The Cycle of Drug Addiction: Consumption, Withdrawal, and Relapse

Current Topics in Neuroscience

NROD60H3

(Friday 10:00-12:00 pm; MW 264)

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COURSE DESCRIPTION

This course is designed to provide an overview of current topics in the field of drug addiction research, with a specific focus on the major phases of the addiction cycle, including drug use (intoxication), withdrawal, and relapse. Consideration will be given to what basic motivational and corresponding neurobiological processes influence behavior during the various phases of the addiction cycle, by examining the empirical findings within the context of some of the major theoretical models guiding the field. A series of seminars, led by students, will highlight recent and exciting advances in the field, and will emphasize complimentary work carried out in human subjects and laboratory animals. In addition to leading a seminar, students will develop a research proposal based on their seminar topic. These two assignments are intended to provide students with the opportunity to engage in an in-depth exploration and critical analysis of a relevant topic in the field of addiction research, and to consider the implications of the literature for future research.

SUMMARY OF COURSE COMPONENTS AND EVALUATION

	Percent of final grade
Seminar	35
Thought papers	15
Class participation	10
Research Proposal	40

Note: Information on individual course components are provided at the end of this document.

SCHEDULE OF LECTURES/ SEMINARS

Week 1 Sept 11	**INTRODUCTION AND OVERVIEW**
Week 2 Sept 18	**LECTURE** *The reinstatement procedure: A model of relapse that encompasses the cycle of addiction*
Week 3 Sept 25	**DISCUSSION** *Discussion of Week 2 Lecture material and assigned readings. Discussion will be based on student responses to a series of questions that will be assigned at the end of class Sept 18.*
Week 4 Oct 2	**LECTURE** *Guidelines for seminars and research proposal assignment*
Week 5 Oct 9	**LIBRARY WORKSHOP**
Week 6 Oct 16	**STUDENT SEMINARS** *Patterns of drug self-administration associated with the development of dependence: Animal studies*
Week 7 Oct 23	**STUDENT SEMINARS** *Role of conditioning factors in drug craving and relapse: Animal studies*
Week 8 Oct 30	**STUDENT SEMINARS** *Role of conditioning factors in drug craving and relapse: Human studies*
Week 9 Nov 6	**STUDENT SEMINARS** *Role of stress in drug craving and relapse: Animal studies*
Week 10 Nov 13	**STUDENT SEMINARS** *Role of stress in drug craving and relapse: Human studies*
Week 11 Nov 20	**STUDENT SEMINARS** *Stimulant sensitization and relationship to reinstatement: Animal studies*
Week 12 Nov 27	**STUDENT SEMINARS** *Rate of drug administration and susceptibility to sensitization: Animal studies*

ASSIGNED READINGS

*****Students are responsible for finding, downloading, and reading all articles in advance of each class. The links to the articles can be found by searching the PubMed data base (http://www.ncbi.nlm.nih.gov/pubmed/).*****

Week 2

Sept 18 *The reinstatement procedure: A model of relapse that encompasses the cycle of addiction*

Assigned readings (Weeks 2 and 3)

Koob GF. Neurobiological substrates for the dark side of compulsivity in addiction. Neuropharmacology. 2009;56 Suppl 1:18-31.

Robinson TE, Berridge KC. Review. The incentive sensitization theory of addiction: some current issues. Philos Trans R Soc Lond B Biol Sci. 2008 Oct 12;363(1507):3137-46.

Shaham Y, Shalev U, Lu L, De Wit H, Stewart J. The reinstatement model of drug relapse: history, methodology and major findings. Psychopharmacology (Berl). 2003 Jul;168(1-2):3-20.

Week 6

Oct 16 *Patterns of drug self-administration associated with the development of dependence: Animal studies*

Assigned readings

Ahmed SH, Kenny PJ, Koob GF, Markou A (2002) Neurobiological evidence for hedonic allostatsis associated with escalating cocaine use. Nature Neuroscience, 5: 625-6.

Ahmed SH, Walker JR, Koob GF. (2000) Persistent increase in the motivation to take heroin in rats with a history of drug escalation. Neuropsychopharmacology, 22: 413-421.

Ahmed SH, Koob GF. Changes in response to a dopamine receptor antagonist in rats with escalating cocaine intake. Psychopharmacology (Berl). 2004 Apr;172(4):450-4.

Ahmed SH, Lin D, Koob GF, Parsons LH. Escalation of cocaine self-administration does not depend on altered cocaine-induced nucleus accumbens dopamine levels. J Neurochem. 2003; 86(1):102-13.

Week 7
Oct 23 *Role of conditioning factors in drug craving and relapse: Animal studies*

Assigned Readings

Grimm JW, Hope BT, Wise RA, Shaham Y. Neuroadaptation. Incubation of cocaine craving after withdrawal. Nature. 2001 Jul 12;412(6843):141-2.

Lu L, Grimm JW, Dempsey J, Shaham Y. Cocaine seeking over extended withdrawal periods in rats: different time courses of responding induced by cocaine cues versus cocaine priming over the first 6 months. Psychopharmacology (Berl). 2004 Oct;176(1):101-8.

Tran-Nguyen LT, Fuchs RA, Coffey GP, Baker DA, O'Dell LE, Neisewander JL. Time-dependent changes in cocaine-seeking behavior and extracellular dopamine levels in the amygdala during cocaine withdrawal. Neuropsychopharmacology. 1998 Jul;19(1):48-59.

Week 8
Oct 30 *Role of conditioning factors in drug craving and relapse: Human studies*

Assigned Readings

Goldstein RZ, Tomasi D, Alia-Klein N, Honorio Carrillo J, Maloney T, Woicik PA, Wang R, Telang F, Volkow ND (2009) Dopaminergic response to drug words in cocaine addiction. Journal of Neuroscience, 29: 6001-6006.

Langleben DD, Ruparel K, Elman I, Busch-Winokur S, Pratiwadi R, Loughead J, O'Brien CP, Childress AR (2008) Acute effect of methadone maintenance dose on brain FMRI response to heroin related cues. Am J Psychiatry. 165: 390-4.

Volkow ND, Fowler JS, Wang GJ, Baler R, Telang F (2008) Imaging dopamine's role in drug abuse and addiction. Neuropharmacology, 56 (Suppl 1): 3-8.

Volkow ND, Wang GJ, Telang F, Fowler JS, Logan J, Childress AR, Jayne M, Ma Y, Wong C. (2008) Dopamine increases in striatum do not elicit craving in cocaine abusers unless they are coupled with cocaine cues. Neuroimage, 39:1266-73.

Week 9
Nov 6 *Role of stress in drug craving and relapse: Animal studies*

Assigned Readings

Shalev U, Highfield D, Yap J, Shaham Y. Stress and relapse to drug seeking in rats: studies on the generality of the effect. Psychopharmacology (Berl). 2000 Jun;150(3):337-46.

Shalev U, Morales M, Hope B, Yap J, Shaham Y. Time-dependent changes in extinction behavior and stress-induced reinstatement of drug seeking following withdrawal from heroin in rats. Psychopharmacology (Berl). 2001 Jun;156(1):98-107.

Sorge RE, Stewart J. The contribution of drug history and time since termination of drug taking to footshock stress-induced cocaine seeking in rats. Psychopharmacology (Berl). 2005 Dec;183(2):210-7.

Week 10
Nov 13 *Role of stress in drug craving and relapse: Human studies*

Assigned Readings

Sinha R, Lacadie C, Skudlarski P, Fulbright RK, Rounsaville BJ, Kosten TR, Wexler BE (2005) Neural activity associated with stress-induced cocaine craving: a functional magnetic resonance imaging study. Psychopharmacology 183:171-80.

Sinha R, Garcia M, Paliwal P, Kreek MJ, Rounsaville BJ (2006) Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. Arch Gen Psychiatry, 63:324-31.

Fox HC, Hong KI, Siedlarz K, Sinha R (2008) Enhanced sensitivity to stress and drug/alcohol craving in abstinent cocaine-dependent individuals compared to social drinkers. Neuropsychopharmacology. 33:796-805.

Week 11
Nov 20 *Stimulant sensitization and relationship to reinstatement: Animal studies*

Assigned Readings

Ahmed SH, Cador M. (2006) Dissociation of psychomotor sensitization from compulsive cocaine consumption. Neuropsychopharmacology, 31:563-71.

De Vries TJ, Schoffelmeer AN, Binnekade R, Raasø H, Vanderschuren LJ (2002) Relapse to cocaine- and heroin-seeking behavior mediated by dopamine D2 receptors is time-dependent and associated with behavioral sensitization. Neuropsychopharmacology, 26:18-26.

Lenoir M, Ahmed SH (2007) Heroin-induced reinstatement is specific to compulsive heroin use and dissociable from heroin reward and sensitization. Neuropsychopharmacology, 32: 616-24.

Week 12
Nov 27 *Rate of drug administration and susceptibility to sensitization: Animal studies*

Assigned Readings

Samaha AN, Li Y, Robinson TE. The rate of intravenous cocaine administration determines susceptibility to sensitization. J Neurosci. 2002 Apr 15;22(8):3244-50.

Samaha AN, Mallet N, Ferguson SM, Gonon F, Robinson TE. The rate of cocaine administration alters gene regulation and behavioral plasticity: implications for addiction. J Neurosci. 2004 Jul 14;24(28):6362-70.

Samaha AN, Yau WY, Yang P, Robinson TE. Rapid delivery of nicotine promotes behavioral sensitization and alters its neurobiological impact. Biol Psychiatry. 2005 Feb 15;57(4):351-60.

DESCRIPTION OF COURSE COMPONENTS

SEMINAR **35% of final grade**

Scheduling

Each student will participate in leading a seminar on one of the 7 topics scheduled between Weeks 6 and 12 (Oct 14 to Nov 25) of the course. Two to four students will participate in each of the seminars. During class on Week 3 (Sept 25), students will be asked to submit a first, second, and third choice for which seminar they wish to participate in. Students wishing to be assigned to the same seminar group should submit one request under both/all names. By Week 4 (Oct 2), seminar assignments will be posted on the intranet.

Content

Each group assigned to a particular seminar topic will be responsible for providing a presentation based on the assigned readings (listed above), and leading a class discussion. Each group will be given 90 min for their presentation (including discussion time). As a group, students may chose to give a series of relatively independent presentations (i.e., they may divide the time equally between/among members), or they may chose to prepare a more integrated presentation. Either way, the seminar should be organized as a group, with an emphasis on the themes/concepts/questions that relate the individual papers. That is, the seminar as a whole should reflect a cohesive conceptual framework. In addition, an effort should be made to relate the material back to the main theme of the course, "The cycle of addiction". That is, an effort should be made to identify how the material is relevant to informing our understanding of the various phases of the addiction cycle (drug use, withdrawal, and relapse).

THOUGHT PAPERS **15% of final grade (5% per paper)**

For 3 of the 7 seminar topics, students will be required to write a "thought" paper of no more than 250 words, describing one central idea, theme, problem, or question that relates the articles assigned for that topic. Students may chose which 3 topics they wish to write on; however, the choices must not include the topic the student is presenting on. Thought papers are due at the start of the class corresponding to that seminar topic**. Late papers or electronic submissions will be accepted only under exceptional circumstances (see H1N1 statement below).**

CLASS PARTICIPATION **10% of final grade**

Students will be graded for attendance and participation in class discussion. A major factor in this component of the evaluation will be the quality of participation; students' contributions should reflect a good level of familiarity with and comprehension of assigned readings.

RESEARCH PROPOSAL **40% of final grade**

Students will write a research proposal, based on a question they develop from their seminar topic. More information about the research proposal will be provided in class on Oct 2. In addition, a library workshop will be held on Oct 9 to provide students with an overview of the most useful search engines/data bases in Neuroscience and strategies/tips for conducting effective literature searches.

Evaluation of the research proposal will be based on the originality and quality of the research question/s, identification and synthesis of the relevant literature (including scope and currency of the literature review), appropriateness and feasibility of the proposed experiment/s (including experimental design), and general stylistic and formatting considerations. Students are strongly encouraged to meet with Professor Erb during office hours (or by appointment) to obtain guidance in the development of proposals.

Final proposals should follow the stylistic guidelines for the Journal of Neuroscience (more information on this will be provided in class Oct 2) and include the following section headings and corresponding content:

Title page

Abstract **(maximum 250 words or 1 double-spaced page)**

The abstract should provide a brief overview of your proposal, including brief statements of background/rationale, objectives and hypotheses, methods, and predicted results.

Introduction **(maximum 1000 words or 4 double-spaced pages)**

This section should provide a brief review and synthesis of the relevant literature, with the key objective of developing the rationale for the proposed experiment/s. The section should conclude with clear statements about your research objectives and hypotheses. In addition to the articles assigned to your seminar topic, a minimum of 10 additional articles from the *primary literature* should be included in your literature review; the majority of these articles (at least 6) should have been published in the last 5 years.

Methods **(maximum 750 words or 3 double-spaced pages)**

This section should be written in the future tense and include relevant subsections (e.g., subjects, drugs, apparatus, procedures, etc). It should include a *very clear description* of your research design, including the nature and number of experimental groups and how many subjects will be included in each group.

Results **(maximum 500 words or 2 double-spaced page)**

Your results section should provide a succinct description of what you anticipate your experimental findings to be (you are not required to discuss methods of statistical analysis, although you may chose to do so). *Do not* include graphs with hypothetical data; rather, describe in words the specific differences in the direction of the dependent measure(s) that you expect to observe between experimental groups.

References **(no restrictions but must be formatted according to the Journal of Neuroscience)**

Papers are due Wednesday December 2, 4:30 pm, in Professor Erb's office. Late or electronic submissions will not be accepted except in exceptional circumstances (see H1N1 statement below).

BLACKBOARD

This course will be organized and managed using the *Blackboard* system. A link to the website is provided on the intranet course page. Students are required to obtain a UTORID in order to access the page.

ACCESSABILITY STATEMENT

Students with diverse learning styles and needs are welcome in this course. In particular, if you have a disability/health consideration that may require accommodations, please feel free to approach me and/or the AccessAbility Services Office as soon as possible. I will work with you and AccessAbility Services to ensure you can achieve your learning goals in this course. Enquiries are confidential. The UTSC AccessAbility Services staff (located in S302) are available by appointment to assess specific needs, provide referrals and arrange appropriate accommodations (416) 287-7560 or ability@utsc.utoronto.ca.

H1N1 STATEMENT

Students are advised to consult the university's preparedness site (http://www.preparedness.utoronto.ca) for information and regular updates regarding procedures relating to H1N1 planning and individual student responsibilities.