

BISC 462: Seminar in Neurobiology The Neurobiology of Dopamine: from Reward Learning to Motor Control Units: 2 Spring 2024: Tuesday 3:00-4:50 pm Location: HNB 107

Instructor: Lauren McElvain mcelvain@usc.edu Office: HNB 209 Office Hours: by appointment

Prerequisite: BISC 421 or equivalent course.

Course Overview

This course examines the dopamine system from cellular, circuit, behavioral, and clinical perspectives. Each week, different students will present a primary research article and will be responsible for providing a brief background, explaining the technology used in the paper, and interpreting the experiments. In addition, the students will lead a discussion on the relative merits of the paper. Students will develop an upstanding of the diverse functions of dopamine in the brain and an appreciation for the central role of neuromodulation in neural circuit function, plasticity, and disease.

The following topics will be discussed:

Date		Торіс
01.9	Course introduction	
01.16	Lecture	
01.23	Lecture	
01.30	Presentation	Neuroanatomy of dopaminergic neurons
02.06	Student presentation	Dopamine and reward prediction
02.13	Student presentation	Learning and plasticity
02.20	Student presentation	Mechanisms of addiction
02.27	Student presentation	Goal-directed behavior and motivation
03.05	Student presentation	Encoding of pain and aversion by dopaminergic neurons
03.12	Spring break	
03.19	Student presentation	Dopamine and motor control: the oculomotor system
03.26	Student presentation	Dopamine and motor control: vigor
04.02	Student presentation	Parkinson's disease as a result of dopaminergic neuron degeneration
04.09	Student presentation	Dopamine in cognition and memory
04.16	Student presentation	The dopamine hypothesis of schizophrenia
04.23	Brief presentations	Group discussion
05.07	No Final	

Provisional Class Schedule

Learning Objectives

By the end of this course, students will be able to outline the various functions of dopamine in the central nervous system. Student will be able to explain and critically assess primary research articles from neurobiology, including experimental results spanning genetic, cellular, electrophysiological, neuroanatomical, and behavioral analyses. The course will enable students to evaluate the technical and conceptual strengths of major hypotheses about dopamine's functions and to appraise the strength of the experimental data underling these hypotheses. Students also will develop a capacity to identify potential new avenues for research.

Grading and expectations

The grade for the course will be determined based on your article presentation (60%), weekly questions (10%), your participation in classroom discussion (30%).

Article presentation

Students will each present a primary research article. Students are expected to provide a brief background, to explain the technical approaches used in the paper, and to lead a discussion on the interpretation of the experiments in the article.

Questions

Before 1:00 pm each Tuesday, each student must email 3 questions about the paper that is being discussed that week to the instructor.

Attendance and Participation

You are expected to attend every class unless you provide a good reason for the absence (e.g. illness, medical school interview, conference presentation, pandemic related issue) that you can document. Students are expected to participate in class by asking the presenter questions about the article and contributing to discussions about the article.

Academic Integrity

The University of Southern California is foremost a learning community committed to fostering successful scholars and researchers dedicated to the pursuit of knowledge and the transmission of ideas. Academic misconduct is in contrast to the university's mission to educate students through a broad array of first-rank academic, professional, and extracurricular programs and includes any act of dishonesty in the submission of academic work (either in draft or final form).

This course will follow the expectations for academic integrity as stated in the <u>USC</u> <u>Student Handbook</u>. All students are expected to submit assignments that are original work and prepared specifically for the course/section in this academic term. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s). Students suspected of engaging in academic misconduct will be reported to the Office of Academic Integrity.

Other violations of academic misconduct include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see the <u>student handbook</u> or the <u>Office of</u> <u>Academic Integrity's website</u>, and university policies on <u>Research and Scholarship</u> <u>Misconduct</u>.

Statement on Academic Conduct and Support Systems

Academic Integrity:

The University of Southern California is a learning community committed to developing successful scholars and researchers dedicated to the pursuit of knowledge and the dissemination of ideas. Academic misconduct, which includes any act of dishonesty in the production or submission of academic work, compromises the integrity of the person who commits the act and can impugn the perceived integrity of the entire university community. It stands in opposition to the university's mission to research, educate, and contribute productively to our community and the world.

All students are expected to submit assignments that represent their own original work, and that have been prepared specifically for the course or section for which they have been submitted. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s).

Other violations of academic integrity include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), collusion, knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university. All incidences of academic misconduct will be reported to the Office of Academic Integrity and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see <u>the student handbook</u> or the <u>Office of</u> <u>Academic Integrity's website</u>, and university policies on <u>Research and Scholarship</u> <u>Misconduct</u>.

Please ask your instructor if you are unsure what constitutes unauthorized assistance on an exam or assignment, or what information requires citation and/or attribution.

Students and Disability Accommodations:

USC welcomes students with disabilities into all of the University's educational programs. <u>The Office of Student Accessibility Services</u> (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and accommodations are determined to be reasonable and appropriate, a Letter of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. More information can be found at <u>osas.usc.edu</u>. You may contact OSAS at (213) 740-0776 or via email at <u>osasfrontdesk@usc.edu</u>.

Support Systems:

<u>Counseling and Mental Health</u> - (213) 740-9355 – 24/7 on call Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

<u>988 Suicide and Crisis Lifeline</u> - 988 for both calls and text messages – 24/7 on call The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline is comprised of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

<u>Relationship and Sexual Violence Prevention Services (RSVP)</u> - (213) 740-9355(WELL) – 24/7 on call

Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

<u>Office for Equity, Equal Opportunity, and Title IX (EEO-TIX)</u> - (213) 740-5086 Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

<u>Reporting Incidents of Bias or Harassment</u> - (213) 740-5086 or (213) 821-8298 Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

<u>The Office of Student Accessibility Services (OSAS)</u> - (213) 740-0776 OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

USC Campus Support and Intervention - (213) 740-0411

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity, Equity and Inclusion - (213) 740-2101

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

<u>USC Emergency</u> - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible. <u>USC Department of Public Safety</u> - UPC: (213) 740-6000, HSC: (323) 442-1200 – 24/7 on call

Non-emergency assistance or information.

<u>Office of the Ombuds</u> - (213) 821-9556 (UPC) / (323-442-0382 (HSC) A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

Occupational Therapy Faculty Practice - (323) 442-2850 or otfp@med.usc.edu

Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.

COVID-19: Students are expected to comply with all aspects of USC's COVID-19 policy.

Disclaimer: It may be necessary to make some changes in the syllabus during the semester.

Course Reading List:

09 January 2024: Class Introduction

16 January 2024: Introductory Lecture 1

23 January 2024: Introductory Lecture 2

30 January 2024: Neuroanatomy of dopaminergic neurons

Beckstead, R. M., et al. (1979). "Efferent connections of the substantia nigra and ventral tegmental area in the rat". <u>Brain Res</u> 175(2): 191-217.

S. M. Williams and P. S. Goldman-Rakic. (1998) "Widespread origin of the primate mesofrontal dopamine system". <u>Cereb Cortex</u> Vol. 8 Issue 4 Pages 321-45

Optional Review Article: Bjorklund, A. and S. B. Dunnett (2007). "Dopamine neuron systems in the brain: an update." <u>Trends Neurosci</u> **30**(5): 194-202.

06 February 2024: Dopamine and reward prediction

Schultz, W., et al. (1993). "Responses of monkey dopamine neurons to reward and conditioned stimuli during successive steps of learning a delayed response task." <u>J</u><u>Neurosci</u> 13(3): 900-913.

Optional Review Article:

Schultz, W. (2000). "Multiple reward signals in the brain." <u>Nat Rev Neurosci</u> 1(3): 199-207.

13 February 2024: Learning and plasticity

Shen, W., et al. (2008). "Dichotomous dopaminergic control of striatal synaptic plasticity." <u>Science</u> 321(5890): 848-851.

Optional Review Articles: Kreitzer, A. C. and R. C. Malenka (2008). "Striatal plasticity and basal ganglia circuit function." <u>Neuron</u> **60**(4): 543-554.

Perrin, E. and L. Venance (2019). "Bridging the gap between striatal plasticity and learning." <u>*Curr Opin Neurobiol*</u> **54**: 104-112.

20 February 2024: Mechanisms of addiction

Ma, T., et al. (2018). "Bidirectional and long-lasting control of alcohol-seeking behavior by corticostriatal LTP and LTD." <u>Nat Neurosci</u> 21(3): 373-383.

Optional Review Articles: Kauer, J. A. and R. C. Malenka (2007). "Synaptic plasticity and addiction." <u>Nat Rev Neurosci</u> **8**(11): 844-858. Wise, R. A. and M. A. Robble (2020). "Dopamine and Addiction." <u>Annu Rev Psychol</u> 71: 79-106.

27 February 2024: Goal-directed behavior and motivation

Mohebi, A., et al. (2019). "Dissociable dopamine dynamics for learning and motivation." <u>Nature</u> 570(7759): 65-70

Optional Review Articles:

Wu, Z., et al. (2022). "Pushing the frontiers: tools for monitoring neurotransmitters and neuromodulators." <u>Nat Rev Neurosci</u> **23**(5): 257-274.

Lerner, T. N., et al. (2021). "Dopamine, Updated: Reward Prediction Error and Beyond." <u>Curr Opin Neurobiol</u> 67: 123-130.

05 March 2024: Encoding of pain and aversion by dopaminergic neurons

Menegas, W., et al. (2018). "Dopamine neurons projecting to the posterior striatum reinforce avoidance of threatening stimuli." <u>Nat Neurosci</u> 21(10): 1421-1430.

Optional Research Article:

Poulin, J. F., et al. (2018). "Mapping projections of molecularly defined dopamine neuron subtypes using intersectional genetic approaches." <u>Nat Neurosci</u> 21(9): 1260-1271.

Optional Review Articles:

Verharen, J. P. H., et al. (2020). "Aversion hot spots in the dopamine system." <u>Curr Opin</u> <u>Neurobiol</u> **64**: 46-52.

Poulin, J. F., et al. (2020). "Classification of Midbrain Dopamine Neurons Using Single-Cell Gene Expression Profiling Approaches." <u>Trends Neurosci</u> **43**(3): 155-169.

12 March 2024: Spring Break

19 March 2024: Dopamine and motor control: the oculomotor system

Sato and Hikosaka 2004 Sato, M. and O. Hikosaka (2002). "Role of primate substantia nigra pars reticulata in reward-oriented saccadic eye movement." <u>J Neurosci</u> 22(6): 2363-2373.

Optional Review Article: Hikosaka, O. (2007). "GABAergic output of the basal ganglia." <u>Prog Brain Res</u> **160**: 209-226.

26 March 2024: Dopamine and motor control: vigor

Panigrahi, B., et al. (2015). "Dopamine Is Required for the Neural Representation and Control of Movement Vigor." <u>Cell</u> 162(6): 1418-1430.

Optional Review Article:

Dudman, J. T. and J. W. Krakauer (2016). "The basal ganglia: from motor commands to the control of vigor." <u>Curr Opin Neurobiol</u> **37**: 158-166.

02 April 2024: Parkinson's disease as a result of dopaminergic neuron degeneration

Gonzalez-Rodriguez, P., et al. (2021). "Disruption of mitochondrial complex I induces progressive parkinsonism." <u>Nature</u> 599(7886): 650-656.

Optional Review Article:

Lees, A. J., et al. (2015). "Four pioneers of L-dopa treatment: Arvid Carlsson, Oleh Hornykiewicz, George Cotzias, and Melvin Yahr." <u>Mov Disord</u> **30**(1): 19-36.

09 April 2024: Dopamine in cognition and memory

Williams, G. V. and P. S. Goldman-Rakic (1995). "Modulation of memory fields by dopamine D1 receptors in prefrontal cortex." <u>Nature</u> 376(6541): 572-575.

Wang, Y. and P. S. Goldman-Rakic (2004). "D2 receptor regulation of synaptic burst firing in prefrontal cortical pyramidal neurons." <u>Proc Natl Acad Sci U S A</u> 101(14): 5093-5098.

Optional Review Articles: Ott, T. and A. Nieder (2019). "Dopamine and Cognitive Control in Prefrontal Cortex." <u>Trends</u> <u>Cogn Sci</u> **23**(3): 213-234.

Cools, R. (2019). "Chemistry of the Adaptive Mind: Lessons from Dopamine." <u>Neuron</u> **104**(1): 113-131.

16 April 2024: The dopamine hypothesis of schizophrenia

McCutcheon, R., et al. (2018). "Defining the Locus of Dopaminergic Dysfunction in Schizophrenia: A Meta-analysis and Test of the Mesolimbic Hypothesis." <u>Schizophr</u><u>Bull</u> 44(6): 1301-1311.

Optional Research Article:

Yun, S., et al. (2023). "Antipsychotic drug efficacy correlates with the modulation of D1 rather than D2 receptor-expressing striatal projection neurons." <u>Nat Neurosci</u> 26(8): 1417-1428.

Optional Review Articles:

Kapur, S. and D. Mamo (2003). "Half a century of antipsychotics and still a central role for dopamine D2 receptors." <u>Prog Neuropsychopharmacol Biol Psychiatry</u> **27**(7): 1081-1090.

Howes, O. D., et al. (2017). "The Role of Genes, Stress, and Dopamine in the Development of Schizophrenia." <u>Biol Psychiatry</u> **81**(1): 9-20.

van den Heuvel, M. P., et al. (2019). "Multiscale Neuroscience of Psychiatric Disorders." <u>Biol Psychiatry</u> **86**(7): 512-522.

23 April 2024: No reading