BIOGRAPHICAL SKETCH

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NAME: **Rhodes, Justin S.**

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

POSITION TITLE: Associate Professor

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
Stanford University – Stanford, CA	B.S.	1995	Biology
University of Washington, Seattle	M.S.	1998	Fisheries
University of Wisconsin, Madison	M.S.	2002	Statistics
University of Wisconsin, Madison	Ph.D.	2002	Zoology
Oregon Health & Science University, Portland	Postdoc	2005	Behavioral Neuroscience

A. Personal Statement

I have 20 years of experience conducting behavioral genetic experiments with mice. My research uses various techniques (behavioral, genetic, molecular, and histological) to measure the effect of lifestyle factors such as diet, drugs of abuse and exercise on the brain and behavior. I direct a privately funded core facility through the Center for Nutrition, Learning and Memory (CNLM) at the University of Illinois that supports several different collaborative projects involving mouse behavior, physiology, and neuroanatomy. In addition to the private funding, over the past 5 years I managed 2 NIH RO1s to explore the functional significance of exercise-induced neurogenesis in learning and extinction of conditioned place preference for cocaine, and a collaborative NSF grant to develop optogenetic tools to implement in mouse behavior testing. Most recently, I am working on two R21 projects, “origins of exercise-brain interactions”, and “In vitro platform for exploring muscle-neuron interactions”. I have a demonstrated record of successful and productive research projects in the area of behavioral neuroscience of high relevance to the proposed work.

B. Positions and Honors

Positions and Employment

1995-1998 Research Assistant, School of Fisheries, University of Washington, Seattle
1998-2002 Predoctoral Fellow and Research Assistant, Department of Zoology, University of Wisconsin, Madison
2003-2005 Postdoctoral Fellow, Department of Behavioral Neuroscience, Oregon Health & Science University, Portland
2005-2012 Assistant Professor, Department of Psychology, University of Illinois at Urbana-Champaign
2013-present Associate Professor, Department of Psychology, University of Illinois at Urbana-Champaign

University of Illinois at Urbana-Champaign Affiliations:

2005-present Beckman Institute; Neuroscience Program; Institute for Genomic Biology Program in Ecology, Evolution, and Conservation Biology; Division of Nutritional Sciences

Other Experience and Professional Memberships

Review Panels:

2009 Ad hoc mail in reviewer, NIH RC1 Challenge Grants
2010-2011 Reviewer, NIH Molecular Neurogenetics study section (06/2010, 10/2010, 02/2011, 06/2011)
2011 Mail in reviewer, Neurogenesis and Cell Fate study section
2012 Reviewer, NIH Special Emphasis panel ZRG1 BDCN-W (03)
2014 Reviewer, NIH Behavioral Neuroscience Fellowships ZRG1 F02a J-20
2015 Reviewer, NIH Neurobiology of Motivated Behavior study section
2016 Reviewer, NIH Neurobiology of Learning and Memory study section
2016 Reviewer, NIH US-China collaborative biomedical research, BDCN N 51
2016 Reviewer, NIH Biobehavioral Regulation, Learning and Ethology study section
2018 Reviewer, NIH Genetics of Health and Disease Study Section

Editorial Boards:

2012-present Editorial board, *Brain, Behavior and Immunity*.
2012-2013 Interim Associate Editor, *Brain, Behavior and Immunity.*
2013 Guest Editor for Named Series on "Neurogenesis, Inflammation, and Behavior," *Brain, Behavior and Immunity.*

Honors and Awards

1996 Quistorff Fellowship, University of Washington, Seattle, WA
1999 Enteman Award, University of Wisconsin, Madison, WI
2000-2002 **Individual Predoctoral Fellowship**, National Research Service Award, NINDS
2003-2005 Institutional Postdoctoral Fellowship, National Research Service Award, NIAAA
2004 Tartar Trust Fellowship, OHSU, Portland, OR
2008 **Young Scientist Award,** International Behavioral and Neural Genetics Society, Portland, OR
2008, 2011 List of teachers ranked excellent by their students (Psych 210)
2010, 2012 Invited Participant, Gordon Research Conferences, Genes & Behavior
2012-2013 **Helen Corley Petit Scholar**, University of Illinois
2013-2014 **Evelyn Satinoff Professorial Scholar** in Psychology, University of Illinois
2013 Best Mentor Award, Medical Scholars (MD/PhD) Program, University of Illinois
2014 Best Mentor Award, Division of Nutritional Sciences, University of Illinois

C. Contributions to Science

1) Exercise-brain interactions

It is increasingly becoming realized that exercise is critical for maintaining cognitive health throughout the lifespan in humans, and that these effects are mediated, in part, through anatomical changes that take place in the hippocampus. One of these anatomical changes likely involves increased adult hippocampal neurogenesis, which results in an increase in the total number of granule neurons and volume of the dentate gyrus in rodent models. We discovered that exercise increases neurogenesis and enhances performance in multiple genotypes of mice depending on the level of running displayed by the strains. We further discovered that it is the exercise component of an enriched environment that has the greatest effect in increasing adult hippocampal neurogenesis. We made a significant contribution to this literature by showing that there is a massive acute activation of the hippocampal formation in direct association with the intensity of physical exercise that does not occur with inactive exploration. We further discovered that new neurons generated from exercise are broadly recruited into multiple functions of the hippocampus. Most recently we discovered a role for mesenchymal stem cells in contracting muscle that may release factors which enter the blood and cross into the brain to support increased neurogenesis. The mechanisms underlying exercise-induced neurogenesis and the function of new neurons in behavior are currently under intense investigation.

a. Clark PJ, Kohman RA, Miller DS, Bhattacharya TK, Brzezinska WJ, **Rhodes JS**. (2011) Genetic influences on exercise-induced adult hippocampal neurogenesis across 12 divergent mouse strains. Genes Brain Behav. 10(3):345-53. PMCID: PMC3139814

b. Clark PJ, Bhattacharya TK, Miller DS, Kohman RA, DeYoung EK, **Rhodes JS**. (2012) New neurons generated from running are broadly recruited into neuronal activation associated with three different hippocampus-involved tasks. Hippocampus. 22(9):1860-7. PMCID: PMC3390440

c. Merritt J, **Rhodes JS**. (2015) Mouse genetic differences in voluntary wheel running, adult hippocampal neurogenesis and learning on the multi-strain-adapted plus water maze. Behav Brain Res. 280:62-71. PMCID: PMC4280099
d. Huntsman HD, Rendeiro C, Merritt JR, Pincua Y, Cobert A, De Lisio M, Kolyvas E, Dvoretskiya S, Dobrucki IT, Kemkemere R, Jensen T, Dobrucki LW, **Rhodes JS**, Boppart MD. 2018. Mechanically stimulated muscle-derived stromal cells facilitate peripheral perfusion and neurogenesis in aged mice. Experimental Gerontology.103:35-46.

2) Exercise accelerates extinction of conditioned place preference for cocaine in mice

One of the major obstacles in the treatment of drug abuse is relapse triggered by re-exposure to drug-paired cues (such as places where drugs were taken). We discovered that voluntary wheel running exercise can accelerate extinction of learned associations between contextual cues and the rewarding effects of cocaine using the conditioned place preference (CPP) paradigm in mice. We further discovered that new neurons generated from running are not required for exercise to abolish cocaine CPP using a nestin-thymidine (nestin-TK) kinase transgenic mouse model. These data have significantly revised our thinking about the role of new neurons in behavior. We now believe that killing new neurons once they have formed does not successfully uncover their function in behavior because compensatory mechanisms (e.g., additional synapses from mature neurons) can compensate for their loss. We are currently developing optogenetic technology to temporarily instantaneously inactivate new neurons while animals are performing on various tasks to elucidate their function in behavior.

a. Mustroph ML, Stobaugh DJ, Miller DS, DeYoung EK, **Rhodes JS**. (2011) Wheel running can accelerate or delay extinction of conditioned place preference for cocaine in male C57BL/6J mice depending on timing of wheel access. Eur J Neurosci. 34(7):1161-9. PMCID: PMC3186851
b. Mustroph ML, Merritt JR, Holloway AL, Pinardo H, Miller DS, Kilby CN, Bucko P, Wyer A, **Rhodes JS**. (2015) Increased adult hippocampal neurogenesis is not necessary for wheel running to abolish conditioned place preference for cocaine in mice. Eur J Neurosci. 41(2):216-26. PMCID: PMC4300275
c. Mustroph ML, Pinardo H, Merritt JR, Rhodes JS. 2016. Parameters for abolishing conditioned place preference for cocaine from running and environmental enrichment in male C57BL/6J mice. Behav Brain Res 312:366-373. PMC4970947

3) Neurobiology of mice selectively bred for increased physical activity

A large literature has established the critical importance of aerobic exercise for maintaining physical and mental health throughout the lifespan, yet average daily levels of physical activity continue to decline in western society. The major obstacle preventing global therapeutic application of exercise is that for many people, the desire to exercise is low, and appears to be declining. Moreover, it is not clear how to increase motivation for exercise. Physical exercise can be rewarding and addictive in certain individuals, suggesting that motivation for physical activity can be increased. However, relatively few studies have investigated the neurobiology of increased motivation for exercise and our understanding of how to neurologically increase desire to exercise is rudimentary at best. As a graduate student I helped conduct a long term selective breeding experiment for increased voluntary wheel running behavior in laboratory mice that resulted in several important discoveries about the genetic and neurobiological basis for increased motivation for exercise. The first discovery I made was that the reward circuit in the brain appeared to be the target for selection, with specific changes occurring in dopamine D1-like receptor signaling pathways in reward regions of the brain. In addition to the early work with the high-running mice, I have established my own long-term selective breeding experiment for increased physical activity, except using continuous video tracking of home cage activity as the selection criterion without running wheels. Recently we discovered that the high-active line of mice display impulsive behavior and a paradoxical response to amphetamines, suggesting that they may be useful as a model for attention deficit hyperactivity disorder.

a. **Rhodes JS**, Garland T. (2003) Differential sensitivity to acute administration of Ritalin, apomorphine, SCH 23390, but not raclopride in mice selectively bred for hyperactive wheel-running behavior. Psychopharmacology (Berl). 167(3):242-50. PMID: 12669177
b. **Rhodes JS**, Garland T Jr, Gammie SC. (2003) Patterns of brain activity associated with variation in voluntary wheel-running behavior. Behav Neurosci. 117(6):1243-56. PMID: 14674844

c. Majdak P, Ossyra JR, Ossyra JM, Cobert AJ, Hofmann GC, Tse S, Panozzo B, Grogan EL, Sorokina A, **Rhodes JS**. (2016) A new mouse model of ADHD for medication development. Scientific Reports 6:39472.

d. Saul M, Majdak P, Perez S, Reilly M, Garland T, Jr, **Rhodes JS.** (2016). High motivation for exercise is associated with altered chromatin regulators of monoamine receptor gene expression in the striatum of selectively bred mice. Genes, Brain, and Behavior. 16:328-341 PMID: 27749013

4) Effects of exercise on brain-immune interactions

This work was led by my former postdoctoral student, Dr. Rachel Kohman, who received a K99/R00 under my mentorship and now runs her own lab at the University of North Carolina, Wilmington. Recent evidence suggests that chronic low-grade inflammation in the brain contributes to cognitive decline associated with aging and increased incidence of neurodegenerative diseases. We discovered that exercise reduces this low-grade inflammation in the aged hippocampus by altering gene expression, reducing proliferation of microglia and increasing the proportion of microglia expressing a neuro-protective phenotype. A review are article that we wrote together, "Neurogenesis, inflammation and behavior" in *Brain, Behavior, and Immunity,* published in 2013 has already been cited over 100 times.

a. Kohman RA, Rodriguez-Zas SL, Kelley KW, Dantzer R, **Rhodes JS**. (2011) Voluntary wheel running reverses age-induced changes in hippocampal gene expression. PLoS One. 6(8):e22654. PMCID: PMC3152565

b. Kohman RA, DeYoung EK, Bhattacharya TK, Peterson LN, **Rhodes JS**. (2012) Wheel running attenuates microglia proliferation and increases expression of a proneurogenic phenotype in the hippocampus of aged mice. Brain Behav Immun. 26(5):803-10. PMCID: PMC3275652

c. Kohman RA, Bhattacharya TK, Kilby C, Bucko P, **Rhodes JS**. (2013) Effects of minocycline on spatial learning, hippocampal neurogenesis and microglia in aged and adult mice. Behav Brain Res. 242:17-24. PMCID: PMC3725815

d. Kohman RA, Bhattacharya TK, Wojcik E, **Rhodes JS**. (2013) Exercise reduces activation of microglia isolated from hippocampus and brain of aged mice. J Neuroinflammation. 10:114. PMCID: PMC3848770

5) A simple model of ethanol drinking to intoxication in mice

As a postdoctoral fellow with John Crabbe at the Oregon Health & Science University I developed a simple model of ethanol drinking to intoxication in mice. Previous models failed to achieve pharmacologically significant ethanol concentrations in the blood, or involved lengthy complicated procedures. By experimenting with timing of delivery, ethanol concentration, and short-term access, we developed a simple technique that is now widely used in the rodent alcohol research community, referred to as Drinking-In-the-Dark (DID). The technique involves offering a genetically predisposed strain of mouse limited access to a 20% ethanol solution during the early dark phase of the light-dark cycle over 4 consecutive days. A pubmed search reveals 125 articles used DID up to present, and the original report (Rhodes et al., 2005) has over 400 citations.

a. **Rhodes JS**, Best K, Belknap JK, Finn DA, Crabbe JC. (2005) Evaluation of a simple model of ethanol drinking to intoxication in C57BL/6J mice. Physiol Behav. 84(1):53-63. PMID: 15642607

b. Kamdar NK, Miller SA, Syed YM, Bhayana R, Gupta T, **Rhodes JS**. (2007) Acute effects of Naltrexone and GBR 12909 on ethanol drinking-in-the-dark in C57BL/6J mice. Psychopharmacology (Berl). 192(2):207-17. PMID: 17273875

c. Crabbe JC, Metten P, **Rhodes JS**, Yu CH, Brown LL, Phillips TJ, Finn DA. (2009) A line of mice selected for drinking in the dark to intoxication. Biol Psychiatry. 65(8):662-70. PMCID: PMC3330756

d. Bulwa ZB, Sharlin JA, Clark PJ, Bhattacharya TK, Kilby CN, Wang Y, **Rhodes JS**. (2011) Increased consumption of ethanol and sugar water in mice lacking the dopamine D2 long receptor. Alcohol 45(7):631-9. PMCID: PMC3184387

Complete List of Published Work in MyBibliography:
https://scholar.google.com/citations?user=gjNS208AAAAJ&hl=en&oi=ao

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

Ongoing Research Support

R21 NS109894 Rhodes (PI) 06/01/2019- 05/31/2021
In Vitro Platform for Exploring Muscle-Neuron Interactions.
This project proposes an in vitro platform consisting of contracting muscle cells and interacting neurons as a way to identify and prioritize factors released by muscles that support connectivity and maturation of neuronal circuits.
Role: PI

R21 NS104293 Rhodes (PI) 11/15/18-12/31/20
Origins of Exercise-Brain Interactions
The goal of this project is to determine the extent to which both electrical activation of the hippocampus or contraction of the muscles in isolation increase neurogenesis and enhance behavioral performance.
Role: PI

Private Industry Rhodes (PI) 5/16/2012-5/15/2018
Mouse Cognition and Hippocampal Neurogenesis Core Facility
This core facility provides capability for conducting preclinical studies using mice as a model organism for the members of the Center for Nutrition, Learning and Memory (CNLM).
Role: PI

Completed Research Support from last 3 years

NSF 1450829 Boppart, S (PI) 09/01/2014 – 08/31/2016
BRAIN EAGER
Spatially-Resolved In Vivo Optogenetic Stimulation and Imaging Platform
The goal is to develop optogenetic technology using implanted imaging fiber bundles that will enable in vivo imaging as well as spatially-controlled optical stimulation and optical feedback of large-area neural circuits.
Role: Co-PI

R01 MH083807 Rhodes (PI) 03/19/2009 – 03/18/2015
Mouse Genetic Differences in Exercise-Induced Hippocampal Neurogenesis & Learning
The goal was to discover mechanisms for pro-cognitive effects of exercise at multiple levels of biological organization from genes to physiology to behavior.
Role: PI

R01 DA027487 Rhodes (PI) 09/01/2009 – 08/31/2015
The Functional Significance of Exercise-Induced Neurogenesis in Cocaine Reward.
The goal was to determine the impact of new neurons generated from exercise on cocaine conditioned behavior.
Role: PI