#### **Basic information:**

Faculty: David Silbersweig, MD (dsilbersweig@bwh.harvard.edu)

Chairman Emeritus, Department of Psychiatry **Brigham and Women's Hospital** Stanley Cobb Professor of Psychiatry **Harvard Medical School** 

Administrator: Nellie Andrade nandrade6@bwh.harvard.edu

#### Course description:

Functional brain imaging has revolutionized the study of systems-level behavioral neuroscience and psychiatric disorders, through the ability to localize and characterize distributed brain activity directly associated with perception, cognition, emotion and behavior in disorders where there are not gross brain lesions. This seminar will introduce students to translational neuroimaging methods at the interface of neuroscience, psychology and medicine. It will cover recent and ongoing advances in our understanding of fronto-limbic-subcortical brain circuitry across the range of psychiatric disorders (e.g., mood disorders, anxiety disorders, psychotic disorders, personality disorders, addictions). It will discuss new, emerging biological (as opposed to descriptive) taxonomies and conceptualizations of mental illness and its treatment. It will explore the implications of such knowledge for issues such as consciousness, meaning, free will, emotion, resilience, and religiosity. It will incorporate clinical observations, scientific data and readings, and examine future directions in brain-mind medicine.

#### Course format and requirements:

This is a seminar course and attendance is mandatory. Our class will consist of an informal lectures followed by group discussion. The discussions are robust, and participation is important. The course involves two types of assignments:

- 1. Weekly best questions: To ensure that the stage is set, each student is required to complete a short weekly assignment, called "best questions†(2 pages double spaced maximum). The assignment is based on your choice of two of the readings. The weekly assignment has two parts: one to present your understanding of the reading, and one for you to pose a question, exploring a free choice topic within the theme of the week. That question can be a springboard for class discussion. Uploaded weekly assignments, related to the Thursday class topic/reading, are due Wednesday, the day before class, by 5 pm.
- 2. **A final paper:** A final paper will be on a topic of your interest, incorporating the functional neuroimaging lens of the course. Due to a very short grading deadline, no late submissions will be accepted. Final papers must follow APA guidelines and count 10 pages (not including the title page and the 5 to 15 references). To help you meet the final paper's deadline, we will scaffold the final assignment: you will bring 3 topic ideas to class (for discussion) on week 7; then a 250-word abstract of the paper including 5 references will be due on week 10.
- 3. **Grading:** 
  - Weekly attendance and participation 30%
  - 2. Weekly assignments 40%
  - 3. Final paper 30%

# **Topics and Readings**

(The readings can be found in the "Files and Assignments" tab of the course website)

#### Week 1: Introduction (1/25/24)

### $\textbf{Week 2: What is Neuropsychiatry?} \ (\textbf{Historical, scientific and medical perspectives})$

• Trimble, M (2020). The history and scope of neuropsychiatry. The Oxford Textbook of Neuropsychiatry

• Cummings, J. L., & Mega, M. S. (2003). Introduction. Neuropsychiatry and behavioral neuroscience. Oxford University Press.

 $\underline{https://www.dropbox.com/s/oxs1qbnctajbcmx/Chapter\%201\%20Introduction.\%20Cummings\%20and\%20Mega..pdf?dl=0Links\ to\ an\ external\ site.}$ 

Cummings, J. L., & Mega, M. S. (2003). Neurobiological Basis of Behavior. Neuropsychiatry and behavioral neuroscience. Oxford University Press.

# Week 3: Functional Brain Imaging (context and methods)

• New and emerging imaging techniques for mapping brain circuitry. Pan H, Epstein J, Silbersweig DA & Stern E.

Pan, H., Epstein, J., Silbersweig, D. A., & Stern, E. (2011). New and emerging imaging techniques for mapping brain circuitry. *Brain Research Reviews*, 67(1-2), 226â€"251.

 $\bullet\,$  Neuroimaging in psychiatry: a quarter century of progress. Silbersweig DA and Rauch S.

Silbersweig, David A., and Scott L. Rauch. "Neuroimaging in Psychiatry: A Quarter Century of Progress.†*Harvard Review of Psychiatry*, vol. 25, no. 5, Sept. 2017, pp. 195â€″197

 $\underline{https://www.dropbox.com/s/ucp2y2ufkivz7j1/Neuroimaging\%20in\%20Psychiatry\%20A\%20Quarter\%20Century\%20of\%20Progress.pdf?dl=0Links\ to\ an\ external\ site.}$ 

### Week 4: Behavioral Neuroanatomy

• Neuroanatomical foundations of neuropsychiatry and behavioral neurology. Schmahmann JD. in Neuropsychiatry and Behavioral Neurology, Principles and Practice. Silbersweig D, Safar L, Daffner K, eds. McGraw Hill, 2021.

01\_Silbersweig\_Ch01.pdf (dropbox.com)

• Principles of Behavioral and Cognitive Neurology. Mesulam (Chapter 1: sections 1, 2, 3 10, 13, 15, 20) Marsel Mesulam, Marsel. *Principles of Behavioral and Cognitive Neurology*. (15 Feb 2000) Oxford; New York, Oxford University Press.

Cummings, J. L., & Mega, M. S. (2003). Principles of Neuropsychiatry. Neuropsychiatry and behavioral neuroscience. Oxford University Press.

 $\label{lem:https://www.dropbox.com/s/dmn7jlgwkdngsg9/Chapter%202%20of%20Neuropsychiatry\%20 and \%20 behavioral\%20 neuroscience\%20 Jeffrey\%20 L.\%20 Cummings\%2C\%20 Microbia dl=0$ 

## Week 5: Key developments in cognitive/behavioral/affective/social - neuropsychology-neuroscience

• Networks underpinning emotion: a systematic review and synthesis of functional and effective connectivity. Underwood et al. Neuroimage. 2021.

https://canvas.harvard.edu/courses/128363/files/folder/Course%20Readings?preview=19272820

• The Neuropsychiatric Spectrum of Motivational Disorders. Jane Epstein & David Silbersweig.

Epstein, Jane, and David Silbersweig. "The Neuropsychiatric Spectrum of Motivational Disorders.†*The Journal of Neuropsychiatry and Clinical Neurosciences*, vol. 27, no. 1, 7 Oct. 2016, pp. 7â€″18

 ${\color{blue} https://www.dropbox.com/s/7c82h80do7il0kl/The \%20 Neuropsychiatric \%20 Spectrum \%20 of \%20 Motivational \%20 Disorders.pdf?dl=0}$ 

• The neuroscience of social feelings: mechanisms of adaptive social functioning. Eslinger et al. Neurosci Biobehav Rev. 2021

The neuroscience of social feelings: mechanisms of adaptive social functioning - PubMed (nih.gov)

Reactivating hippocampally-mediated memories during reconsolidation to disrupt fear (S Ramirez)

Ramirez, Steve. "Reactivating Hippocampal-Mediated Memories during Reconsolidation to Disrupt Fear.†*BioRxiv*, vol. 460695, 16 Sept. 2021.

 $\underline{https://www.dropbox.com/s/hpy455ze9z5ono7/Reactivating\%20Hippocampal-Mediated\%20Memories\%20During\%20Reconsolidation.pdf? \\ \underline{dl=0}$ 

#### Week 6: Neural circuit dysfunction and biological classification in major psychiatric diseases, biomarkers

- Butler, Tracy, et al. "Neuroimaging of Frontal-Limbic Dysfunction in Schizophrenia and Epilepsy-Related Psychosis: Toward a Convergent Neurobiology.†*Epilepsy & Behavior : E&B*, vol. 23, no. 2, 1 Feb. 2012, pp. 113â€"122

 $\frac{\text{https://www.dropbox.com/s/gpzxfntpf3a1br2/Neuroimaging\%20of\%20frontal\%20limbic\%20dysfunction\%20in\%20schizophrenia\%20and\%20epilepsy-related\%20psychosis\%20toward\%20a\%20convergent\%20neurobiology.pdf?dl=0}{\text{https://www.dropbox.com/s/gpzxfntpf3a1br2/Neuroimaging\%20of\%20frontal\%20limbic\%20dysfunction\%20in\%20schizophrenia\%20and\%20epilepsy-related\%20psychosis\%20toward\%20aw20convergent\%20neurobiology.pdf?dl=0}$ 

 Amygdala reactivity to emotional faces in the prediction of general and medication-specific responses to antidepressant treatment in the randomized iSPOT-D trial (Williams)

Williams, Leanne M, et al.  $\hat{a} \in \omega$  Amygdala Reactivity to Emotional Faces in the Prediction of General and Medication-Specific Responses to Antidepressant Treatment in the Randomized ISPOT-D Trial.  $\hat{a} \in \omega$  Neuropsychopharmacology, vol. 40, no. 10, 31 Mar. 2015, pp.  $2398\hat{a} \in 2408$ 

 $\label{lem:https://www.dropbox.com/s/h2hv2f826ubuw8k/Amygdala%20Reactivity\%20to\%20Emotional\%20Faces\%20in\%20the\%20Prediction\%20of\%20General\%20and\%20MedicationSpecific%20Responses\%20to\%20Antidepressant\%20Treatment\%20in\%20the\%20Randomized\%20iSPOT-D\%20Tria\%20\%281\%29.pdf?dl=0$ 

• A thalamocentric neural signature for restructuring negative self beliefs. (Steward CBT paper)

Steward, Trevor, et al. "A Thalamo-Centric Neural Signature for Restructuring Negative Self-Beliefs.†Molecular Psychiatry, 1 Jan. 2022

• Default mode subnetworks, connectivity, depression and its treatment: toward brain-based biomarker development. Silbersweig D.

Silbersweig, David.  $\hat{a} \in \mathbb{C}$  Default Mode Subnetworks, Connectivity, Depression and Its Treatment: Toward Brain-Based Biomarker Development.  $\hat{a} \in \mathbb{C}$  Biological Psychiatry, vol. 74, no. 1, July 2013, pp.  $5\hat{a} \in \mathbb{C}$ 

https://www.dropbox.com/s/dhzy8r7pkf9q6mw/Default%20Mode%20Subnetworks%2C%20Connectivity%2C%20Depression%20and%20its%20treatment.pdf?dl=0

• Precision psychiatry meets network medicine: Network psychiatry. Silbersweig D and Loscalzo J.

Silbersweig, David, and Joseph Loscalzo. "Precision Psychiatry Meets Network Medicine.†JAMA Psychiatry, vol. 74, no. 7, 1 July 2017, p. 665, 10.

# Week 7: Connectomics, Brain Circuit Therapeutics

### (Come to class with three possible paper topics for discussion)

The Brain's Default Mode Network, Marcus Raichle.

 $\underline{https://canvas.harvard.edu/courses/128363/files/folder/Course\%20Readings?preview=19272846220Readings?preview=19272846220Readings.preview=1927284620Readings.previ$ 

• On the existence of a generalized non-specific task-dependent network. Kenneth Hugdahl, Marcus Raichle, Anish Mitra and Karsten Specht.

https://canvas.harvard.edu/courses/128363/files/folder/Course%20Readings?preview=19191517

Li, Ningfei, et al.  $\hat{a} \in A$  Unified Functional Network Target for Deep Brain Stimulation in Obsessive-Compulsive Disorder.  $\hat{a} \in Biological$  Psychiatry, vol. 90, no. 10, 15 Nov. 2021, pp.  $701\hat{a} \in 713$ .

 $\frac{\text{https://www.dropbox.com/s/wxnil9lxgizzlpn/A}\%20Unified\%20Functional\%20Network\%20Target\%20for\%20Deep\%20Brain\%20Stimulation\%20in\%20Obsessive-Compulsive\%20Disorder.pdf?dl=0}{\text{compulsive}\%20Disorder.pdf?dl=0}$ 

Siddiqi, Shan H., et al.  $\hat{a} \in \text{Distinct Symptom-Specific Treatment Targets}$  for Circuit-Based Neuromodulation.  $\hat{a} \in \text{American Journal of Psychiatry}$ , vol. 177, no. 5, 1 May 2020, pp.  $435\hat{a} \in \text{May}$  174.

• Real-time fMRI neurofeedback reduces auditory hallucinations and modulates resting state connectivity of involved brain regions: part 2: Default mode network-preliminary evidence (Whitfield-Gabrieli)

Bauer, Clemens C.C., et al. "Real-Time FMRI Neurofeedback Reduces Auditory Hallucinations and Modulates Resting State Connectivity of Involved Brain Regions: Part 2: Default Mode Network -Preliminary Evidence.†*Psychiatry Research*, vol. 284, Feb. 2020.

# Week 8

Spring Recess â€" No Class or Assignment due this week (3/14/24)

# Week 9: Psychiatric Disorders and Interview, BWH/HMS clinical visit

DSM overview

 $\underline{https://canvas.harvard.edu/courses/128363/files/folder/Course\%20Readings?preview=19191523}$ 

- Linking RDoC and HiTOP: a new interface for advancing psychiatric nosology and neuroscience (Michelini)
- Michelini. "Linking RDoC and HiTOP: A New Interface for Advancing Psychiatric Nosology and Neuroscience.†Clinical Psychology Review, vol. 86, 1 June 2021, p. 102025.

• The Psychiatric Interview Chapter

#### Week 10: Implications of psychiatric neuroimaging findings for mental health

#### (250 word abstract due including 5 references )

• Neural contributors to trauma resilience: a review of longitudinal neuroimaging studies. Roeckner et al. Transl Psych. 2021.

(insert ref)

• Wu, Gang, et al. "Understanding Resilience.†Frontiers in Behavioral Neuroscience, vol. 7, no. 10, 2013.

 $\underline{https://www.dropbox.com/s/ahoss81gzhg86yb/Understanding\%20 resilience.pdf?dl=0 Links\ to\ an\ external\ site.}$ 

(podcast in class)

# Week 11: Implications of brain imaging findings for models of mind, mental activity/consciousness

• Damasio chapters 8, 9 and 10

Damasio, Antonio, Self Comes To Mind, Building a Conscious Mind, (2010)

Damasio, Antonio. Self Comes To Mind. The Autobiographical Self. (2010)

Damasio, Antonio. Self Comes To Mind. Putting It Together. (2010)

https://www.dropbox.com/s/06agsqx1wknusr4/Antonio Damasio Self Comes to Mind Chapters%208 10%20only.pdf?dl=0

Buzsaki, Gyorgy, The brain from inside out, (2019). 10.1002

https://www.dropbox.com/s/hhpzjlfu728cem5/Buzsaki.pdf?dl=0Links to an external site.

Seth, Anil K., and Tim Bayne. "Theories of Consciousness.†Nature Reviews Neuroscience, 3 May 2022, 10.1038/s41583-022-00587-4.

 $\underline{https://www.dropbox.com/s/h68hny2rxycqdlg/TheoriesofConsciousness.pdf?dl=0}$ 

#### Week 12: Implications for issues in philosophy of mind: consciousness, free will

Frith, Chris D. "Action, Agency and Responsibility.†Neuropsychologia, vol. 55, Mar. 2014, pp. 137â€"142, 10.1016.

Libet, Benjamin. "Do We Have Free Will?†Conscious Will and Responsibility, 24 Nov. 2010, pp. 1–10, 10.1093.

https://www.dropbox.com/s/mglw7fo0obibuy1/Libet 1999 Do%20we%20have%20free%20will.pdf?dl=0

Darby, Ryan, Joutsa, Juho, Burke, Matthew, Fox Michael. (16 Aug 2018). Lesion network localization of free will. 115 (42) 107-10797.

### Week 13: Implications for issues in philosophy of mind: religious experience, belief and meaning; morality, politics, policy

• Current understanding of religion, spirituality and their neurobiological correlates. Harvard Rev Psych. Rim et al. 2019

• (insert ref)

Devinsky, Orrin, and George Lai.  $\hat{a} \in \omega$ Spirituality and Religion in Epilepsy.  $\hat{a} \in Epilepsy \& Behavior$ , vol. 12, no. 4, 1 May 2008, pp. 636 $\hat{a} \in \omega$ 643.

 $\underline{https://www.dropbox.com/s/8xube29wocqp2p5/Spirituality\%20and\%20Religion\%20in\%20Epilepsy.pdf?dl=0Links\ to\ an\ external\ site.}$ 

Saver, J, and J Rabin.  $\hat{a} \in \mathbb{C}$  The Neural Substrates of Religious Experience.  $\hat{a} \in \mathbb{C}$  The Journal of Neuropsychiatry and Clinical Neurosciences, vol. 9, no. 3, Aug. 1997, pp.  $498\hat{a} \in \mathbb{C}$  510, 10.1176/jnp.9.3.498.

Mendez, Mario F. "A Neurology of the Conservative-Liberal Dimension of Political Ideology. †The Journal of Neuropsychiatry and Clinical Neurosciences, vol. 29, no. 2, Apr. 2017, pp. 86†"94, 10.

• The prefrontal cortex and (uniquely) human cooperation: a comparative perspective (Crockett)

Zoh, Y., Chang, S.W.C. & Crockett, M.J. The prefrontal cortex and (uniquely) human cooperation: a comparative perspective. *Neuropsychopharmacol.* 47, 119–133 (2022).

 $\frac{https://www.dropbox.com/s/emwitucu57fq7uz/The%20prefrontal%20cortex%20and%20%28uniquely%29%20human%20cooperation%20a%20comparative%20prespective.pdf?dl=0$ 

Nummenmaa L, Lukkarinen L, Sun L, Putkinen V, Seppälä K, Karjalainen T, Karlsson HK, Hudson M, Venetjoki N, Salomaa M, Rautio P, Hirvonen J, Lauerma H, Tiihonen J, Brain Basis of Psychopathy in Criminal Offenders and General Population. Cereb Cortex. 2021 Jul 29;31(9):4104-4114.

### **Course Schedule**

Thursday, January 25, 2024	No assignment due
Thursday, February 1, 2024	Best question for week 2 due by 5:00 pm, Wednesday, January 31st
Thursday, February 8, 2024	Best question for week 3 due by 5:00 pm, Wednesday, February $7^{\mbox{th}}$
Thursday, February 15, 2024	Best question for week 4 due by 5:00 pm, Wednesday, February $14^{\mbox{th}}$
Thursday, February 22, 2024	Best question for week 5 due by 5:00 pm, Wednesday, February 21st
Thursday, February 29, 2024	Best question for week 6 due by 5:00 pm, Wednesday, February 28th
Thursday, March 7, 2024	Best question for week 7 due by 5:00 pm, Wednesday, March $6^{\mbox{th}}$
	Upload 3 paper topics to the class site on Canvas

Thursday, March 14, 2024	Spring Recess $\hat{\mathbf{a}} \mathbf{\ell}''$ No Class or Assignment due this week
Thursday, March 21, 2024	Best question for week 9 due by 5:00 pm, Wednesday, March $20^{\mbox{th}}$
Thursday, March 28, 2024 with 5 references to the class site	Best question for week 10 due by 5:00 pm, Wednesday, March $27^{\mbox{th}}$
Thursday, April 4, 2024	Best question for week 11 due by 5:00 pm, Wednesday, April $3^{\mbox{rd}}$
Thursday, April 11, 2024	Best question for week 12 due by 5:00 pm, Wednesday, April $10^{\mbox{th}}$
Thursday April 18, 2024	Best question for week 13 due by 5:00 pm, Wednesday, April $17^{\mbox{th}}$
	Last Class

Final paper due by 5 pm

Upload 250 word abstract

# Course/Assignment Schedule

Thursday, May 2, 2024

Week 1	Thursday, January 25, 2024	No assignment due
Week 2	Thursday, February 1, 2024	Best question for week 2 due by 5:00 pm, Wednesday, January 31
Week 3	Thursday, February 8, 2024	Best question for week 3 due by 5:00 pm, Wednesday, February 7
Week 4	Thursday, February 15, 2024	Best question for week 4 due by 5:00 pm, Wednesday, February 14
Week 5	Thursday, February 22, 2024	Best question for week 5 due by 5:00 pm, Wednesday, February 21
Week 6	Thursday, February 29, 2024	Best question for week 6 due by 5:00 pm, Wednesday, February 28
		Best question for week 7 due by 5:00 pm, Wednesday, March 6
Week 7 Thursday	Thursday, March 7, 2024	Upload 3 paper topics to the class site on Canvas.
Week 8	Thursday, March 14, 2024	Spring Recess $\hat{a} \mathfrak{E}''$ No Class or Assignment due this week
Week 9	Thursday, March 21, 2024	Best question for week 9 due by 5:00 pm, Wednesday, March 20
Week 10	Thursday, March 28, 2024	Best question for week 10 due by 5:00 pm, Wednesday, March 27 Upload 250 word abstract with 5
Week 11	Thursday, April 4, 2024	references to the class site on Canvas.  Best question for week 11 due by 5:00 pm, Wednesday, April 3
Week 12	Thursday, April 11, 2024	Best question for week 12 due by 5:00 pm, Wednesday, April 10
Week 13 Last Class	Thursday April 18, 2024	Best question for week 13 due by 5:00 pm, Wednesday, April 17
	Thursday, May 4, 2023	Final paper due by 5 pm