Inhibited Temperament and HPA Axis Function in Healthy Adults. Annual Meeting of the American College of Neuropsychopharmacology, December 2005.
- A33. Carpenter, L.L., **Tyrka, A.R.**, Carvalho, J.P., Wier, L., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. Annual Meeting of the American College of Neuropsychopharmacology, December 2005.
- A34. Kelly, M. M., Carpenter, L. L., **Tyrka, A. R.**, Anderson, G., M., & Price, L. H. Parental bonding and stress reactivity: The mediating effects of trait anxiety. 26th annual meeting of the Anxiety Disorders Association of America, Miami, FL, March 2006.

- A35. Carvalho, J.P., **Tyrka, A.R.**, Rikhye, K., Price, L., and Carpenter, L.L. Does a History of Abuse Influence Recall of Psychobiological Responses to a Standardized Stress Test? Tenth Annual Brown University Research Symposium, April 2006.
- A36. Carpenter, L.L., Carvalho, J.P., **Tyrka, A.R.**, Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Decreased Cortisol Response to the Trier Social Stress Test in Healthy Adults with Significant Childhood Adversity. Tenth Annual Brown University Research Symposium, April 2006.
- A37. **Tyrka, A.R.**, Carpenter, L.L., Wier, L.M., Wilkinson, C.W., Anderson, G.M., and Price, L.H. Inhibited Temperament and HPA Axis Function in Healthy Adults. Tenth Annual Brown University Research Symposium, April 2006.
- A38. Wyche, M.C, **Tyrka, A.R.**, Kelly, M.M., Wier, L.M., Carvalho, J.P., Rikhye, R., Price, L.H., and Carpenter, L.L. Childhood Abuse and Adult Personality: Does Type of Maltreatment Matter? Tenth Annual Brown University Research Symposium, April 2006.
- A39. Wier, L.M., Carpenter, L.L., Carvalho, J.P., Rikhye, K., Wyche, M.C., Price, L.H., and **Tyrka, A.R.** The Relationship Between Childhood Parental Loss and Adult Psychological Function. Tenth Annual Brown University Research Symposium, April 2006.
- A40. Kelly, M.M., Carpenter, L.L, **Tyrka, A.R.**, Anderson, G.M., and Price, L.H. Parental Bonding and Stress Reactivity: The Mediating Effects of Trait Anxiety. Tenth Annual Brown University Research Symposium, April 2006.
- A41. Kelly, M.M., **Tyrka, A.R.**, Anderson, G.M., Price, L.H., and Carpenter, L.L. Sex Differences in Emotional and Physiological Responses to the Trier Social Stress Test. Tenth Annual Brown University Research Symposium, April 2006.
- A42. **Tyrka, A.R.**, Carvalho, J.P., Wier, L.M., Gagne, G.G., Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., Price, L.W., and Carpenter, L.L. Attenuated cortisol and ACTH responses to the Trier Social Stress Test in healthy adults with a history of childhood maltreatment. Annual Meeting of the Society of Biological Psychiatry, May, 2006.
- A43. Kelly, M. M., **Tyrka, A. R.**, Anderson, G. M., Price, L. & Carpenter, L. L. Sex differences in emotional and physiological responses to the Trier Social Stress Test. 40th annual meeting of the Association for Behavioral and Cognitive Therapies, Chicago, IL., November 2006.
- A44. Wyche, M.C., **Tyrka, A.R.**, Kelly, M.M., Wier, L.M., Carvalho, J.P., Rikhye, K., and Price, L.H., and Carpenter LL. Childhood Abuse and Adult Personality: Does Type of Maltreatment Matter? 14th Annual Research Celebration, Rhode Island Hospital, Providence, RI. November 9, 2006.
- A45. Wier, L.M., Carpenter, L.L., Carvalho, J.P., Rikhye, K., Wyche, M.C., Price, L.H., and **Tyrka, A.R.** The Relationship Between Childhood Parental Loss and Adult Psychological Function.

14th Annual Research Celebration, Rhode Island Hospital, Providence, RI. November 9, 2006.

- A46. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Annual Meeting of the American College of Neuropsychopharmacology, December 2006.
- A47. Kelly, M. M., **Tyrka, A. R.**, Graber, J. A., Warren, M., Brooks-Gunn, J. Associations of internalizing and externalizing symptoms with HPA axis stress reactivity in a longitudinal study of boys. Annual Meeting of the American Psychopathological Association, March, 2007
- A48. Wier, W., Carpenter, L.L., Price, L.H., Ross, N., Anderson, G.M., Wilkinson, C.W., and **Tyrka, A.R.** Parental loss in childhood and pituitary-adrenal response to the dexamethasone/corticotropin-releasing hormone test in healthy adults. Eleventh Annual Brown University Research Symposium, April 2007.
- A49. Ross, N., **Tyrka, A.R.**, Price, L.H., Anderson, G.M., and Carpenter, L.L. Childhood maltreatment, female sex, and perceived stress burden: significant determinants of cortisol response to the Dex/CRH test in healthy adults. Eleventh Annual Brown University Research Symposium, April 2007.
- A50. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Eleventh Annual Brown University Research Symposium, April 2007.
- A51. Wyche, M.C., Tyrka, A.R., Kelly, M.M., Graber, J.A., Warren, M.P., and Brooks-Gunn, J. Associations of Internalizing and Externalizing Symptoms with HPA Axis Stress Reactivity in a Longitudinal Study of Boys. Eleventh Annual Brown University Research Symposium, April 2007.
- A52. Carpenter, L.L., Ross, N.S., **Tyrka, A.R.**, Mello, A.F., Mello, M.F., Anderson, G.M., Wilkinson, C.W., and Price, L.H. Childhood abuse, depression and gender are significant determinants of cortisol and ACTH response to the dex/crh test. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A53. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Kelly, M.M., and Price, L.H. COMT genetic variation and depression: gene-environment interaction and HPA axis correlates. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A54. **Tyrka, A.R.**, Wier, L., Price, L.H., Anderson, G., and Carpenter, L.L. Childhood parental loss and cortisol response to the dexamethasone/corticotropin-releasing hormone test in healthy adults. Annual Meeting of the Society of Biological Psychiatry, May, 2007.
- A55. Kelly, M. M., **Tyrka, A. R.**, Price, L. H., & Carpenter, L. L. Sex differences in the use of coping strategies: Predictors of anxiety and depressive symptoms. 41st Annual Meeting of the Association for Behavioral and Cognitive Therapies, Philadelphia, PA, November, 2007.

- A56. Dougherty, D.D., Malone, D., Carpenter, L., **Tyrka, A.**, Friehs, G., Rezai, A. Eskander, E., Machado, A., Kubu, C., Malloy, P., Salloway, S., Rauch, S.L., Price, L., Rasmussen, S. Greenberg, B. Long-term outcomes of ventral capsule/ventral striatum DBS for highly treatment-resistant depression. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.
- A57. **Tyrka, A.R.**, Carpenter, L.L., Gelernter, J., Price, L.H. Serotonin transporter polymorphism, childhood maltreatment, and cortisol response to the Dex/CRH test in healthy adults: Preliminary findings. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.
- A58. Carpenter, L.L., **Tyrka, A.R.**, Anderson, G..M., Wilkinson, C.W., Price, L.H. Depression, childhood maltreatment, and gender are significant determinants of cortisol response to the Dex/CRH test. Annual Meeting of the American College of Neuropsychopharmacology, December 2007.
- A59. Carpenter, L.L., Malone, D.A. Jr, Dougherty, D.A., Rezai, A.R., Friehs, G.M., Eskandar, E.N., Rauch, S.L., Rasmussen, S.A., Machado, A.G., Kubu, C.S., **Tyrka, A.R.**, Price, L.H, Stypulkowski P.H., Giftakis, J.E., Rise, M.T., Malloy, P.F., Salloway, S.P., Greenberg, B.D. Deep brain stimulation (DBS) of the ventral capsule/ventral striatum for treatment resistant major depression. Twelfth Annual Brown University Research Symposium March, 2008.
- A60. Carpenter, L.L., Price, L.H, Gelernter, J., Ross, N.S., Anderson, G., **Tyrka, A.R.** Serotonin transporter polymorphism, childhood maltreatment, and cortisol response to the Dex/CRH test in healthy adults: Preliminary findings. Twelfth Annual Brown University Research Symposium March, 2008.
- A61. **Tyrka, A.R.**, Price, L.H., Gelernter, J., Anderson, G., Tracy, A.P., Carpenter, L.L. Corticotropin releasing hormone receptor (CRHR1) polymorphisms interact with early life stress to influence the cortisol response to the Dex/CRH test. Twelfth Annual Brown University Research Symposium March, 2008.
- A62. Khoury, L.M., Carpenter, L.L., Price, L.H., Anderson, G., **Tyrka, A.R.** Early life stress and HPA axis function. Twelfth Annual Brown University Research Symposium March, 2008.
- A63. Philip, N.S., Carpenter, L.L., Tyrka, A.R., Price, L.H. Depression and suicidality in outpatients during varenicline (Chantix) treatment: A preliminary report. Twelfth Annual Brown University Research Symposium March, 2008.
- A64. Schoedl AF, Costa MCP, **Tyrka AR**, Carpenter LL, Price LH, Mari JJ, Feijo Melo M. The clinical correlates of reported childhood sexual abuse: An association between age at trauma onset and severity of depression and PTSD in adults. International Symposium on Violence and Mental Health #71, p 51, June, 2008.
- A65. Cui D.H., Zhang H.P., Kranzler H.R., Blumberg H.P., **Tyrka A.R.**, Yang B.Z., Wei F., Carpenter

L., Price L., Gelernter J. Association between NGFB and affective disorder suggests potentially different genetic backgrounds between primary and drug dependence-comorbid affective disorders. The American Society of Human Genetics (ASHG) 58th Annual Meeting, November, 2008.

- A66. **Tyrka, A.R.**, Price, L.H., Kao, H.T., Porton, B., Marsella, S., and Carpenter, L.L. Reported childhood maltreatment linked to shortened telomere length in healthy adults: A pilot study. Brain Research Meeting: Stress, Coping and Disease, November, 2008.
- A67. Carpenter L.L., Lee J.K., **Tyrka A.R.**, Anderson G.M., Price L.H. Elevated IL-6 response to stress in healthy adults with early life adversity. Brain Research Meeting: Stress, Coping and Disease, November, 2008.
- A68. **Tyrka, A.R.**, Price, L.H., Kao, H.T., Porton, B., Marsella, S., and Carpenter, L.L. Reported childhood maltreatment linked to shortened telomere length in healthy adults: A pilot study. Annual Meeting of the American College of Neuropsychopharmacology, December 2008.
- A69. Carpenter L.L., Lee J.K., **Tyrka A.R.**, Anderson G.M., Price L.H. Elevated IL-6 response to stress in healthy adults with early life adversity. Annual Meeting of the American College of Neuropsychopharmacology, December 2008.
- A70. Malone, D.A.*, Dougherty, D.D.*, Rezai, A.R., Carpenter, L.L., Friehs, G.M., Eskander, E., Rauch, S.L., Rasmussen, S.A., Machado, A.G., Kubu, C.S., **Tyrka, A.R.**, Price, L.H., Stypulkowski, P.H., Giftakis, J., Malloy, P.F., Salloway, S.P., and Greenberg, B.D. Deep brain stimulation of the ventral capsule/ventral striatum for treatment-resistant depression. American Psychiatric Association Annual Meeting, May 2009.
- A71. Cui, D.H., Kranzler, H.R., Zhang, H., Listman, J., Price, L.H., Carpenter, L.L., Tyrka, A.R., and Gelernter, J. A candidate genes association study by customized low-density gene array indicates different pathways in primary affective disorders vs. comorbid with substance dependence disorders. The Chinese Society of Psycho-Neuroscience Annual Meeting, October, 2009.
- A72. Strong, D. R., Haber, S., **Tyrka, A.**, Rasmussen, S., Greenberg, B.D. Deep brain stimulation of the ventral capsule/ventral striatum and experienced reward in two depressed smokers. Presented at the 16th annual meeting for the Society for Research on Nicotine and Tobacco, Baltimore, MD, 2009.
- A73. Walters, C., Carpenter, L.L., Price, L.H., and **Tyrka, A.R.** Association of indices of the metabolic syndrome with altered cortisol responses to neuroendocrine challenge. 17th Annual Research Celebration, Rhode Island Hospital, Providence, RI. October, 2009.
- 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.

- A74. **Tyrka, A.R.**, Price, L.H., Walters, C., Anderson, G.M., and Carpenter, L.L. Hypothalamic-pituitary-adrenal axis activity and indices of the metabolic syndrome. Annual Meeting of the American College of Neuropsychopharmacology, December, 2009.
- A76. Carpenter, LL, **Tyrka, AR**, Geraciotti, TD, Shattuck, TT, and Price, LH. Diminished cortisol response to stress in healthy adults reporting physical abuse. Annual Meeting of the American College of Neuropsychopharmacology, December, 2009.
- A77. **Tyrka, A.R.**, Price, L.H., Walters, C., Anderson, G.M., and Carpenter, L.L. Indices of the metabolic syndrome in healthy adults: Associations with hypothalamic-pituitary-adrenal axis function. Annual Meeting of the Society of Biological Psychiatry, May, 2010.
- A78. Carpenter, L.L., Shattuck, T.T., Tyrka, A.R., Geraciotti, T.D, and Price, L.H. Childhood physical abuse is associated with dampened cortisol stress response in adulthood. Annual Meeting of the Society of Biological Psychiatry, May, 2010.
- A79. Shea, M.T., Tyrka, AR, Reddy, M, and Sevin, E. Psychosocial Risk Factors for PTSD in National Guard and Reserve Veterans Following War-Zone Deployment. 44th annual conference of the Association for Behavioral and Cognitive Therapies, San Francisco, CA, 2010.
- A80. Tyrka, A.R., Price, L.H., Marsit, C., Carpenter, L.L. Methylation of leukocyte glucocorticoid receptor in healthy adults: Associations with childhood parenting experience. Epigenetics, October, 2010.
- A81. Tyrka, A.R., Price, L.H., Gelernter, J., Walters, C., Carpenter, L.L. BDNF Val/Met polymorphism interacts with early-life stress to predict HPA axis function. American College of Neuropsychopharmacology, December, 2010
- A82. Tyrka, A.R., Lee, J.K., Graber, J.A., Clement, A.M., Kelly, M.M., DeRose, L.M., Warren, M.P., Brooks-Gunn, J. Neuroendocrine predictors of behavioral adjustment in boys: Longitudinal follow-up of a community sample. Society for Research in Child Development, March, 2011.
- A83. Tyrka, AR, Reddy, MK, Burgers, DE, Lee, JK, McGeary, J, Sevin, E, Carpenter, LL, Price, LH, and Shea, MT. War-Zone Deployment: Stress, Neurobiology, and PTSD Outcomes. Fourteenth Annual Research Symposium on Mental Health Sciences, Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, March, 2011.
- A84. Philip, N.S., Sweet, L.H., Tyrka, A.R., Niaura, R., Price, L.H., and Carpenter, L.L. Effect of early life stress on the default network. To be presented at the Annual Meeting of the Society of Biological Psychiatry, May 2011.
- A85. Tyrka, A.R., Price, L.H., Marsit, C., Walters, O.K., Wilkinson, C.W., and Carpenter, L.L. Epigenetic modulation of leukocyte glucocorticoid receptor in healthy adults: Effects of childhood parenting experiences. To be presented at the Annual Meeting of the Society of Biological Psychiatry, May 2011.

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.
5. "Trauma and Psychopathology: Psychosocial and Biological Factors Influencing Risk and Resilience." Second Annual Joint Conference Butler Hospital and Family Service of Rhode Island, 3/24/06, Regional Presentation.
6. "Risk for Major Depression: Genes, Stress, and the HPA Axis," American Psychiatric Association 159th Annual Meeting, Toronto, May, 2006, National Presentation.
7. "Current Research and Significance of Childhood Trauma: Effects on Adulthood" . Women and Infants Hospital Annual Women's Health Conference, 5/15/07, Regional Presentation.
8. "Stress Sensitivity and Risk for Psychopathology: Genes, Experience and HPA Axis Function." Distinguished Faculty Speaker, Twelfth Annual Brown University Research Symposium, March, 2008, Regional Presentation.
9. "Corticotropin releasing hormone receptor (CRHR1) polymorphisms interact with early life stress to influence the cortisol response to the Dex/CRH test: Preliminary findings." Paper presented at the Annual Meeting of the Society of Biological Psychiatry, May, 2008, National Presentation.
10. "Neurobiology of Anxious Depression." American Psychiatric Association 162nd Annual Meeting, San Francisco, May 2009, National Presentation.
11. "Depression and Bipolar Disorder: Ask the Doctor Panel" Depression and Bipolar Support Alliance National Conference, September, 2009, National Presentation.
12. "Alternative Treatments: Evaluating Your Options" Depression and Bipolar Support Alliance National Conference, September, 2009, National Presentation.
13. "Genetics of Mental Health Outcomes in Relation to Childhood Maltreatment" NIMH Workshop: Child Maltreatment and Trauma: Integrating Biological, Cognitive and Social Trajectories of Development, Bethesda, MD, August, 2010, National Presentation.

14. "Gene–Environment Interactions – Role in Depressive and Anxiety Disorders" European College of Neuropsychopharmacology, Amsterdam, August 2010, International Presentation.
15. "Exposure to Violence in Childhood: Neurobiology of the Stress Response" Butler Hospital / Family Service of Rhode Island 6th Annual Professional Education Lecture, March, 2011, Regional Presentation.
16. "Childhood Adversity and Leukocyte Telomere Shortening: Effects of Early Stress on Cellular Aging" paper invited for accepted symposium entitled "Cell Aging and Telomere Attrition in Major Depression," To be presented at the Annual Meeting of the Society of Biological Psychiatry, May, 2011, National 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
6. Medtronic, Inc., "Electrical Stimulation of the Anterior Limb of the Internal Capsule to Treat Major Depressive Disorder," role: **Co-Investigator**, 10/02-9/04, \$315,000.
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.
8. Pfizer, Inc. "Sertraline Treatment and Cortisol Response to the DEX/CRH Test", Investigator-Initiated, role: **Co-Investigator**, 1/04-11/06, \$300,684.
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
10. UCB Pharma, Inc. "Keppra Treatment and Cortisol Response to the DEX/CRH Test in Healthy Subjects," Investigator-Initiated, role: **Co-Investigator**, 6/04-5/07, \$111,624.
11. NCCAM/NIMH AT001742, "Double-blind, placebo-controlled study of SAME vs. escitalopram in MDD," role: **Study Physician**, 4/04 - 3/09, \$1,087,938.

12. United States Department of Defense, "Biomarkers of risk for post-traumatic stress disorder (PTSD)," role: **Principal Investigator**, 4/01/07-4/01/10, \$276,422.
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-
15. R01 MH0687670 "DEX/CRH Response: Mood/Anxiety Disorder Endophenotype? Phase 2." role: **Co-Investigator**, 12/08-11/13, \$3,514,780.
16. R01 MH083704 "Childhood Maltreatment: Biomarkers of Risk and Resilience," role: **Principal Investigator**, 12/09-11/14, \$2,863,342
17. R01 NR012005 "RCT of Hatha Yoga for Persistent Depression," role: **Co-Investigator**, 2/11 - 01/15, \$1,718,041
18. R21 MH091508 "Childhood Maltreatment: Epigenetic Modulation of the Glucocorticoid Receptor," role: **Principal Investigator**, 4/08/11-3/31/13, \$393,156.

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

Supervisor, Brown University Neuroscience Concentrator senior student Independent Research Project 2008-2009 (C. Schepker, BA)

HOSPITAL TEACHING ROLES

Supervisor/preceptor, 3rd- and 4th-year Brown medical student clerks, 2003-2007

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

Doctor-on-call supervisor, Butler Hosp. Patient Assessment Service, 2003-present.

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