Syllabus

PSYC GU4493 Stress and the Brain

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I. Bulletin description

PSYC GU4493. Stress and the Brain (seminar).

4 pts.

Office hours: *By appointment (Please email to arrange)*

Prerequisites: Basic background in neurobiology (for instance PSYC 1010, 2430, 2450, 2460, 2470, 2480, or GU4498) and the instructor's permission.

This course will use clinical studies and experimental research on animals to understand the impact of stress during various periods of development on brain function and behavior. We will address the long- and short-term consequences of stress on cognition, emotion, and ultimately psychopathology through investigating how various stressors can induce neurobiological and behavioral outcomes through genetic, epigenetic, and molecular mechanisms in the brain.

II. Full course description:

Stress is a complex biological process that has long-term and lasting effects on brain function and behavior. Experiencing stress during crucial timepoints in development or even as a mature adult can have diverse consequences for various types of neurobiological outcomes and psychopathology. This course is designed to introduce students to a well-established field of stress research that is rapidly evolving with new techniques and concepts within the field of neuroscience.

The first part of the course will familiarize students with literature and techniques used in the stress neurobiology field and provide a base understanding of the HPA axis and stress response in both humans and animals. The course will also include an investigation into the genetic underpinnings of stress susceptibility and resilience that have been elucidated in human and animal literature and introduce students to the novel field of epigenetics, in which environment and genes work in concert to regulate brain function and behavior. With a thorough understanding of stress and genetics/epigenetics, the next part of the course will then begin to characterize the effects of developmental stress on various realms of behavior, including learning, memory, and emotion, including aberrant behavior leading to psychopathology and how these changes can be altered with interventions or treatments.

The topics of the course will be introduced through overview lectures given by the instructor, followed by journal article presentations by students. The readings will consist of review articles and primary research articles, and will draw upon examples from both human and experimental/animal research. In addition to several classic papers to lay the foundation for the neurobiology of stress, the readings emphasize the most contemporary research and understanding of each topic area. The whole class is expected to have read the journal articles in advance and participate in discussion.

Finally, students will have the opportunity to explore and demonstrate a detailed understanding of a topic of their choice relevant to Stress and the Brain through a final paper.

III. Rationale for giving the course:

This course is designed to familiarize the students with basic and more advanced concepts of a well-established yet rapidly evolving field of stress neurobiology. Neurobiological effects of stress have been well-characterized in the major neuroscience-related areas, such as studies of neurodevelopment, animal models of behavioral and psychiatric disorders, studies on learning and memory, neuroendocrinology, psychopharmacology, and psychiatric epidemiology. The first part of the course will cover the basics of stress and the HPA axis as well as laboratory techniques used to investigate such topics, and will prepare students for more specific topics as well as enable them to critically evaluate stress literature. The second part of the course will provide a synthesis on the role of stress in regulating aberrant brain function and its contribution to the development of psychopathology. The readings will consist of both review articles and primary research articles. Throughout the course, we will explore the landmark studies that paved the way for the establishment of the field.

The primary goal of this course is for students to gain in-depth understanding of stress neurobiology as it pertains to the fields of Psychology and Neuroscience, through introduction of twelve applied topics. In order to aid in *remembering*, *understanding*, and *applying* the knowledge gained from the readings and lectures, students will be encouraged to ask questions and participate in discussion throughout the lectures and journal article presentations. Through presentation of journal articles and leading class discussion, students will gain a detailed understanding of a topic, *draw connections* to other course topics, *evaluate* the research, and *create* their own framework for presenting it to the class. The final literature review paper on a topic of the student's choice will further enable students to *synthesize* information from multiple sources, critically *evaluate* it as a whole, and *author* their own review of the sub-field.

More broadly, students will learn how to read primary scientific research articles, think critically, synthesize information, and write organized, evaluative papers. These skills are necessary to be informed citizens in our increasingly technological society, and in all chosen post-graduate disciplines and careers.

The Psychology Program Goals that will be advanced in this seminar (see http://www.columbia.edu/cu/psychology/dept/ugrad/goals.html) include 1. Knowledge

base; 2. Research methods; 4. Critical thinking; 5. Values in psychology; 6. Application of psychology; 7. Communication skills—written; 8. Communication skills—oral; 9. Information and technological literacy.

PSYC GU4493 is an advanced seminar, designed particularly for graduate students, for advanced undergraduates who are majoring in Psychology or in Neuroscience and Behavior, and for students participating in the Psychology Postbac Certificate Program. These students will have priority in registration, followed by junior majors followed by non-majors. While not required as pre-requisites, the seminar will be well suited to students who have completed two or more lecture courses beyond UN1001, such as UN1010 (Mind, Brain, and Behavior), UN2215 (Cognition and the Brain), UN2430 (Cognitive Neuroscience), UN2450 (Behavioral Neuroscience), UN2460 (Drugs and Behavior), UN2470 (Fundamentals of Human Psychology) or UN2220 (Cognition: Memory and Stress).

<u>It fulfills the following degree requirements:</u>

• For Psychology Graduate Students, with prior DGS approval, PSYC GU4493 could potentially apply toward the “two seriously graded seminars” requirement of the Master’s degree.

• For the Psychology major or concentration in the College and in G.S. and for the Psychology Postbac Certificate, GU4493 meets the Group II (Psychobiology and Neuroscience) distribution requirement and the seminar requirement.

• For the Neuroscience and Behavior joint major, GU4493 will fulfill the P5 requirement: “one advanced psychology seminar from a list approved by the Psychology Department advisor to the program.”

Graduate students, and undergraduate students who are majoring in Psychology or in Neuroscience and Behavior, and postbac Psychology certificate students will have priority in registration.

V. Course requirements and grading:

Grades:

25% Participation in journal article discussions and in-class activities

25% Presentation of original research journal article

10% Topic and bibliographic citations for literature review

40% Literature review paper

Participation (25%: 50 points): All students are expected to participate in weekly discussions. To effectively participate, it is expected that all students read the assigned articles in advance of the class. Each student should come prepared with at least one substantive question for the original research article(s) being presented. If medical or other emergencies prevent students from attending a class, an email to Dr. Blaze is required *in advance of class* to explain the absence. Each student is allowed one absence without penalty, and each additional absence will result in a 5-point deduction from the participation grade for the semester.

Presentation (25%: 50 points): Each student will present 1-2 original research articles throughout the semester and lead the class discussion. Journal articles are pre-selected by the instructor. Students are expected to walk the class through the background/rationale, methods, results, and discussion, including what is novel, and potential pitfalls/misinterpretation, and possible future directions. Students should try to engage class in discussion through questions. Each presentation should be ~30m.

Topic and references (10%: 20 points): All students are required to select a topic relevant to Stress and the Brain for a final literature review paper. The topic may expand on a topic presented in the course, may be a relevant topic not covered within the course, or may synthesize information across areas of the course. The student will submit the topic/title, a short rationale for its selection, and at least 10 FULL citations (**APA format**) for their proposed literature review paper on or before the class meeting on **[DUE DATE]** with no exceptions. Each day the assignment is late will result in a 3-point deduction (assignment is worth ten points total). Topics will be approved by the instructor, and in some instances the instructor may suggest ways to broaden or focus the topic as appropriate. For the citations: review papers are acceptable but should be kept to a minimum (Maximum of 2 reviews).

Literature review paper (40%: 80 points): All students will write a substantial, *original* 8-12 page paper (double spaced, not including references) on the chosen topic. At least 15 citations in APA format must be included (with a total of 3 reviews maximum). The paper will be submitted on the final day of class, with no exceptions. Each additional day that the paper is late will result in a 10-point penalty. **[DUE DATE]**

Course topics and assigned readings (PDFs of all articles will be available through CourseWorks/Canvas):

Topic: Individual differences in stress reactivity: susceptibility vs. resilience

Review: Russo et al. (2012) Neurobiology of resilience. *Nature Neuroscience*, 15(11):1475-1484.

Caspi et al. (2003) Influence of Life Stress on Depression: Moderation by a Polymorphism in the 5-HTT Gene. *Science*, 301: 386-389.

Vialou et al. (2010) **Δ**FosB in brain reward circuits mediates resilience to stress and antidepressant responses. *Nature Neuroscience*, 13(6): 745-752.

Topic: Programming effects of early-life stress on stress responsivity

Review: Chen and Baram (2016) Toward Understanding How Early-Life Stress Reprograms Cognitive and Emotional Brain Networks. *Neuropsychopharmacology*, 41: 197-206.

Ivy et al. (2010) Hippocampal Dysfunction and Cognitive Impairments Provoked by Chronic Early-Life Stress Involve Excessive Activation of CRH Receptors. *Journal of Neuroscience*, 30(39): 13005-13015.

Tottenham et al. (2010) Prolonged institutional rearing is associated with atypically large amygdala volume and difficulties in emotion regulation. *Developmental Science*, 13(1): 46-61.

Topic: Epigenetics of stress: gene-environment interactions through DNA methylation: Developmental stress (prenatal and early-life)

Review: Blaze and Roth (2015) Evidence from clinical and animal model studies of the long-term and transgenerational impact of stress on DNA methylation. *Seminars in Cell and Developmental Biology*, 43: 76-84. **Pages 76-79 only**

Roth et al. (2009) Lasting Epigenetic Influence of Early-Life Adversity on the BDNF gene. *Biological Psychiatry*, 65: 760-769.

McGowan et al (2009) Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. *Nature Neuroscience*, 12(3): 342-348.

Topic: Epigenetics of stress: gene-environment interactions through DNA methylation: Adult stress

Review: Blaze and Roth (2015) Evidence from clinical and animal model studies of the long-term and transgenerational impact of stress on DNA methylation. *Seminars in Cell and Developmental Biology*, 43: 76-84. **Pages 79-80 only**

Uchida et al. (2010) Epigenetic Status of Gdnf in the Ventral Striatum Determines Susceptibility and Adaptation to Daily Stressful Events. *Neuron*, 69: 359-372.

Unternaehrer et al (2012) Dynamic changes in DNA methylation of stress-associated genes (OXTR, BDNF) after acute psychosocial stress. *Translational Psychiatry*, 2: e150.

Topic: PTSD

Review: Daskalakis et al. (2018) Recent Genetic and Epigenetics Approaches to PTSD. *Current Psychiatry Reports*, 20(30): 1-12.

Knox et al. (2016) Neural circuits via which single prolonged stress exposure leads to fear extinction retention deficits. *Learning & Memory*, 23: 689-698.

Vinkers et al. (2019) Successful treatment of post-traumatic stress disorder reverses DNA methylation marks. *Molecular Psychiatry*.

Topic: Stress and neuronal plasticity/learning and memory

Review: McEwen (1999) Stress and hippocampal plasticity. *Annual Review of Neuroscience*, 22: 105-22.

Bagot et al. (2009) Maternal care determines rapid effects of stress mediators on synaptic plasticity in adult rat hippocampal dentate gyrus. *Neurobiology of Learning and Memory*, 92: 292-300.

Nasca et al. (2015) Stress dynamically regulates behavior and glutamatergic gene expression in hippocampus by opening a window of epigenetic plasticity. *Proceedings of the National Academy of Science*, 112(48): 14960-14965.

Topic: Sex differences in stress responses

Review: Bale and Epperson (2015) Sex differences and stress across the lifespan. *Nature Neuroscience*, 18(10): 1413-1420.

Hodes et al. (2015) Sex Differences in Nucleus Accumbens Transcriptome Profiles Associated with Susceptibility versus Resilience to Subchronic Variable Stress. *Journal of Neuroscience*, 35(50): 16362–16376.

Shepard et al. (2016) Sensitivity of the Prefrontal GABAergic System to Chronic Stress in Male and Female Mice: Relevance for Sex Differences in Stress-related Disorders. *Neuroscience*, 332: 1-12.

Topic: Gut-brain connection and stress

Review: Cryan and Dinan (2012) Mind-altering microorganisms: the impact of the gut microbiota on brain and behavior. *Nature Reviews Neuroscience*, 13: 701-712.

Desbonnet et al. (2010) Effects of the Probiotic *Bifidobacterium Infantis* in the Maternal Separation Model of Depression. *Neuroscience*, 170: 1179-1188.

Jasarevic et al. (2015) Alterations in the Vaginal Microbiome by Maternal Stress Are Associated With Metabolic Reprogramming of the Offspring Gut and Brain. *Endocrinology*, 156(9): 3265-3276.

Topic: Stress and the immune system

Review: Hodes et al. (2015) Neuroimmune mechanisms of depression. *Nature Neuroscience*, 18(10): 1386-1393.

Goshen et al. (2008) Brain interleukin-1 mediates chronic stress-induced depression in mice via adrenocortical activation and hippocampal neurogenesis suppression. *Molecular Psychiatry*, 13: 717-728.

Wang et al. (2018) Epigenetic modulation of inflammation and synaptic plasticity promotes resilience against stress in mice. Nature Communications, 9:477.

Topic: Effects of stress on telomere length

Review: Lindqvist et al. (2019) Psychiatric disorders and leukocyte telomere length: Underlying mechanisms linking mental illness with cellular aging. *Neuroscience and Biobehavioral Reviews*, 55: 333-364.

Asok et al. (2014) Infant-Caregiver Experiences Alter Telomere Length in the Brain. *PLOS One*, 9:7.

Lu et al. (2019) Perceived racism in relation to telomere length among African American women in the Black Women's Health Study. *Annals of Epidemiology*, 36: 33-39.

Topic: Transgenerational inheritance of stress phenotypes

Review: Yehuda et al. (2018) The public reception of putative epigenetic mechanisms in the transgenerational effects of trauma. *Environmental Epigenetics*, 1-7.

van Steenwyk et al. (2018) Transgenerational inheritance of behavioral and metabolic effects of paternal exposure to traumatic stress in early postnatal life: evidence in the 4th generation. *Environmental Epigenetics*, 1-8.

Yehuda et al. (2016) Holocaust Exposure Induced Intergenerational Effects on FKBP5 Methylation. *Biological Psychiatry*, 80: 372-380.

Topic: Behavioral interventions for stress-induced phenotypes

Review: Davidson and McEwen (2012) Social influences on neuroplasticity: stress and interventions to promote well-being. *Nature Neuroscience*, 15: 689-695.

Schloesser et al. (2010) Environmental enrichment requires adult neurogenesis to facilitate the recovery from psychosocial stress. *Molecular Psychiatry*, 15: 1152-1163.

Mul et al. (2018). Voluntary wheel running promotes resilience to chronic social defeat stress in mice: a role for nucleus accumbens ΔFosB. *Neuropsychopharmacology,* 43: 1934-1942.

VI: Other

Academic honesty

As members of this academic community, we are responsible for maintaining the highest level of personal and academic integrity: "[E]ach one of us bears the responsibility to participate in scholarly discourse and research in a manner characterized by intellectual honesty and scholarly integrity.… The exchange of ideas relies upon a mutual trust that sources, opinions, facts, and insights will be properly noted and carefully credited. In practical terms, this means that, as students, you must be responsible for the full citations of others' ideas in all of your research papers and projects… [and] you must always submit your own work and not that of another student, scholar, or internet agent" (from the Columbia University Faculty Statement on Academic Integrity. All allegations of academic misconduct will be immediately referred to the office of Student Conduct and Community Standards.

https://www.college.columbia.edu/faculty/resourcesforinstructors/academicintegrity/statement).

Plagiarism – whether intentional or inadvertent – is a serious violation of academic integrity. If you have any questions about what constitutes plagiarism and/or how to properly cite sources, please come to me. I am more than happy to help. Similarly, if you put yourself in a situation, e.g., starting an assignment very late, in which you think your best option might be to cut some corners, see me. It is far better to have a few points deducted from a paper than to compromise your academic integrity and potentially put your academic standing in jeopardy.

Disability Services

Students with special needs who may require classroom/test accommodations should make an appointment with me before or during the first week of class. You should also contact the Office of Disability Services (ODS) in Lerner Hall before the start of the course to register for these accommodations. The procedures for registering with ODS can be found at http://health.columbia.edu/services/ods or by calling (212) 854-2388.

Writing Center

I encourage you to visit the Writing Center, where you can receive free individual consultations on your writing at any stage in the writing process, including brainstorming. Writing consultants work with all members of the Columbia community on any academic or nonacademic writing. You can make an appointment and view drop in hours on their website [www.college.columbia.edu/core/uwp/writing-center].