BIOGRAPHICAL SKETCH

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NAME: Janes, Amy C.

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POSITION TITLE: Director, Functional Integration of Addiction Research Laboratory
Assistant Professor, Harvard Medical School

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
Rutgers University New Brunswick, NJ	B.A.	05/2001	Psychology/Biology
Boston University Boston, MA	M.A.	05/2003	Psychology
Boston University Boston, MA	Ph.D.	05/2007	Psychology
McLean Hospital, Belmont, MA	Post-doc	11/2009	Neuroimaging

A. Personal Statement

I have extensive experience studying the neurobiology of substance abuse disorders. My early research focused on preclinical models of addiction including the molecular processes underlying cocaine cue-reactivity, while my more recent work, centers on clinical neuroimaging studies of addiction. I currently direct the Functional Integration of Addiction Research Laboratory and the Mclean Hospital Imaging center. My lab uses multi-modal neuroimaging techniques to understand how neurobiological disruptions contribute to relapse vulnerability and how individual factors impact the brain and treatment outcome. Such factors include biological variation such as sex, psychiatric influences such as co-morbid disorders, and differences in cognitive aspects such as reward-function and reactivity to conditioned stimuli. I received a 2019 Presidential Early Career Award for Scientists and Engineers award, which is the highest honor bestowed by the United States Government to scientists beginning their independent research careers.

B. Positions and Honors

Professional experience

1996-2001 (May-August): Lab Assistant, Environmental Science, Rutgers University, New Brunswick, NJ
1999-2001: Research Assistant, Center for Alcohol Studies, Rutgers University, New Brunswick, NJ
2007- 2009: Postdoctoral Fellow, Mclean Hospital, Belmont, MA
2009- 2012: Instructor in Psychiatry, Harvard Medical School
2012-current: Assistant Professor, Harvard Medical School
2013-current: Director, Functional Integration of Addiction Research Laboratory
2014-current: Research Assistant Professor, Suffolk University

Academic and Professional Honors

2001-2003 & 2005-2006:Teaching Fellowship, Boston University
2003-2005 & 2006-2007: Research Assistantship, Boston University
2006: Clara Mayo Fellowship, Boston University
2008: National Research Service Award (NIDA T32), Postdoctoral Fellowship
2008: NIDA Women & Sex/Gender Junior Investigator Travel Award
2009: Mysell Research Award, Department of Psychiatry, Harvard Medical School
2009: College on Problems of Drug Dependence Travel Award
2009: International Society for Magnetic Resonance in Medicine Educational Stipend

2010: Clinical Research Day Award, Department of Psychiatry, Massachusetts General
2010: Alfred Pope Award for Young Investigators, McLean Hospital
2011: NIDA Women & Sex/Gender Junior Investigator Travel Award CPDD
2011: Mentored Research Scientist Development Award (K01)
2013: American College of Neuropsychopharmacology (ACNP) Travel Award
2013: Society of Biological Psychiatry (SOBP) Travel Fellowship Award
2019: Presidential Early Career Award for Scientists and Engineers

Professional Memberships
2008 – current: College on Problems of Drug Dependence (CPDD, elected Associate Member)
2012– current: Finance Committee Member, CPDD
2014: Organization for Human Brain Mapping
2016: American College of Neuropsychopharmacology (elected Associate Member)
2016: Finance Committee Member, CPDD
2017: Board of Directors, CPDD

Ad Hoc Reviewer for
Addiction, Addictive Behavior, American Journal of Psychiatry, JAMA Psychiatry, Biological Psychiatry, Biology of Sex Differences, Cerebral Cortex, Drug and Alcohol Dependence, European Journal of Pharmacology, Frontiers in Addictive Disorders and Behavioral Dyscontrol, General Hospital Psychiatry, Human Brain Mapping, Journal of Addiction Medicine, Neuropharmacology, Neuropsychologia, Neuropsychopharmacology, Neuroscience & Biobehavioral Reviews, Nicotine & Tobacco Research, The International Journal of Pharmacology, The Journal of Neuroscience, Physiology & Behavior, PlosOne, Psychiatry Research: Neuroimaging, Psychopharmacology

Professional Service
2009 – 2010: McLean Postdoctoral Association Steering Committee Member
2010: Boston Brain Bee Volunteer Judge
2010: Coordinator Neuroimaging Center Research Seminar
2010 – 2012: Coordinator McLean Neuroscience Seminar
2011: NIH Blueprint Workgroup on Neuro-Image Data Sharing
2011: McLean Ad Hoc Mentoring Committee Member
2012 – current: Mentor, Suffolk University Pre-doctoral Mentoring Collaboration
2012: Mentor, McLean Student Visitor Program
2012: Mentor, Citizen School's Spotlight on Science: Career Exploration Day
2012: National Science Foundation (NSF) *Ad Hoc* Reviewer
2012: Harvard Catalyst Pilot Funds *Ad Hoc* Reviewer
2014 - current: Co-Chair McLean Neuroscience Seminar Committee
2014: NIH Reviewer: Loan Repayment Program
2015-2019: NIH Reviewer

C. Contribution to Science

1. **<u>Individual differences contributing to substance abuse</u>**: A main focus of my work is identifying individual differences in substance abusers to guide personalized treatment. Currently, the majority of treatments are not guided by individual traits, which may limit efficacy. Our research is a first step toward personalizing therapy as we are using a battery of methods including fMRI, behavior, genetics, and magnetic resonance spectroscopy, which measures brain chemistry, to define underlying neurobiological differences between subsets of drug users. Thus far, we have shown that individual variability in pre-quit levels of brain reactivity to tobacco smoking cues predict relapse vulnerability[1]. Relapse vulnerable smokers also show enhanced behavioral interference to smoking cues, which may make ignoring smoking cues difficult. This work has been cited over 200 times, was highlighted in the 2010 NIDA news scan and in the German Magazine Gehirn & Geist. Moving forward with this line of questioning we reported that individuals with enhanced behavioral interference to smoking cues had the lowest levels of gamma-aminobutyric acid (GABA) in the dorsal anterior cingulate cortex (dACC)[2], a brain region associated with cognitive control and reward-based decision making. Importantly, this finding linked disrupted drug-related behavior with individual variability in brain chemistry, suggesting a

potential target for future treatment avenues. We went on to show that the strength of inherent connectivity between the dACC and insula, a brain region that is critically involved in maintaining nicotine dependence, influences subsequent brain reactivity to smoking cues[3]. This finding supports the concept that inherent brain organization impacts subsequent function and individual variability in connectivity may influence how specific smokers respond to stimuli likely to provoke craving and relapse. Finally, we showed that genetic differences in the alpha-5 cholinergic receptor influences brain reactivity to smoking cues such that higher alpha-5 efficiency relates to greater cue-reactivity[4]. This finding was recently supported by preclinical work showing that this alpha-5 receptor genetic profile influences the encoding of rewarding/salient stimuli.

a. **Janes AC**, Pizzagalli DA, Richardt S, Frederick B deB, Chuzi S, Pachas G, Culhane MA, Holmes AJ, Fava M, Evins AE, Kaufman MJ. (2010) Brain reactivity to smoking cues prior to smoking cessation predicts ability to maintain tobacco abstinence. *Biol Psychiatry* 2010 67:722-9. PMC2954596.
b. **Janes AC**, Jensen JE, Farmer SL, Frederic, BB, Pizzagalli DA, Lukas SE (2013) GABA levels in dorsal anterior cingulate cortex associated with difficulty ignoring smoking-related cues in tobacco-dependent volunteers. *Neuropsychopharmacology* 38: 1113-20. PMC3629395
c. **Janes AC,** Farmer S, Peechatka A, Blaise deB Frederick, Lukas SE (2015) Insula-dorsal anterior cingulate cortex coupling is associated with enhanced brain reactivity to smoking cues. *Neuropsychopharmacology* 40:1562-8. PMCID in process
d. **Janes AC**, Smoller JW, David SP, Frederick BB. Haddad S, Basu A, Fava M, Evins AE, Kaufman MJ. (2012) Association between CHRNA5 genetic variation at rs16969968 and brain reactivity to smoking images in nicotine dependent women. *Drug and Alcohol Depend* 120:7-13. PMC3203995

2. **Reactivity to drug-related stimuli**: To study individual differences in nicotine dependent individuals as discussed above, my work has focused heavily on how smokers respond to smoking-related cues, which have the ability to precipitate craving and relapse. In addition to the work described above, we have shown that brain reactivity to smoking cues is enhanced following traditional cessation treatment with nicotine replacement therapy (NRT)[1], which may explain the poor efficacy of NRT. Images from this work were presented in the undergraduate textbook *Essentials of Understanding Psychology*. We also related brain reactivity to smoking cues with behavioral interference[2], which more clearly links brain and behavior. We evaluated the cognitive underpinnings of smoking-cue processing by evaluating how memory processing for smokers differs when they are asked to encode, maintain, or retrieve information that is either related or unrelated to smoking. Results indicate that the neurobiological processes for smoking-related memory differs from neutral memory[3]. Finally, we used neuroanatomical methods to show that craving induced by smoking cues is related to the morphology of the striatum[4], a brain region linked to addictive disorders by decades of research.

a. **Janes AC**, Frederick BdeB, Richardt S, Burbridge C, Merlo-Pich E, Renshaw PF, Evins AE, Fava M, Kaufman MJ. (2009) Brain fMRI responses to smoking-related images prior to and during extended smoking abstinence. *Exper Clin Psychopharm* 17: 6:365-73. PMC3742373.
b. **Janes AC**, Pizzagalli DA, Richardt S, Frederick B deB, Chuzi S, Pachas G, Culhane MA, Holmes AJ, Fava M, Evins AE, Kaufman MJ. (2010) Brain reactivity to smoking cues prior to smoking cessation predicts ability to maintain tobacco abstinence. *Biol Psychiatry* 2010 67:722-9. PMC2954596.
c. **Janes AC**, Ross RS, Farmer S, Frederick BB, Nickerson L, Lukas SE, Stern CE (2015) Memory retrieval of smoking-related images induce greater insula activation as revealed by an fMRI based delayed matching to sample task. *Addiction Biology*. PMCID in process
d. **Janes AC,** Park MTM, Farmer S, Chakravarty MM (2015) Striatal morphology is associated with tobacco cigarette craving. *Neuropsychopharmacology*, 40: 406-11

3. **Brain connectivity**: Another primary focus of my research is investigating the role of brain connectivity within the context of addictive and psychiatric disorders. Currently, we have shown that disruptions in insula connectivity are associated with smoking relapse vulnerability[1] and as described above insula connectivity with the dorsal anterior cingulate cortex impacts subsequent brain reactivity to smoking cues. We also reported brain connectivity differences between smokers and non-smokers[2], a finding that was shown in the undergraduate textbook *An Introduction to Brain and Behavior*. Furthermore, we described a dynamic change in brain connectivity as inherent connectivity between reward-related brain regions enhances as a function of

craving[3]. Finally, I am the senior author on a manuscript showing that reduced interhemispheric coupling in cocaine dependent individuals is associated with cocaine craving[d].

a. **Janes AC**, Pizzagalli DA, Richardt S, Frederick B deB, Chuzi S, Pachas G, Culhane MA, Holmes AJ, Fava M, Evins AE, Kaufman MJ. (2010) Brain reactivity to smoking cues prior to smoking cessation predicts ability to maintain tobacco abstinence. *Biol Psychiatry* 2010 67:722-9. PMC2954596.
b. **Janes AC**, Nickerson L, Frederick BB, Kaufman MJ. (2012) Prefrontal and limbic resting state brain network functional connectivity differs between nicotine-dependent smokers and non-smoking controls. *Drug and Alcohol Dependence*, 125: 252-259. PMC3389311
c. **Janes AC**, Farmer S, Frederick BB, Nickerson LD, Lukas SE (2014) An increase in tobacco craving is associated with enhanced medial prefrontal cortex network coupling. *PlosOne*
d. McCarthy JM, Zuo CS, Shepherd JM, Dias N, Lukas SE, **Janes AC** (2017) Reduced interhemispheric executive control network coupling in men during early cocaine abstinence: A pilot study. *Drug and Alcohol Dependence* 181: 1-4. PMC5683918

4. **Co-morbid addiction and psychiatric disorders**: We have investigated the interaction of psychiatric disorders such as major depressive disorder (MDD) and schizophrenia with nicotine dependence. This is clinically relevant as smoking rates are significantly higher in these groups, relative to the general population. Specifically, we have evidence that nicotine "normalizes" reward function[a] and related circuitry[b] in those with MDD, while decreasing cognitive control deficits in those with schizophrenia[c]. These findings support the idea that nicotine may be used to self-medicate under certain conditions, which may make it harder for some populations to abstain from using nicotine. Further, those with schizophrenia have lower brain reactivity to smoking cues[d], supporting the concept that self-medication, rather than conditioned responding to smoking cues, may enhance relapse in this population

a. **Janes AC**, Pedrelli P, Whitton AE, Pechtel P, Douglas S, Martinson MA, Huz I, Fava M, Pizzagalli DA, Evins AE. (2015) Reward responsiveness varies by smoking status in women with a history of major depressive disorder. Neuropsychopharmacology. 40:1940-1946. PMID: 25662839
b. **Janes AC**, Zegel M, Ohashi K, Betts J, Molokotos E, Olson D, Moran L, Pizzagalli DA. (2018) Nicotine normalizes cortico-striatal connectivity in non-smoking individuals with major depressive disorder. Neuropsychopharmacology. 43: 2445-2451. PMID 29795403
c. Moran LV, Stoeckel LE, Wang K, Caine CE, Villafuerte R, Calderon V, Baker JT, Ongur D, **Janes AC**, Evins AE, Pizzagalli DA. (2018) Nicotine-induced activation of caudate and anterior cingulate cortex in response to errors in schizophrenia. Psychopharmacology. 235: 789-802. PMID: 29181816
d. Moran LV, Betts JM, Ongur D, **Janes AC**. (2018) Neural responses to smoking cues in schizophrenia. Schizophrenia Bulletin. 44: 525-534. PMID: 29106683

For a full reference list see: http://www.ncbi.nlm.nih.gov/pubmed/?term=Amy+Janes

D. Research Support
Ongoing Research Support

R03 DA048941 Janes(PI) 7/2019-7/21
NIH/NIDA
Targeting orexin to treat nicotine dependence
Substantial preclinical research indicates that orexin antagonism blunts the internally and externally triggered motivation to attain abused substances. The current application will translate these preclinical findings into the clinical domain by administering the FDA approved orexin antagonist, suvorexant, to nicotine dependent smokers. The impact of suvorexant on motivational factors of nicotine use (cue-induced craving, subjective experiences of smoking) as well as more general reward responsivity will be evaluated in a dose dependent manner using a repeated-measures, double blind, cross over design.
Role: PI

K02 DA042987 Janes (PI) 9/1/17-8/31/22
NIH/NIDA

Individual differences in nicotine dependence: A multi-modal neuroimaging approach
This K02 Independent Scientist Career Development Award provides 5 years of protected time to solidify the PI's independent laboratory, which focuses on defining individual risk factors for addictive disorders and their related neurobiological mechanisms, and to allow the PI time to mentor junior scientists and extend her research portfolio through collaborations. Further, to study brain temporal dynamics, the novel neuroimaging technique, electroencephalogram (EEG), will be integrated into the PI's ongoing funded work.
Role: PI

R01 DA041866 Kaufman (PI) 9/1/17-8/31/22
NIH/NIDA
Brain effects of long-term anabolic-androgenic steroid use: Multimodal imaging and cognition studies.
Determine the impact of anabolic-androgenic steroid use on brain circuitry underlying emotion and cognition.
Role: Co-I

R01 AA012923 Barlow(PI) 07/1/17-06/30/21
NIH/NIAAA
Interdisciplinary study of two novel anticonvulsants in alcoholism. The primary purpose of this double-blind randomized controlled study is to assess treatment mechanisms and the effectiveness of the anticonvulsant medication Zonisamide in reducing alcohol consumption in patients with alcohol use disorders.
Role: Co-I

R01 DA039125 Janes (PI) 07/15/15-05/31/20
NIH/NIDA
Defining Individual Differences in Tobacco Smokers Using Multimodal Neuroimaging
Objective: Differences in brain reactivity to smoking cues predict relapse vulnerability and suggest the need for more personalized cessation treatment. Multi-modal neuroimaging techniques will be used to comprehensively phenotype high and low cue-reactive smokers, which will be a first step toward the development of personalized smoking cessation therapy.

Completed Research Support

K01DA029645 Janes (PI) 04/01/11-03/31/17
NIH/NIDA
Training in Cognitive Function and Neuroimaging of Smoking-Related Cues
Objective: The goal of this project is to develop a deeper understanding of tobacco smoking relapse risk factors and their interactions using neuroimaging, cognitive, and psychological trait and state measures. Such studies may improve smoker phenotyping and advance research aimed at developing more effective personalized smoking cessation treatments.
Role: PI