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

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14. ABSTRACT The objective of this proposal is to study genetic and neuroendocrine biomarkers of risk in a carefully assessed population of military personnel who have recently returned from war zones. The target sample includes 300 men and women who have recently returned from hazardous deployment and are undergoing a comprehensive assessment of symptoms and stressors in a related 12-month longitudinal study. To date, we have enrolled 125 subjects. Samples of saliva have been obtained from all 125 enrolled subjects for analysis of DNA and candidate genes. Cortisol samples have been obtained from 96 of these subjects. Hormone and genetic data will be used to predict the development of PTSD and chronic PTSD. In addition, interactions of these biomarkers with trauma severity and other stressors as well as social supports will be examined.					
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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

This year we consented 125 subjects who were eligible for the study and collected genetics samples on all of them. We received salivary cortisol back from 96 subjects this year. All specimens have been catalogued, processed, and stored. All collection materials have been ordered. We renewed our IRB approval. We plan to conduct assays and analyses in years two and three of the grant.

Key Research Accomplishments

Consented 125 subjects
Collected genetic samples on a 125 subjects
Collected salivary cortisol on 96 subjects
Processed and stored all specimens
Renewed IRB approval

Reportable Outcomes

N/A

Conclusion

Recruitment and collection of genetic and salivary cortisol specimens has been proceeding according to timeline.

References

N/A

Appendix

Dr. Tyrka's CV is attached.

Supporting Data

N/A

CURRICULUM VITAE
AUDREY R. TYRKA, M.D., PH.D.

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EDUCATION

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

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 Medical Scientist Training Program

1994-1999 NIMH 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 Outstanding Teaching Award in General Psychiatry, The Warren Alpert Medical School of Brown University, Department of Psychiatry and Human Behavior

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-

OTHER APPOINTMENTS

Advisory Board Member, Acta Psychiatrica Scandinavica, 2007-

Director, Trainee Advisory Board, Acta Psychiatrica Scandinavica, 2007-

Reviewer, Special Emphasis Panel “NIMH Centers for Pediatric Mental Health.” ZMH1-ERB-A-05

Reviewer, Special Emphasis Panel Department of Defense PTSD/TBI Post Traumatic Stress Disorder
Intramural #2

Ad Hoc Reviewer: American Journal of Psychiatry
Biological Psychiatry
Bipolar Disorders
Developmental Psychobiology
European Neuropsychopharmacology
Journal of Abnormal Psychology
Journal of Adolescent Health
Journal of Affective Disorders
Molecular Psychiatry
Neuropsychopharmacology
Psychological Medicine
Psychoneuroendocrinology
Psychopharmacology
Psychophysiology

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

UNIVERSITY COMMITTEES

Brown Medical School: Medical Curriculum Committee, Subcommittee on Years 3 and 4, 2004-

MEMBERSHIPS IN SOCIETIES

American Psychiatric Association 1989-

Rhode Island Psychiatric Society, 2004-

Society of Biological Psychiatry, 2005-

American College of Neuropsychopharmacology Associate Member, 2007-

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.
3. Weller, A., Corp, E. S., **Tyrka, A.**, Ritter, R. C., Brenner, L., Gibbs, J., and Smith, G. P. Trypsin inhibitor and maternal reunion increase plasma cholecystokinin in neonatal rats. Peptides, 13(5): 939-941, 1992.
4. **Tyrka, A.**, Gayle, C. and Smith, G. P. Raclopride decreases sucrose intake of rat pups in independent ingestion tests. Pharmacology Biochemistry & Behavior, 43(3):863-869, 1992.
5. Miesner, J., Smith, G. P., Gibbs, J., and **Tyrka, A.** Intravenous infusion of CCK-A receptor antagonist increases food intake in rats. American Journal of Physiology, 262(2):R216-R219, 1992.
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.
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8. **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.
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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.

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13. **Tyrka, A.R.**, Carpenter, L.L., McDougle, C.J., Kirwin, P.D., Owens, M.J., Nemeroff, C.B., Strong, D.R., and Price, L.H. Increased CSF corticotropin-releasing factor during tryptophan depletion in healthy adults. Biological Psychiatry, 56, 531-534, 2004.
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.
15. Carpenter, L.L., Milosavljevic, N., Schechter, J.M., **Tyrka, A.R.**, and Price, L.H. Augmentation with open-label atomoxetine for partial or nonresponse to antidepressants. Journal of Clinical Psychiatry, 66, 1234-8, 2005.
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20. 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.
21. 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.
22. Carpenter, L.L., Bayat, L., Moreno, F., Kling, M.A., Price, L.H., **Tyrka, A.R.**, Kinkead, B., Owens, M.J., and Nemeroff, C.B. Decreased cerebrospinal fluid concentrations of substance P in treatment resistant

depression and lack of alteration after acute adjunct vagus nerve stimulation therapy. Psychiatry Research, 157, 123-129, 2008.

23. 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. Journal of Behavior Therapy and Experimental Psychiatry, 39, 87-98, 2008.
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28. **Tyrka, A.R.**, Wier, L.M., Price, L.H., Anderson, G.M., Wilkinson, C.W., and Carpenter, L.L. Childhood Parental Loss and Pituitary-Adrenal Response to the Dexamethasone/Corticotropin-Releasing Hormone Test in Healthy Adults. Biological Psychiatry, in press.
29. 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. Long-term outcome of deep brain stimulation for highly resistant depression, Biological Psychiatry, in press.
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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.
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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.
5. **Tyrka, A.R.**, Wyche, M.C.. Anxiety Disorders. In K.A. McGarry and I. Tong (Eds), *5-Minute Consult Clinical Companion to Women's Health*, Philadelphia: Lippincott Williams & Williams, pp. 25-27, 2007.

OTHER NON PEER REVIEWED PUBLICATIONS

- 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.

PUBLICATIONS SUBMITTED OR IN PREPARATION

1. Carpenter, L.L., Carvalho, J., Kelly, M.M., **Tyrka, A.R.**, and Price, L.H. Does a history of childhood maltreatment influence recall of responses to a psychosocial stress task? Submitted to Child Abuse and Neglect, 10/1/07.
2. **Tyrka, A.R.**, Kelly, M.M., Graber, J.A., Lee, J.A., Warren, M.P., and Brooks-Gunn, J Behavioral Adjustment in a Community Sample of Boys: Links with Basal and Stress-Induced Salivary Cortisol Concentrations. In preparation.

3. **Tyrka, A.R.**, Kelly, M.M., Graber, J.A., Ross, N.S., Warren, M.P. and Brooks-Gunn, J. Neuroendocrine Predictors of Behavioral Adjustment in Boys: A Prospective Longitudinal Study of a Community Sample. In preparation.
4. **Tyrka A.R.**, Price, L.H., Gelernter, J., Anderson, G., Carpenter, L.L. Corticotropin Releasing Hormone Receptor Gene Polymorphisms, Reported Childhood Maltreatment, and HPA Axis Function. In preparation.

ABSTRACTS

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- 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.**, Schecter 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**, Schecter 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.**, Schecter, 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.
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- 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 DEX/CRH Test in Healthy Adults. Ninth Annual Brown University Research Symposium, March 2005.
- 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. 13th Annual Research Celebration, Rhode Island Hospital, 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. 13th Annual Research Celebration, Rhode Island Hospital, 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. 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
- A47. **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.
- 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.**, Friebs, 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., Friebs, 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. Tyrka, A.R. biological abstract
- A65. Carpenter et al. sobp
- A66. 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.

INVITED PRESENTATIONS

1. "Psychotic Depression." Butler Hospital Case Conference Series, 2/26/04, Regional Presentation.
2. "New Views on Women and Depression." Women and Infants Hospital Annual Women's Health Conference, 1/15/05, Regional Presentation.
3. "Risk for Depression: It's Nature *and* Nurture." Academic Meeting of the Butler Hospital Board of Trustees, 3/22/05, Regional Presentation.
4. "Sensitivity to Stress and Risk for Depression." Academic Presentation to the Butler Hospital Staff Association, 4/7/05, Regional Presentation.
5. "Clinical Psychiatry: Diagnosis and Management." Lecturer for Falcon Reviews, 6/05-5/06, National Presentation.
6. "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.
7. "Risk for Major Depression: Genes, Stress, and the HPA Axis," American Psychiatric Association 159th Annual Meeting, Toronto, May, 2006, National Presentation.
8. "Current Research and Significance of Childhood Trauma: Effects on Adulthood" . Women and Infants Hospital Annual Women's Health Conference, 5/15/07, Regional Presentation.
9. "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.

GRANTS

1. 5 F30 MH10819-03 Predoctoral National Research Service Award, "Neuropsychological Indicators of Risk for Schizophrenia," Principal Investigator, 9/94-5/00.
2. NARSAD (Young Investigator Award), "Hypothalamic-Pituitary-Adrenal Function in Adults with a History of Early Life Stress," Principal Investigator; 6/03-5/05, \$60,000.
3. Janssen Pharmaceutica Faculty Development Award in Psychopharmacology, 5/18/03, \$25,000.
4. RSGPB PBP-103382 American Cancer Society, "Improving Smoking Cessation in Smokers with Depressive Symptoms", role: study physician, 7/02-6/04
5. Medtronic, Inc., "Electrical Stimulation of the Anterior Limb of the Internal Capsule to Treat Major Depressive Disorder," Co-Investigator, 10/02-9/04, \$315,000.

6. 1K23MH067947-1A1 Mentored Patient-Oriented Research Career Development Award, “Risk for Depression, Stress, and Neuroendocrine Function,” Principal Investigator; 12/03-11/08, \$905,000.
7. Pfizer, Inc. “Sertraline Treatment and Cortisol Response to the DEX/CRH Test”, Investigator-Initiated, Co-Investigator, 1/04-11/06, \$300,684.
8. 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,” Co-Investigator, 7/04-6/05, \$40,000
9. UCB Pharma, Inc. “Keppra Treatment and Cortisol Response to the DEX/CRH Test in Healthy Subjects,” Investigator-Initiated, Co-Investigator, 6/04-5/07, \$111,624.
10. NCCAM/NIMH AT001742-01, "Double-blind, placebo-controlled study of SAME vs. escitalopram in MDD," Co-Investigator, 4/04 - 3/09, \$1,087,938.
11. United States Department of Defense, “Biomarkers of risk for post-traumatic stress disorder (PTSD),” Principal Investigator, 4/07-4/10, \$276,422.
12. R01 MH0687670-01 “DEX/CRH Response: Mood/Anxiety Disorder Endophenotype? Phase 2.” Co-Investigator, 12/08-11/13, \$3,514,780, pending.
13. R01 MH083704-01 “Childhood Maltreatment: Biomarkers of Risk and Resilience.” Principal Investigator, 4/09-3/14, pending.
14. R01 “Onset and Maintenance of PTSD in Iraq Veterans: A Longitudinal Study of Psychosocial and Biological Risk Factors.” Co-Principal Investigator, 7/09-6/14, \$3,907,421, pending.

UNIVERSITY TEACHING ROLES

Psychiatric Interviewing, PGY 1 Residents, 2003-

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

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

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

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

Research Supervisor, Post-Doctoral Psychology Fellows 2004-2007

Dissertation Committee Member, Pre-Doctoral Psychology Student 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 2007-2008

Supervisor, Brown University Neuroscience Concentrator senior student Independent Research Project 2008-

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-.

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