

***Addiction Science (GMS MS710)***  
***Course Syllabus Fall 2020***  
***Thursdays 10AM-12PM***  
***E201***

**Description:** This introductory course will cover the broad field of addiction with a focus on drug dependence. In one segment of the course, students will learn about the spectrum of drug dependence disorders and modalities for diagnosis and treatment. Another segment will present a wide variety of approaches for studying addiction using the tools of epidemiology, genetics, pharmacology, neurobehavior, and animal models. Emphasis will be placed on transdisciplinary approaches which are essential for understanding and combating addiction disorders. In addition, students will be exposed to the impact of addiction on the family and society, and to public policy issues addressing the prevention of addiction.

**Lecture Series Overview**

1. Sep 3 *Introduction / History of Addiction Research* - **Lindsay Farrer**
2. Sep 10 *Clinical Trials for Substance Use Disorders* - **Richard Saitz**
3. Sep 17 *Epidemiology of Addiction* - **Tim Heeren**
4. Sep 24 *Genetic Basis of Addiction* - **Lindsay Farrer**
5. Oct 1 *Current Approaches in Diagnosis & Treatment of Substance Use Disorders* -  
**Alexander Walley**
6. Oct 8 *Genetic Models for Addiction* - **Camron Bryant**
7. Oct 22 *Neurochemistry & Neurobiology of Addiction* - **Pietro Cottone / Valentina Sabino**
8. Oct 29 *Development of Pharmacological Treatments for Substance Use Disorders* -  
**Gary Kaplan**
9. Nov 5 *Animal Models of Addiction* - **Kathleen Kantak**
10. Nov 12 *A Trauma-Informed Approach to Substance Use Prevention and Treatment with  
Latinos(as)* - **Luz Lopez**
11. Nov 19 *Neonatal Abstinence Syndrome – Presentation, Treatment, and Emerging Research*  
- **Elisha Wachman**
12. Dec 3 *The Politics of Addiction Prevention: From Tobacco to Alcohol to Cannabis* - **David  
Jernigan**
13. Dec 10 **student presentations**

# Lecture Outlines

## **Lecture 1 (September 3): Introduction / History of Addiction Research**

**Lindsay A. Farrer, Ph.D.**

*BU Distinguished Professor of Genetics*

*Chief, Biomedical Genetics*

*Professor of Medicine, Neurology, Ophthalmology, Epidemiology, and Biostatistics*

**Summary:** This lecture will introduce the students to addiction as it pertains to diagnosis, treatment, research, and public policy. Insight into contemporary approaches in these domains will be provided by historical analysis.

**Objectives:** To give to the student some understanding of the history and attitudes and beliefs of drug abuse through the years by both the lay public and investigators.

### **Outline:**

1. Introduction
  - a) Overview of course and learning objectives
  - b) Class organization
  - c) Evaluation and grading
2. Definition of Substance Use Disorders
3. History of substance use and societal views
4. Brain reward system
5. Animal models in the study of drug addiction

### **Required Readings:**

- Wikler, A. A Psychodynamic Study of a Patient During Experimental Self-Regulated Re-addiction to Morphine *Psychiatric Quarterly*, 26:270-293, 1952
- Yale Reports. The Doctor and the Treatment of Narcotic Addiction –Daniel X. Freedman, Conan Kornetsky and Vincent Dole, 2/6/66.
- Robins LN, Helzer JE, Hesselbrock M, Wish E. Vietnam veterans three years after Vietnam: How our study changed our view of heroin. *Am J Addictions* 19:203-211, 2010.

## Lecture 2 (September 10): Clinical Trials for Substance Use Disorders

### **Richard Saitz MD, MPH**

*Chair, Department of Community Health Sciences (CHS), Boston University School of Public Health*

*Professor of Community Health Sciences & Medicine, Boston University Schools of Public Health and Medicine*

*Addiction Medicine Physician, Boston Medical Center*

**Summary:** During this session we will describe and critically appraise clinical trials of treatments for people with addictions. We will review key examples and design issues and outline the design for a new trial.

### **Objectives:**

1. Learners will become familiar with an example of an addiction clinical trial
2. Learners will gain skills in critical appraisal of addiction clinical trials
3. Learners will be able to list the key design issues relevant to addiction clinical trials

### **Outline:**

1. Review of an addiction clinical trial
2. Principles of critical appraisal
  - a. Validity
  - b. Results
  - c. Generalizability
3. Critical appraisal of an addiction clinical trial
4. Special challenges in studying addiction treatments
  - a) Surrogate outcomes
  - b) Anonymity/confidentiality
  - c) Motivation to change
5. Key design issues
  - a) Experimental design
  - b) Participant selection
  - c) Intervention fidelity
  - d) Control groups
  - e) Blinding
  - f) Follow-up
  - g) Outcomes
  - h) Effectiveness versus efficacy
6. Exercise: design a trial

### **Required Readings:**

- Therapy (randomized trials). Chapter 7, in Gordon Guyatt, Drummond Rennie, Maureen O. Meade, Deborah J. Cook. *Users' Guides to the Medical Literature: A Manual for Evidence-*

*Based Clinical Practice*, 3rd ed. McGraw Hill, USA. To Access, Search BU Libraries for JAMAevidence. JAMAevidence using evidence to improve care 2009. Click on online access. Focus on Box 7-1, this is critical appraisal. <https://jamaevidence.mhmedical.com/book.aspx?bookid=847#69031499>

- Lee JD , Nunes EV Jr , Novo P et al. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. *Lancet*. 2018 Jan 27;391(10118):309-318. doi: 10.1016/S0140-6736(17)32812-X. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5806119/>

## Lecture 3 (September 17): Epidemiology of Addiction

**Tim Heeren, Ph.D.**

*Professor of Biostatistics*

*Boston University School of Public Health*

**Summary:** This lecture will first give a brief overview of some of the goals, strengths, and weaknesses of addictions-related epidemiologic research. Then, focusing on a few students, we will discuss early predictors of substance use problems in early adulthood. Finally, we will take a look at some statistical methods currently being used in epidemiologic studies of substance use and substance use disorders.

### Objectives:

1. To provide an introduction to epidemiological research into substance use and substance use disorders.
2. To provide an overview into early life predictors of substance use disorders in early adulthood
3. To provide an overview of some current methods in epidemiological research into substance use disorders.

### Outline:

1. Overview: the use of epidemiology in alcohol and substance use research
2. Case studies: epidemiological studies of substance use disorders in emerging and early adulthood
  - a) Prenatal alcohol exposure
  - b) Early life predictors of adult drinking
  - c) Age of onset and substance use disorders
3. Case studies: current methods in epidemiological substance use research
  - a) Drinking trajectories
  - b) Latent class analysis of alcohol use disorder criteria
  - c) Structural equation modeling of the relationship between impulsivity and

alcohol misuse

### **Required Readings:**

- Rossow I and Norstrom T. The use of epidemiology in alcohol research. *Addiction*, 108:20-25, 2012.
- Stone AL, Becker LG, Huber AM, Catalano RF. Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addictive Behaviors*, 37:747-775, 2012.

### **Suggested Readings:**

- Alati R, Mamun AA, Williams GM, O'Callaghan M, Najman JM, Bor W. In utero alcohol exposure and prediction of alcohol disorders in early adulthood: a birth cohort study. *Arch Gen Psychiatry*, 63:1009-1016, 2006.
- Alati R, Najman JM, Kinner SA, Mamun AA, Williams GM, O'Callaghan M, Bor W. Early predictors of adult drinking: a birth cohort study. *American Journal of Epidemiology*, 162(11):1098-1107, 2005.
- King KM and Chassin L. A prospective study of the effects of age of initiation of alcohol and drug use on young adult substance dependence. *J Stud Alcohol Drugs*, 68:256-265, 2007.
- Maggs JL and Schulenberg JE. Trajectories of alcohol use during the transition to adulthood. *Alcohol Research and Health*, 28(4):195-201, 2005.
- Beseler CL, Taylor LA, Kraemer DT, Leeman RF. A latent class analysis of DSM-IV alcohol use disorder criteria and binge drinking in undergraduates. *Alcoholism: Clinical and Experimental Research*, 36(1):153-161, 2012.
- Courtney KE, Arellano R, Barkley-Levenson E, Galvan A, Poldrack RA, MacKillop J, Jentsch JD, Ray LA. The relationship between measures of impulsivity and alcohol misuse: an integrative structural equation modeling approach. *Alcoholism: Clinical and Experimental Research*, 36(6):923-931, 2012.

## **Lecture 4 (September 24): Genetic Basis of Addiction**

**Lindsay A. Farrer, Ph.D.**

*BU Distinguished Professor of Genetics*

*Chief, Biomedical Genetics*

*Professor of Medicine, Neurology, Ophthalmology, Epidemiology, and Biostatistics*

**Summary:** This lecture will explore the genetic basis for addiction in humans. The session will begin with a discussion of the evidence from family and twin studies for the genetic component to dependence on various substances including nicotine, alcohol, cocaine, opioids and cannabis. There will be some didactic on methodologies for genetic linkage and association studies including genome-wide association studies. This will be followed by a demonstration of how

these approaches have been applied in substance dependence with a focus on phenotype definition and discussion of qualitative versus quantitative trait outcomes. Finally, the lecture will introduce contemporary genetics research approaches in addictions including next generation sequencing and bioinformatics.

**Objectives:** At the end of the session, students will be able to:

1. Describe methodologies for determining the strength of the genetic component for addictions;
2. Differentiate the strengths and limitations for genetic linkage, candidate gene association, GWAS and next generation sequencing approaches to identify genes for addiction;
3. Articulate principles for family-based and case-control designs for genetic discovery in the addictions;
4. Read and understand scientific papers focused on these topics.

**Outline:**

1. Review of basic principles of genetics
  - a) Mendelian Inheritance
  - b) Complex Inheritance
  - c) Quantitative traits
  - d) Linkage and association
2. Twin studies of addiction
3. Candidate gene studies of addiction
4. Genome-wide association studies of addiction

**Required Readings:**

- Tsuang, M.T., Lyons, M.J., Eisen, S.A., Goldberg, J, True, Lin N, W, Meyer, J.M., Tooney R, Faraone SV, and Eaves, L. Genetic influences on DSM-III-R drug abuse and dependence: A study of 3,372 twin pairs. *Am J Med Genet (Neuropsych. Genet)* 1996;67:473-477
- Smith AH, Jensen KP, Li J, Nunez Y, Farrer LA, Hakonarson H, Cook-Sather SD, Kranzler HR, Gelernter J. Genome-wide association study of therapeutic opioid dosing identifies a novel locus upstream of OPRM1. *Mol Psychiatry* 2017; 22:346-352.
- Edenberg HJ, Gelernter J, Agrawal A. Genetics of Alcoholism. *Curr Psychiatry Rep* 2019; 21(4):26.
- Crist RC, Reiner BC, Berrettini WH. A review of opioid addiction genetics. *Curr Opin Psychol.* 2019; 27:31-35

**Suggested Readings:**

- Xie P, Kranzler HR, Krystal JH, Farrer LA, Zhao H, Gelernter J. Deep resequencing of 17 glutamate system genes identifies rare variants in *DISC1* and *GRIN2B* affecting risk of opioid dependence. *Addiction Biology* 2014; 19:955-964.
- Gelernter J, Sherva R, Koesterer R, Zhao H, Kranzler HR, Farrer LA. Genomewide association study of cocaine dependence and related traits: FAM53B identified as a risk gene. *Molecular Psychiatry* 2014; 19:717-723.

- Gelernter J, Kranzler HR, Sherva R, Koesterer R, Sun J, Bi J, Almasy L, Zhao H, Farrer LA. Genomewide association study of opioid dependence and related traits: multiple associations mapped to calcium and potassium pathways. *Biological Psychiatry* 2014; 76:66-74.
- Sherva R, Wang Q, Kranzler HR, Zhao H, Koesterer R, Herman A, Farrer LA, Gelernter J. Genome wide association study of cannabis dependence severity reveals novel risk variants, genes previously implicated in schizophrenia risk, and shared risk with major depressive disorder. *JAMA Psychiatry* 2016; 73:472-480.
- Cox JW, Sherva RM, Lunetta KL, Johnson EC, Martin NG, Degenhardt L, Agrawal A, Nelson EC, Kranzler H, Gelernter J, Farrer LA. Genome-wide association study of opioid cessation. *J Clin Med* 2020; 9:180.

## **Lecture 5 (October 1): Current Approaches in Diagnosis & Treatment of Substance Use Disorders**

**Alexander Y. Walley, MD, MSc**

*Associate Professor of Medicine*

*Clinical Addiction Research and Education Unit, General Internal Medicine*

*Boston University School of Medicine*

**Summary:** This lecture will review the diagnostic criteria and current treatment approaches for substance use disorders. Treatment approaches include existing evidence-based behavioral therapy and FDA-approved medications. The lecture will also include an introduction to treatment delivery systems.

### **Objectives:**

1. Learners will be able to list the current diagnostic criteria for substance use disorders
2. Learners will understand the existing clinical treatment approaches for substance use disorders, including alcohol, opioids, stimulants, and benzodiazepines

### **Outline:**

1. Diagnostic criteria for substance use disorders – DSM IV and V
2. Alcohol Disorders
  - a) Behavioral treatment
  - b) Pharmacological treatment
3. Opioid Disorders
  - a) Maintenance treatment with methadone
  - b) Maintenance treatment with buprenorphine
  - c) Naltrexone treatment
4. Stimulant Disorders
  - a) Cocaine

- b) Methamphetamine
- c) Contingency management
- 5. Benzodiazepine Disorders
  - a) Medically managed withdrawal treatment (detoxification)
- 6. Polysubstance Disorders

### **Required Readings:**

- Helping Patients Who Drink Too much: A Clinician's Guide. [www.niaaa.nih.gov/guide](http://www.niaaa.nih.gov/guide)
- McLellan TA et al. Drug Dependence: A Chronic Medical Illness. JAMA 2000 284: 1689-95.
- Prendergast M, Podus D, Finney J, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: A meta-analysis. Addiction. 2006;101(11):1546-1560.
- Hasin DS, O'Brien CP, Auriacombe M, Borges G, Bucholz K, Budney A, Compton WM, Crowley T, Ling W, Petry NM, Schuckit M. DSM-5 criteria for substance use disorders: recommendations and rationale. American Journal of Psychiatry. 2013 Aug;170(8):834-51.<http://www.ncbi.nlm.nih.gov/pubmed/17034434><<http://www.ncbi.nlm.nih.gov/pubmed/17034434>>

### **Suggested Readings:**

- McLellan TA et al. Drug Dependence: A Chronic Medical Illness. JAMA 2000 284: 1689-1695  
<http://www.ncbi.nlm.nih.gov/pubmed?term=11015800>
- Helping Patients Who Drink Too much: A Clinician's Guide <http://www.niaaa.nih.gov/guide>
- Prendergast M, Podus D, Finney J, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: A meta-analysis. Addiction. 2006; 101(11):1546-1560.  
<http://www.ncbi.nlm.nih.gov/pubmed/17034434>
- Hasin DS, O'Brien CP, Auriacombe M, Borges G, Bucholz K, Budney A, Compton WM, Crowley T, Ling W, Petry NM, Schuckit M. DSM-5 criteria for substance use disorders: recommendations and rationale. American Journal of Psychiatry. 2013 Aug;170(8):834-51.  
<http://www.ncbi.nlm.nih.gov/pubmed/17034434>
- Prendergast M, Podus D, Finney J, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: A meta-analysis. Addiction. 2006;101(11):1546-1560.



## Lecture 6 (October 8): Genetic Models for Addiction

**Camron D. Bryant, Ph.D.**

*Associate Professor of Pharmacology and Psychiatry*

### Summary:

Despite the overwhelming evidence that substance use disorders have a genetic component, the vast majority of heritability has yet to be explained. Addiction genetic approaches in rodents offer powerful, complementary, rapid, and efficient means for discovering and validating causal genes and variants underlying drug-induced behaviors that are relevant to substance use disorders in humans. The high degree of genetic homology between rodents and humans means that genes discovered in rodents can almost always be identified, leveraged, and tested for their association in humans.

### Objectives:

The objective of this lecture is to introduce heritable, addiction-relevant behaviors in rodents and genetic analysis of these behaviors in contemporary experimental crosses and populations. Forward genetic approaches will be described that have led to the identification of novel genetic factors underlying behavioral variation in addiction traits. Examples of successful validation of candidate genes and variants identified through genetic analysis will be presented.

### Outline:

#### I. SUD-relevant traits for gene discovery

- A. Behavioral models and heritability
- B. Genetic variants and genotyping
- C. Linkage (QTL) and association (GWAS)
- D. Gene expression, eQTLs, and Omics to aid in gene identification and biological mechanisms
- D. Pharmacogenomics and pharmacogenetics

#### II. Forward genetic approaches (gene discovery)

- A. F2 crosses, inbred panels, and congenics
  - 1. Reduced Complexity Crosses – *Cyfp2*, *Gabra2*, *Taar1*
  - 2. Congenics for fine mapping
- B. Advanced intercrosses for high resolution mapping
  - 1. AILs (LG x SM)
  - 2. Outbred stocks (CFW)
  - 3. Diversity Outbred (DO)

#### III. Reverse genetics (gene validation and functional studies)

- A. Functional gene and variant identification via gene editing
- B. Humanized mice to validate human variants – mu opioid receptor, nicotinic receptor

#### IV. Limitations, considerations, future directions

- A. Genetic background and epistasis
- B. G x E
- C. Modeling human GWAS variants on multiple genetic variants

## Required Readings:

- [Genome-wide association studies in mice](#). Flint J, Eskin E. Nat Rev Genet. 2012 Nov;13(11):807-17. doi: 10.1038/nrg3335. Epub 2012 Oct 9. PMID: 23044826 Free PMC article. Review.
- Bryant CD, Smith DJ, Williams RW, Damaj MI, Redei EE, Chen H, Mulligan MK (2020). Facilitating complex trait analysis via reduced complexity crosses. *Trends in Genetics*; 36(8): 549-562. [PMC7365571](#)
- Yazdani N, Parker CC, Shen Y, Reed ER, Guido MA, Kole LA, Kirkpatrick SL, Lim JE, Sokoloff G, Cheng R, Johnson WE, Palmer AA, Bryant CD (2015). *Hnrnp1* is a quantitative trait gene for methamphetamine sensitivity. *PLOS Genetics* 11(12):e1005713.
- Ruan QT, Yazdani N, Reed ER, Beierle JA, Peterson LP, Luttik KP, Szumlinski KK, Johnson WE, Ash PEA, Wolozin B, Bryant CD (2020). 5' UTR variants in the quantitative trait gene *Hnrnp1* support reduced 5' UTR usage and hnRNP H protein as a molecular mechanism underlying reduced methamphetamine sensitivity. *The FASEB Journal*, 34(7): 9223-2344. [10.1096/fj.202000092R](#)
- Mulligan MK, Abreo TJ, Neuner SM, Parks CL, Watkins CE, Houseal MT, Shapaker TM, Hook M, Tan H, Wang X, Ingels J, Peng J, Lu L, Kaczorowski CC, Bryant CD, Homanics GE, Williams RW (2019). Identification of a functional non-coding variant in the GABAA receptor  $\alpha 2$  subunit of the C57BL/6J mouse reference genome: Major implications for neuroscience research. March 29 *Frontiers in Genetics* 10: 188. [PMC6449455](#)
- [A Human Polymorphism in CHRNA5 Is Linked to Relapse to Nicotine Seeking in Transgenic Rats](#). Forget B, Scholze P, Langa F, Morel C, Pons S, Mondoloni S, Besson M, Durand-de Cuttoli R, Hay A, Tricoire L, Lambomez B, Mourot A, Faure P, Maskos U. *Curr Biol*. 2018 Oct 22;28(20):3244-3253.e7. doi: 10.1016/j.cub.2018.08.044. Epub 2018 Oct 4. PMID: 3029372

## Suggested Readings:

- Ruan QT, Yazdani N, Blum BC, Beierle JA, Lin W, Coelho MA, Fultz EK, Healy AF, Shahin JR, Kandola AK, Luttik KP, Zheng K, Smith NJ, Cheung J, Mortazavi F, Apicco DJ, Varman DR, Ramanmoorthy S, Ash PEA, Rosene DL, Emili A, Wolozin B, Szumlinski KK, Bryant CD (2020). A mutation in *Hnrnp1* that decreases methamphetamine reinforcement, reward, and dopamine release and increases synaptosomal hnRNP H and mitochondrial proteins. *J Neurosci* 40(1): 107-130. [PMC6939476](#)
- [Genome-wide association study of behavioral, physiological and gene expression traits in outbred CFW mice](#). Parker CC, Gopalakrishnan S, Carbonetto P, Gonzales NM, Leung E, Park YJ, Aryee E, Davis J, Blizard DA, Ackert-Bicknell CL, Lionikas A, Pritchard JK, Palmer AA. *Nature Genetics* 2016 Aug;48(8):919-26. doi: 10.1038/ng.3609. Epub 2016 Jul 4. PMID: 27376237
- [Taar1 gene variants have a causal role in methamphetamine intake and response and interact with Oprm1](#). Stafford AM, Reed C, Baba H, Walter NA, Mootz JR, Williams RW, Neve KA, Fedorov LM, Janowsky AJ, Phillips TJ. *Elife*. 2019 Jul 9;8:e46472. doi: 10.7554/eLife.46472. PMID: 31274109 Free PMC article.

- [Mouse model of OPRM1 \(A118G\) polymorphism has sex-specific effects on drug-mediated behavior.](#) Mague SD, Isiegas C, Huang P, Liu-Chen LY, Lerman C, Blendy JA. *PNAS*; 2009 Jun 30;106(26):10847-52. doi: 10.1073/pnas.0901800106. Epub 2009 Jun 15. PMID: 19528658 Free PMC article.
- [Genetic Background Limits Generalizability of Genotype-Phenotype Relationships.](#) Sittig LJ, Carbonetto P, Engel KA, Krauss KS, Barrios-Camacho CM, Palmer AA. *Neuron*. 2016 Sep 21;91(6):1253-1259. doi: 10.1016/j.neuron.2016.08.013. Epub 2016 Sep 8. PMID: 27618673

## Midterm Exam – October 17

### Lecture 7 (October 22): Neurochemistry and Neurobiology of Addiction

#### **Pietro Cottone, Ph.D.**

*Assistant Professor of Pharmacology & Experimental Therapeutics and Psychiatry  
Laboratory of Addictive Disorders*

#### **Valentina Sabino, Ph.D.**

*Assistant Professor of Pharmacology & Experimental Therapeutics and Psychiatry*

**Summary:** This lecture will provide information about the molecular mechanisms of action of the most common drugs of abuse. Neurocircuitries involved in the different stages of drug addiction will be described, with a focus on the neurochemical and molecular changes taking place in the transition to dependence.

**Objectives:** At the end of the session, students will be able to:

1. Describe the mechanism of action of psychostimulants, opiates, alcohol, and cannabinoids
2. Describe the neuroanatomy and neurochemistry of drug addiction
3. Explain the neurochemical and molecular adaptations characterizing the transition to dependence.

#### **Outline:**

1. Addiction Definitions: Drug Use, Abuse, Dependence, Addiction
2. Classification of drugs of abuse
3. Mesolimbic system and reward neurotransmission
4. Mechanism of action of most common drugs of abuse (psychomotor stimulants, opiates, alcohol, cannabinoids)
5. Transition to addiction and stages of the addiction cycle

6. Molecular neuroadaptations in addiction
7. Animal models

**Required Readings:**

- Neurocircuitry of addiction. Koob GF, Volkow ND. *Neuropsychopharmacology* (2010); 35(1): 217-38.
- Experimental psychiatric illness and drug abuse models: from human to animal, an overview. Edwards S, Koob GF. *Methods Mol Biol.* (2012); 829: 31-48.

**Suggested Readings:**

- *Neurobiology of Addiction*, by George F. Koob and Michel Le Moal, 2006, Elsevier, Inc., London.

## **Lecture 8 (October 29): Development of Pharmacological Treatments in Addiction**

**Gary B. Kaplan, MD,**

*Professor of Psychiatry and Pharmacology & Experimental Therapeutics, Boston University School of Medicine; Director of Translational Psychiatry Research, VA Boston Healthcare System*

**Summary:** This lecture will explore the pharmacological basis for addiction treatment. The lecture begins with a review of the role of drug agonists, antagonists, and inverse agonists and their role in addiction pharmacotherapy. This will be followed by a discussion of the application of pharmacological treatment at the different phases of substance use disorders. It focuses on the different receptor and neurotransmitter targets for addiction pharmacotherapy. Finally, it describes how synaptic and structural plasticity in addiction are relevant to future medication development in addiction.

**Objectives:** At the end of the session, students will be able to:

1. Understand how basic pharmacological approaches for drug agonists, antagonists, inverse agonists relate to addiction treatment
2. Understand how pharmacological agents can be applied at different phases of addiction treatments such as withdrawal, maintenance and relapse prevention
3. Describe the different targets for addiction pharmacotherapy at GABA, glutamate, and opioid receptors and at different ion channels
4. Explain how changes in synaptic plasticity in key neuroanatomical pathways represent targets for future addiction pharmacotherapy

**Outline:**

1. Patient Assessment and Measurement of Outcomes
2. Understanding Basic Pharmacology and its Translation to Addiction Pharmacotherapy
3. Use of Drug Agonists, Partial Agonists and Antagonists in Addiction
4. Overdose reversal
5. Detoxification
6. Drug Substitution
7. Drug Antagonists
8. Aversive pharmacology (disulfiram)
9. Anti-craving agents
10. New Treatments Based on Glutamatergic Transmission
11. New Treatments Based on GABAergic Transmission
12. Synaptic Plasticity in Addiction and Novel Targets

### **Required Readings**

- Kalivas PW, Volkow ND, New medications for drug addiction hiding in glutamatergic neuroplasticity. *Mol Psychiatry*. 2011 Oct;16(10):974-86. doi: 10.1038/mp.2011.46.
- O'Brien CP. Review. Evidence-based treatments of addiction. *Philos Trans R Soc Lond B Biol Sci*. 2008 Oct 12;363(1507):3277-86. doi: 10.1098/rstb.2008.0105.
- Addolorato G, Leggio L, Hopf FW, Diana M, Bonci A. Novel therapeutic strategies for alcohol and drug addiction: focus on GABA, ion channels and transcranial magnetic stimulation. *Neuropsychopharmacology*. 2012 Jan;37(1):163-77. PMID: 22030714

### **Supplemental Readings**

- Lüscher C, Malenka RC (2011): Drug-evoked synaptic plasticity in addiction: from molecular changes to circuit remodeling. *Neuron* 69: 650-663.
- Vocci FJ, Acri J, Elkashef A. Medication development for addictive disorders: the state of the science. *Am J Psychiatry*. 2005 Aug;162(8):1432-40. PMID: 16055764
- Kaplan GB, Heinrichs S, Carey RC (2011). Treatment of addiction and anxiety using extinction approaches: neural mechanisms and their treatment implications, *Pharmacol Biochem Behav* 97:619–625, 2011

## Lecture 9 (November 5): Animal Models of Addiction

**Kathleen Katak, Ph.D.**

*Director Laboratory of Behavioral Neuroscience*

*Department of Psychological and Brain Sciences*

**Summary:** This lecture will explore the methods commonly used to study drug addiction in preclinical animal models ranging from fruit flies to non-human primates. Particular attention is paid to how different phases of the addiction cycle are modeled in animals.

### **Objectives:**

1. To acquire basic knowledge of a variety of behavioral approaches to study drug addiction in animals. This lecture will prepare students for upcoming lectures in which the various behavioral models of addiction are used to study the neurochemistry, neurobiology and pharmacology of addiction.
2. To gain perspectives on the advantages and limitations of each species used in the preclinical assessment of drug addiction.
3. To instill an appreciation for the translational relevance of the addiction cycle, as studied in animals, to the human condition.

### **Outline:**

1. Common behavioral approaches
  - a) Self-Administration
  - b) Conditioned Place Preference
  - c) Intracranial Self-Stimulation
  - d) Conditioned Reinforcement, Tolerance and Withdrawal
2. Model organisms for addiction research
  - a) Drosophila
  - b) Zebrafish
  - c) Mice
  - d) Rats
  - e) Monkeys
3. Modeling the addiction cycle in animals
  - a) Acquisition
  - b) Maintenance
  - c) Escalation
  - d) Extinction
  - e) Relapse/Craving

### **Required Readings:**

- Kuhn BN, Kalivas PW, Bobadilla AC. Understanding Addiction Using Animal Models. *Front Behav Neurosci.* 13:262, 2019.
- Lynch, WJ, Nicholson KL, Dance ME, Morgan RW, Foley PL. Animal Models of Substance Abuse and Addiction: Implications for Science, Animal Welfare, and Society. *Comparative Medicine* 60(3) :177-188, 2010.

### **Suggested Readings:**

- Kaun KR, Devineni AV, Heberlein U. *Drosophila melanogaster* as a model to study drug addiction. *Hum Genet.*131:959-75, 2012.
- Klee EW, Schneider H, Clark KJ, Cousin MA, Ebbert JO, Hooten WM, et al. Zebrafish: a model for the study of addiction genetics. *Hum Genet.*131:977-1008, 2012.
- Fowler CD, Kenny PJ. Utility of genetically modified mice for understanding the neurobiology of substance use disorders. *Hum Genet.*131:941-57, 2012.
- O'Connor EC, Chapman K, Butler P, Mead AN. The predictive validity of the rat self-administration model for abuse liability. *Neurosci Biobehav Rev.*35:912-38, 2011.
- Weerts EM, Fantegrossi WE, Goodwin AK. The value of nonhuman primates in drug abuse research. *Exp Clin Psychopharmacol.* 15:309-27, 2007.
- Koob GF, Ahmed SH, Boutrel B, Chen SA, Kenny PJ, Markou A, et al. Neurobiological mechanisms in the transition from drug use to drug dependence. *Neurosci Biobehav Rev.* 27:739-49, 2004.
- Nic Dhonnchadha BA, Kantak KM. Cognitive enhancers for facilitating drug cue extinction: insights from animal models. *Pharmacol Biochem Behav.* 99:229-44 2011.
- Epstein DH, Preston KL, Stewart J, Shaham Y. Toward a model of drug relapse: an assessment of the validity of the reinstatement procedure. *Psychopharmacology (Berl).* 189:1-16, 2006.
- O'Brien CP, Gardner EL. Critical assessment of how to study addiction and its treatment: human and non-human animal models. *Pharmacol Ther.* 108:18-58, 2005

## **Lecture 10 (November 12): A Trauma-Informed Approach to Substance Use Prevention and Treatment with Latinos(as)**

**Luz M López, PhD, MPH, LCSW**

*Clinical Professor, Associate Director, Dual Degree Program in Social Work & Public Health, Director Global Health Core, Center for Innovation in Social Work and Health, Boston University School of Social Work*

**Summary:** This lecture will examine the relationship between trauma/violence, substance use, and related mental health symptoms. These topics will be analyzed within a socio-cultural context working with Latino/as and other ethnically diverse groups. Utilizing a human rights and resilience framework, we will also explore a community participatory approach to conduct outreach and research among homeless Latino/as survivors of trauma and addiction.

### **Objectives:**

- 1) Identify the connection between addiction, trauma/violence & mental health
- 2) Analyze socio-cultural perspectives, taboos and stigma in the treatment of trauma and addiction among Latinos.
- 3) Describe two effective evidenced based trauma intervention models for substance use treatment.
- 4) Illustrate ways to increase access to trauma informed prevention and substance use services for Latino/as and other ethnically diverse groups.

### **Outline:**

- I. Addiction opioid crisis among Latino/as
- II. Substance use myths and controversies
- III. Addiction: cultural taboos and stigma
- IV. Strategies for outreach and research with homeless Latino/as with addiction using a community participatory approach
- V. Discuss the application of three evidenced based trauma informed interventions
  - a. Seeking Safety, Lisa Najavitz
  - b. Trauma Recovery Empowerment Model (TREM) by Maxine Harris & M-TREM, Trauma Recovery Empowerment Model for Men by Roger Falot & Maxine Harris
- VI. Small groups case discussion

### **Suggested Readings:**

- Alegría, M., Page, B.J., Hansen, H., Cauce, A.M., Robles, R., Blanco, C., Cortés, D.E., Amaro, H., Morales, A., Berry, P. (2006). Improving drug treatment services for Hispanics: Research gaps and scientific opportunities. *Drug and Alcohol Dependence*, 84(Supplement 1), 76-84.
- Falot, R. D., & Harris, M. (2002). The Trauma Recovery and Empowerment Model (TREM): Conceptual and practical issues in a group intervention for women. *Community Mental Health Journal*, 38, 475-485.



-Najavits, LM (2017; revised edition 2019). *Finding Your Best Self. Recovery from Addiction, Trauma or Both*. New York: The Guilford Press

-Najavits, LM, Krinsley, K., Waring, M. E., Gallagher, M. W., & Skidmore, W. (2018). A randomized controlled trial for veterans with PTSD and substance use disorder: Creating Change versus Seeking Safety. *Substance Use and Misuse*, doi: 10.1080/10826084.2018.1432653.

-Najavits, LM, Krinsley, K., Waring, M. E., Gallagher, M. W., & Skidmore, W. (2018). A randomized controlled trial for veterans with PTSD and substance use disorder: Creating Change versus Seeking Safety. *Substance Use and Misuse*, doi: 10.1080/10826084.2018.1432653

-Roberts, NP, Roberts, PA, Jones, N, Bisson, JI (2016). Psychological therapies for post-traumatic stress disorder and comorbid substance use disorder. *Cochrane Database Syst Rev*. 2016 Apr 4: CD010204. doi: 10.1002/14651858.CD010204.pub2. Review. PMID: 27040448

## **Lecture 11 (November 19): Neonatal Abstinence Syndrome – Presentation, Treatment, and Emerging Research**

**Elisha Wachman, MD**

*Associate Professor of Pediatrics*

*Division of Neonatology, Boston Medical Center*

*Boston University School of Medicine*

**Summary:** This lecture will review the diagnosis, assessment, and current treatment approaches for neonatal abstinence syndrome (NAS) / Neonatal Opioid Withdrawal Syndrome (NOWS) secondary to in-utero opioid exposure. This will include a review of both non-pharmacologic and pharmacologic treatment strategies, and new research contributing to NAS outcomes.

### **Objectives:**

1. Learners will be able to identify signs and symptoms of NAS, and ways to assess NAS.
2. Learners will understand the existing treatment approaches, both non-pharmacologic and pharmacologic, to NAS.
3. Learners will be able to identify some contributors to NAS outcomes.

### **Outline:**

1. Definition and epidemiology of NAS
2. NAS symptoms and assessment tools
3. Clinical variables affecting NAS presentation and outcomes
4. Non-Pharmacologic Management of NAS

5. Pharmacologic Treatment of NAS
6. Emerging research – predictors of NAS outcomes
7. Long-term outcomes

#### **Required Readings:**

- 1) Wachman EM, Schiff DM, Silverstein M. Neonatal Abstinence Syndrome: Advances in Diagnosis and Treatment.(review) *JAMA*, 319(13):1362-1374.
- 2) Wachman EM, Grossman M, Schiff DM, Philipp B, Minear S, Hutton E, Saia K, Nikita F, Khattab A, Nolin A, Alvarez C, Barry K, Combs G, Stickney D, Driscoll J, Humphreys R, Burke J, Farrell C, Shrestha H, Whalen BL. Quality Improvement Initiative to Improve Inpatient Outcomes for Neonatal Abstinence Syndrome. *J Perinatology*, 2018; May 8.
- 3) PNQIN NAS Toolkit, available on-line at: <https://www.neoqicma.org/sen-toolkit> (Password is “pnqin2018”).

#### **Suggested Readings:**

- 1) Davis JM, Shenberger J, Terrin N, Breeze J, Hudak M, Silverstein M, Wachman EM, et al. Methadone versus Morphine in the Treatment of Neonatal Abstinence Syndrome: A Randomized Comparison Trial. *JAMA Pediatrics*, 2018, Jun 18. doi: 10.1001/jamapediatrics.2018.1307.
- 2) MacMillan KDL, Rendon CP, Verma K, et al. Association of Rooming-in With Outcomes for Neonatal Abstinence Syndrome: A Systematic Review and Meta-analysis. *JAMA Pediatr*, 2018; 172(4): 345-351.

**NO CLASS (November 28) – Thanksgiving vacation**

## **Lecture 12 (December 3): The Politics of Addiction Prevention: From Tobacco to Alcohol to Cannabis**

**David Jernigan, PhD**

*Professor, Department of Health Law, Policy and Management  
Boston University School of Public Health*

**Summary:** This session will explore the politics of policy making in the addiction field, focusing primarily on alcohol policy. The leading drugs of addiction for young people in the U.S. are tobacco, alcohol and cannabis. All three are increasingly in the hands of industries whose primary responsibility is return of profit to owners and shareholders rather than prevention of addiction. Based on 35 years of work on alcohol policies, the lecture will begin by reviewing prevalence of drug use among youth, and then focus on the policies shown most effective in preventing youth alcohol use. Examples will be drawn both from public health and policy

research into the structure and activities of the alcohol industry, and its efforts to influence alcohol policy making, up through the COVID-19 pandemic. It will address the role of research in policy development in the field of addiction prevention, and describe industry efforts to shape and counter that research.

**Objectives:** At the end of the session, students will be able to:

1. Describe the policies most effective in reducing youth alcohol use;
2. Articulate and illustrate key conflicts of interest in addiction policy-making, with particular reference to alcohol;
3. Understand the implications of the alcohol and tobacco experiences for cannabis policy-making.

**Outline:**

1. Overview of youth drug use
2. CDC and WHO recommendations for the reduction and prevention of alcohol-related harm, including youth alcohol use
3. Structure of consumption of alcohol and alcohol industry conflicts of interest
  - a. Case studies in conflict of interest in alcohol research
4. Review of the structure and tactics of the alcoholic beverage industry
  - a. Industry concentration
  - b. Implications of concentration for policy making
  - c. Use of social aspects organizations
  - d. Case studies in alcohol industry efforts to influence policy
5. Public health responses
6. Implications for cannabis policy

**Required Readings:**

- Jernigan D, Ross CS. The Alcohol Marketing Landscape: Alcohol Industry Size, Structure, Strategies, and Public Health Responses. *J Stud Alcohol Drugs Suppl.* 2020 Mar; Sup 19:13-25.
- Jernigan DH, Trangenstein PJ. What's next for WHO's global strategy to reduce the harmful use of alcohol? *Bulletin of the World Health Organization* 98(3):222-223, 2020. Available at <https://www.who.int/bulletin/volumes/98/3/19-241737/en/>
- Jernigan, D. Global alcohol producers, science and policy: The case of the International Center for Alcohol Policies. *American Journal of Public Health* 102(1):80-89, 2012.

**Student Presentations – December 3**

**Final Exam – December 17**