BIOGRAPHICAL SKETCH

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NAME: Stephen J. Kohut

eRA COMMONS USER NAME (credential, e.g., agency login): STEPHEN.KOHUT

POSITION TITLE: Assistant Professor of Psychiatry, Harvard Medical School; Director, Behavioral Neuroimaging Laboratory, McLean Hospital

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
La Salle University, Philadelphia, PA	B.A.	05/2003	Psychology
Loyola College in Maryland, Baltimore, MD	M.S.	05/2003	Clinical Psychology
NIDA-IRP/NIH, Baltimore, MD	Clin. Externship	05/2005	Clinical Psychopharm.
American University, Washington, D.C.	Ph.D.	10/2009	Experimental Psych.
NIDA-IRP/NIH, Baltimore, MD	Post-Doctoral	04/2011	Medications Discovery

A. Personal Statement

Stephen J. Kohut, PhD, focuses his research primarily on two main interacting lines of investigation: understanding how alterations in underlying neurobiology alter behavioral responses to drugs, especially stimulants and opioids, and medications discovery for drug abuse and addiction.

Dr. Kohut's current research, funded by several awards from the National Institute on Drug Abuse, combines behavioral pharmacology with cutting-edge neuroimaging methodologies to understand the neural consequences of drug-taking behavior and the extent to which they can be mitigated by behavioral and pharmacological interventions.

Supporting peer reviewed publications:

1. Bardo MT, Denehy ED, Hammerslag LR, Dwoskin LP, Blough BE, Landavazo A, Bergman J, **Kohut SJ** (2019). Effects of methamphetamine isomers on d-methamphetamine self-administration and food-maintained responding in male rats. *Psychopharmacology*, in press. PMID: 31346628
2. **Kohut SJ**, Hiranita T, Hong SK, Ebbs AL, Tronci V, *et al* (2014). Preference for distinct functional conformations of the dopamine transporter alters the relationship between subjective effects of cocaine and stimulation of mesolimbic dopamine. *Biol Psychiatry*, 76(10): 802-809. PMID: 24853388
3. **Kohut SJ,** Bergman J, Blough BE (2016). Effects of l-methamphetamine treatment on cocaine-and food-maintained behavior in rhesus monkeys. *Psychopharmacology*, 233(6): 1067-1075. PMID: 26713332

B. Positions and Honors

Positions

2003-2005 Research Associate, The Johns Hopkins School of Medicine, Baltimore, MD
2005 Guest Researcher, Office of the Clinical Director, NIDA-IRP/NIH/DHHS, Baltimore, MD
2005-2009 Graduate Student Researcher, Dept. of Psychology, American Univ., Washington, DC

2006-2007 Lecturer, Dept. of Psychology, George Washington Univ., Washington, DC
2006-2010 Guest Researcher, The Johns Hopkins School of Medicine, Baltimore, MD
2009 Lecturer, Dept. of Psychology, American University, Washington, DC
2009-2011 Fellow, Medications Discovery Research Branch, NIDA-IRP/NIH/DHHS, Baltimore, MD
2011-2016 Instructor, Harvard Medical School, Boston, MA
2011-2016 Research Psychologist, McLean Hospital. Belmont, MA
2016-Present Assistant Professor of Psychiatry, Harvard Medical School, Boston, MA
2016-Present Associate Psychobiologist, McLean Hospital, Belmont, MA
2018-Present Assistant Professor (Affiliate), Center for Drug Discovery, Northeastern Univ., Boston, MA
2019-Present Director, Behavioral Neuroimaging Laboratory, McLean Hospital

Honors

2008 NIDA "Sex and Gender Differences" Travel Award – College on Problems of Drug Dependence
2012 NIDA/NIAAA Early Career Investigator Travel Award – American Psychological Association
2014 Young Scientist Travel Award – American Society for Pharmacology and Exp. Therapeutics
2019 Maharaj Ticku Memorial Travel Fellowship for New Investigators, Behavior, Biology, and Chemistry Translational Research in Addiction
2019 Joseph Cochin Young Investigator Award, College on Problems of Drug Dependence

C. Contributions to Science

URL to full list of published work: http://www.ncbi.nlm.nih.gov/pubmed/?term=Kohut+SJ

1) *Norepinephrine-preferring monoamine releasers as candidate medications for stimulant use disorder in nonhuman primates and rodents.* Monoamine releasers with prominent dopaminergic actions, i.e., d-methamphetamine (d-MA) significantly reduce cocaine use and craving in clinical and preclinical laboratory studies. However, d-MA and related drugs are highly abused, which limits their acceptability as agonist replacement medications for substance use disorder. The L-isomer of methamphetamine (l-MA), unlike d-MA, has preferential noradrenergic actions and is used medicinally with low, if any, abuse liability. We conducted studies in nonhuman primates and rodents to determine whether l-MA may have advantages over d-MA as a candidate agonist medication for cocaine use disorder. These studies found that l-MA shares discriminative stimulus effects with cocaine and nearly eliminates cocaine self-administration with minimal effects on food-maintained behavior. Follow-up studies have recently found that l-MA is self-administered to a lesser extent and has considerably reduced stimulant-like effects compared with d-MA. These studies have encouraged other investigators to evaluate the behavioral effects of l-MA for other indications (e.g., antinociception, ADHD). My contribution to this work was as the lead in all phases of experimental design, data collection and analysis, and manuscript writing.

1. **Kohut SJ,** Bergman J, Blough BE (2016). Effects of l-methamphetamine treatment on cocaine-and food-maintained behavior in rhesus monkeys. *Psychopharmacology*, 233(6): 1067-1075. PMID: 26713332
2. **Kohut SJ**, Jacobs DS, Rothman RB, Partilla JS, Bergman J, Blough BE (2017). Cocaine-like discriminative stimulus effects of "norepinephrine-preferring" monoamine releasers: time course and interaction studies in rhesus monkeys. *Psychopharmacology*, 234(23-24): 3455-3465. PMID: 28889212
3. Bardo MT, Denehy ED, Hammerslag LR, Dwoskin LP, Blough BE, Landavazo A, Bergman J, **Kohut SJ** (2019). Effects of methamphetamine isomers on d-methamphetamine self-administration and food-maintained responding in male rats. *Psychopharmacology*, in press. PMID: 31346628

2) *In vivo pharmacology and neurochemistry of atypical dopamine uptake inhibitors in rodents.* The dopamine system has been the primary target for the development of stimulant abuse medications. However, as described above, most drugs that act as dopamine indirect agonists, produce stimulant-like effects, including increased locomotor activity and reinforcing effects. Atypical dopamine-uptake inhibitors (DUIs) bind to the dopamine transporter but appear to have low abuse potential and do not produce stimulant-like effect suggesting that they may serve as leads for the development of stimulant-abuse treatments. We conducted studies in rodents to evaluate the ability of atypical DUIs to decrease cocaine and methamphetamine self-administration and their ability to increase extracellular dopamine in the nucleus accumbens. These studies found that atypical DUIs can decrease cocaine and methamphetamine self-administration across a range of doses. Further, atypical DUIs increase dopamine levels similar to those of typical DUIs such as cocaine. However, increased dopamine by

atypical DUIs is not associated with cocaine-like behavioral effects. The results of these studies have stimulated interest in identifying compounds that bind atypically to the dopamine transporter as candidate medications for stimulant abuse and several new generations of compounds have now been developed. My role in these studies was in data collection, discussion of data interpretation, and writing and editing drafts of manuscripts. In microdialysis studies, my role was in experimental design, data collection and analysis, and manuscript writing.

1. Hiranita T, Soto PL, **Kohut SJ**, Kopajtic TA, Cao J, Newman AH, (2011). Decreases in cocaine self-administration with dual inhibition of dopamine transporter and {sigma} receptors. *J Pharmacol Exp Ther.* 339(2): 662-677. PMID: 21859929
2. Hiranita T, **Kohut SJ**, Soto PL, Tanda G, Kopajtic TA, Katz JL (2014). Preclinical efficacy of N-substituted benztropine analogs as antagonists of methamphetamine self-administration in rats. *J Pharmacol Exp Ther,* 348(1): 174-191. PMID: 24194527
3. **Kohut SJ**, Hiranita T, Hong SK, Ebbs AL, Tronci V, *et al* (2014). Preference for distinct functional conformations of the dopamine transporter alters the relationship between subjective effects of cocaine and stimulation of mesolimbic dopamine. *Biol Psychiatry*, 76(10): 802-809. PMID: 24853388

3) *Behavioral economic demand analysis to investigate strength of drug reinforcers*. There has been a long-standing need in behavioral pharmacology to develop and refine procedures to quantify the relative reinforcing strength of various reinforcers that could facilitate their comparison. Our studies were among the first to utilize the Exponential Model of Demand to compare the reinforcing strength of cocaine and food. These studies compared cocaine self-administration in two different inbred rat strains that show differential levels of drug intake. These results showed that the Essential Value of cocaine is greater in Fischer (F344) compared to Lewis rats and Essential Value for food was greater in Lewis compared to F344 rats. However, Essential Value for food was greater than cocaine for both strains suggesting that the reinforcing strength of food is greater than for cocaine. These studies have stimulated research into food reinforcement and obesity and have served as an important finding in developing theories of addiction and underscores the need to use nondrug reinforcers as an important comparison in drug studies. Recently, I have extended my work studying demand for reinforcers in nonhuman primates in several new directions: 1) I completed a study comparing demand for several amphetamine-like compounds with distinct pharmacological profiles, 2) I used demand analysis to quantify changes to the reinforcing strength of drugs of abuse before and during treatment with several candidate medications, 3) I used demand analysis to study the reinforcing effects of nicotine. The nicotine studies included an analysis of several doses, the effects of extended nicotine self-administration history, and comparison with cocaine and food. Recent studies have further extended this work by using demand analysis to evaluate alterations in the reinforcing effects of nicotine during and following termination of chronic nicotine treatment. A manuscript describing this work is currently in preparation.

1. **Kohut SJ**, Bergman J (2016). Reinforcing effectiveness of nicotine in nonhuman primates: effects of nicotine dose and history of nicotine self-administration. *Psychopharmacology*; 233(13):2451-8. PMID: 27076210
2. Christensen CJ, **Kohut SJ**, Handler SL, Silberberg A, Riley AL (2009). Demand for food and cocaine in Fischer and Lewis rats. *Behav Neurosci*; 123(1):165-71. PMID: 19170441
3. Freeman KB, Kearns DN, **Kohut SJ**, Riley AL (2009). Strain differences in patterns of drug-intake during prolonged access to cocaine self-administration. *Behav Neurosci*; 123(1):156-64. PMID: 19170440

4) *Characterizing alterations in the abuse-related effects of drugs by environmental stressors.* It has long been known that exposure to various environmental stressors can alter behavioral responses to drugs of abuse and that stressors activate similar neural pathways. However, little is known about how stressors alter the discriminative stimulus effects of drugs such as cocaine. In a series of studies, we found that exposure to various types of stressors, or environmental enrichment, differentially alters the discriminative stimulus effects of cocaine and that those changes are accompanied by distinct alterations in monoaminergic systems. The results of these studies have informed several high impact studies about how changes to dopamine transporters, for example, alters responses to cocaine and has been extended to other drugs, such as nicotine and ethanol. These studies comprised a large component of my graduate school dissertation. As such, my contribution was as the lead in all phases of experimental design, data collection and analysis, and manuscript writing.

1. **Kohut SJ**, Roma PG, Davis CM, Zernig G, Saria A, Dominguez JL, Rice KC, Riley AL (2009). The impact of early environmental rearing conditions on the discriminative stimulus effects and FOS expression induced by cocaine in adult male and female rats. *Psychopharmacology*, 203(2):383-97. PMID: 18953528
2. **Kohut SJ**, Decicco-Skinner K, Johari S, Hurwitz ZE, Baumann MH, Riley AL, (2012). Differential modulation of cocaine's discriminative cue by repeated and variable stress exposure: Relation to monoamine transporter levels. *Neuropharmacology*, 63(2): 330-337. PMID: 22516586
3. **Kohut SJ**, Riley AL. The effects of home-cage access to a sweet solution on the discriminative stimulus effects of cocaine. *Behav Pharmacol* 21; 241-245. PMID: 20445440

5) *Medications evaluation for nicotine and nicotine + cocaine polydrug abuse.* The concurrent use of nicotine and cocaine is a prevalent form of substance abuse and yet, no systematic evaluations of potential medications to combat this form of addiction had been conducted. Our studies sought 1) to characterize the potential interactive reinforcing effects of nicotine and cocaine that leads to increased intake when combined and 2) to evaluate medications that may attenuate this effect. These studies found that combinations of nicotine and cocaine are self-administered to a greater extent that either drug alone. Further, medications such as varenicline and bupropion produce behaviorally selective reductions in drug intake. The results of these studies suggest that these or similar medications may offer viable approaches for the management of nicotine + cocaine polydrug addiction. I was directly responsible for scientific progress including experimental design, dose selection, data collection and analysis and I also contributed to manuscript writing.

1. Jacobs DS, Barkin CE, Kohut MR, Bergman J, **Kohut SJ** (2017). Effects of lorcaserin (Belivq) on nicotine- and food-maintained responding in non-human primates. *Drug Alcohol Depend,* 10; 181-194.
2. Mello NK, Fivel PA, **Kohut SJ**, (2013). Effects of chronic buspirone treatment on nicotine and concurrent nicotine + cocaine self-administration *Neuropsychopharmacol,* 38(7): 1264-1275. PMID: 23337868
3. Mello NK, Fivel PA, **Kohut SJ**, Carroll FI (2014). Effects of chronic varenicline treatment on nicotine, cocaine, and concurrent nicotine + cocaine self-administration. *Neuropsychopharmacol*, 39(5): 1222-31. PMID: 24304823
4. **Kohut SJ**, Bergman J (2016). Reinforcing effectiveness of nicotine in nonhuman primates: effects of nicotine dose and history of nicotine self-administration. *Psychopharmacology*; 233(13):2451-8. PMID: 27076210

D. Additional Information: Research Support and/or Scholastic Performance

K01 DA039306 Kohut (PI) 04/01/15-03/31/2020
NIH/NIDA
Translational Models of Brain Activation Patterns During Nicotine Self-Administration and Reinstatement
The research goal of this grant is to develop and characterize the neurobiological correlates of drug addiction by utilizing phMRI analysis in awake, behaving nonhuman primates to aid in the development of more effective treatment strategies to facilitate treatment approaches.
Role: PI

R01 DA047130 Booth, Kohut (PI) 03/01/15-02/29/2019
NIH/NIDA
Delineating the role of serotonin 5-HT2 receptors in opioid use disorders: Development of novel 5-HT modulators with translational studies in rodents and primates
The goal of this research is to identify and evaluate novel serotonin-based medications for the treatment of opioid use disorder
Role: MPI

R01 DA048150 Kohut (PI) 03/01/15-02/29/2019
NIH/NIDA
Synthetic Psychoactive "Bath Salt" Effects on Brain Activity and Behavior
The goal of this proposal is to identify patterns of brain activation induced by methamphetamine, MDMA, and various synthetic cathinones with diverse pharmacological activity.

Role: PI

R01 DA047575 Bergman, Kohut, Kangas, Spealman (PI) 03/01/15-02/29/2019
NIH/NIDA
Neural, cognitive and abuse-related consequences of chronic THC exposure during adolescence in nonhuman primates

The goal of this proposal is to determine how THC exposure during adolescence alters behavioral and neural indices in adulthood.

Role: MPI