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BIOGRAPHICAL SKETCH

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NAME: Herman, Melissa A.

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

POSITION TITLE: Assistant Professor of Pharmacology

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
Boston University, Boston MA	B.S.	06/2001	Human physiology
Georgetown University, Washington DC	Ph.D.	06/2010	Neuroscience
The Scripps Research Institute, La Jolla CA	Postdoctoral	08/2016	Neuropharmacology

A. Personal Statement

I am an Assistant Professor in the Pharmacology Department and a member of the Bowles Center for Alcohol Studies at the University of North Carolina at Chapel Hill. I have a broad background in neurophysiology and neuropharmacology and have been trained as a multidisciplinary scientist. My research program is focused on the neurophysiological changes that occur in response to alcohol and drug exposure and how neuroadaptations at the circuit, network, and systems level contribute to behaviors associated with adverse clinical outcomes such as alcohol or drug dependence. My interests specifically involve the structure and function of neuronal networks and how activity in these networks change to alter synaptic control in local microcircuits and multi-region circuit connections. I am also interested in how the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) regulates neuronal networks via both synaptic and extrasynaptic forms of inhibition and how alterations in inhibitory networks contribute to co-morbid clinical conditions such as drug addiction or stress. I teach lectures in both the Neuroscience and Pharmacology curricula, act as a faculty mentor in the First Year Group course, and mentor neuroscience and pharmacology Ph.D. students as well as postdoctoral fellows in my laboratory. As a trained neuroscientist I prioritize both formal instruction in the principles of neuroscience and pharmacology as well as hands-on mentoring in conceptual design and experimental techniques. I provide my lab members with a safe, supportive, and inclusive environment to receive training and develop their independent research careers. I support and promote lab members to achieve their career goals, emphasizing the importance of professional development and successful career transitions to independent positions.

B. Positions and Honors

Positions and Employment

2016-present Assistant Professor, Department of Pharmacology, Bowles Center for Alcohol Studies
The University of North Carolina (Chapel Hill, NC)

2010-2015 Research Associate (postdoc), Committee on the Neurobiology of Addictive Disorders
The Scripps Research Institute (La Jolla, USA)

2005-2010 Graduate student, Department of Pharmacology, Interdisciplinary Program in Neuroscience
Georgetown University Medical School (Washington DC)

2001-2005 Research Assistant, Department of Peptide Biology
The Salk Institute for Biological Studies (La Jolla, CA)

Other Experience and Professional Memberships

2020- Member, Basic Science Network, Society for Research on Nicotine and Tobacco
2019- Member, Society for Research on Nicotine and Tobacco
2013- Guest Associate Editor, Frontiers in Psychiatry
2011- Member, Research Society on Alcoholism
2005- Member, Society for Neuroscience

Honors

2020 UNC Emerging Challenges in Biomedical Research Award
2020 NARSAD Young Investigator Award, Brain & Behavior Research Foundation
2018 American College of Neuropsychopharmacology Travel Award: Annual Meeting
2018 University of North Carolina at Chapel Hill Faculty Development Award
2017 Young Investigator Award, NIAAA Special Meeting "Alcoholism and Stress: a Framework for future treatment strategies" Volterra, Italy

C. Contributions to Science

1. **Inhibitory microcircuitry and the effects of ethanol in the central amygdala**. The central nucleus of the amygdala (CeA) is a key brain region in the negative reinforcing properties of ethanol and has been implicated in both the development of alcohol dependence as well as the susceptibility to relapse in dependent individuals. Inhibitory signaling in the CeA has been shown to play a major role in both the effects of acute ethanol as well as the neuroadaptations that occur in response to chronic ethanol exposure. Until recently, the majority of the work done has been focused on phasic or synaptic inhibition and has treated the CeA as a homogenous nucleus, with little investigation into cell type-specific effects. In my work I utilized a transgenic reporter mouse expressing green fluorescent protein (GFP) under the control of the corticotropin releasing factor 1 receptor 1 (CRF1) promoter to identify CRF1-expressing (GFP+) neurons in the CeA. Using these mice, we have uncovered cell type- and sex-specific changes in inhibitory signaling and activity in CeA neurons with differential sensitivity to the effects of ethanol and to CRF. This work highlights the significant role of specific CeA cell populations in ethanol-induced plasticity in inhibitory signaling in the physiological functioning of the CeA and adds sex as an important biological variable in the neuroadaptations that occur with chronic alcohol exposure.

   a) Agoglia AE, Zhu M, Douglass E, Hanback T, Tella J, Ying R, Hodge CW and **Herman MA**. Sex-specific plasticity in CRF regulation of inhibitory control in central amygdala CRF1 neurons after chronic voluntary alcohol drinking. Addiction Biology. 2021 Jun 2:e13067. Online ahead of print. PMID: 34075665

   b) Agoglia AE, Tella J, **Herman MA**. Sex differences in corticotropin releasing factor peptide regulation of inhibitory control and excitability in central amygdala corticotropin releasing factor receptor 1-neurons. Neuropharmacology. 2020 Dec 1;180:108296. PMID: 32950560

   c) Agoglia AE, Crofton EJ, **Herman MA**. Biological intersection of sex, age, and environment in the corticotropin releasing factor (CRF) system and alcohol. Neuropharmacology. 2020 Jun 15;170:108045. PMID: 32217364

2. **Neuroplastic effects of nicotine exposure.** Nicotine is a highly addictive drug that has been shown to dynamically impact brain signaling and alter behavior in a use-dependent manner. These behaviors appear to be mediated by adaptations at the cellular level as the brain responds to repeated drug exposure and withdrawal. With prolonged use, these adaptations can lead to long-lasting changes in neural function and behavior. A number of brain regions have been identified as targets of nicotine-induced plasticity, including the ventral tegmental area (VTA) and the central amygdala (CeA). Despite substantial evidence linking VTA activity to the rewarding effects of nicotine, as well as dysregulation of this signaling in pathological conditions such as addiction and psychiatric disorders like depression, the cellular mechanisms underlying drug-associated VTA plasticity remain unclear. My work has examined inhibitory and excitatory regulation of dopamine neurons in the VTA and the role of neuromodulatory signaling systems on VTA dopamine

neurons activity. Specifically, I have shown that inhibitory control of VTA dopamine neurons is compromised by chronic exposure to nicotine in a mechanism involving upregulation of the CRF system. I have also conducted studies implicating the cannabinoid system and found that the dysregulation in the inhibitory control of VTA dopamine neurons following nicotine exposure can be reversed by targeted inhibition of the synthetic enzyme diacylglycerol lipase. More recent work from my group is investigating the neural and behavioral consequences of nicotine exposure by intermittent vaping, a model with much greater similarity to the human experience of vaping, an increasingly prevalent method of nicotine delivery. Using this vaping model, we found differential changes in CeA activity, thermoregulation, and locomotion following acute and repeated vape sessions, suggesting that vape exposure produces dysregulation both centrally and peripherally.

a) Zhu M, Echeveste Sanchez M, Douglass E, Hanback T, Guhr Lee TN, Esther CR Jr, Cole M, Roberts AJ, **Herman MA**. Electronic nicotine vapor exposure produces differential changes in central amygdala neuronal activity, thermoregulation and locomotor behavior in male mice. eNeuro. 2021 Aug 11;8(4):ENEURO.0189-21.2021. PMID: 34321216

b) **Herman M**, Tarran R. E-cigarettes, nicotine, the lung and the brain: multi-level cascading pathophysiology. J Physiol. 2020 Jun 9. PMID: 32515030

c) Buczynski MW, **Herman MA**, Hsu KL, Natividad LA, Irimia C, Polis IY, Pugh H, Chang JW, Niphakis MJ, Cravatt BF, Roberto M, Parsons LH. Diacylglycerol lipase disinhibits VTA dopamine neurons during chronic nicotine exposure. Proceedings of the National Academy of Sciences of the United States of America. 2016; 113(4):1086-91.

3. Brainstem inhibitory networks regulating gastric function. The role of the autonomic nervous system in the central control of gastric function is well known, however, the specific signaling and circuitry mediating this control remain poorly understood. My early work focused on the role of inhibitory signaling in the brainstem nucleus the Nucleus Tractus Solitarius (NTS) and the role of inhibition in the central control of gastric function. My work revealed an important role for inhibitory signaling in the NTS in the control of basal gastric function. I also reported on a novel form of inhibition in the NTS, tonic or extrasynaptic inhibition, and showed how tonic inhibition acted as a critical regulator of overall network activity in the NTS. In addition, I showed how stimulation of the mu-opioid receptor in the NTS altered inhibitory function by dampening tonic inhibition resulting in diminished gastric tone. Collectively this work demonstrates the importance of inhibitory control in maintaining physiological gastric function and provides a central mechanism by which opioid therapeutics can produce adverse gastric side effects.

   a) Valentino RJ, Guyenet P, Hou XH, **Herman M**. Central Network Dynamics Regulating Visceral and Humoral Functions. J Neurosci. 2017 Nov 8;37(45):10848-10854.

   b) **Herman MA**, Gillis RA, Vicini S, Dretchen K, Sahibzada N. Tonic GABAA receptor conductance in medial subnucleus of the tractus solitarius (mNTS) neurons is inhibited by activation of μ-opioid receptors. J Neurophysiol. 2012 Feb;107(3):1022-31.

   c) **Herman MA**, Alayan A, Sahibzada N, Bayer B, Verbalis JG, Dretchen K, Gillis RA. Mu-opioid receptor stimulation in the medial subnucleus of the tractus solitarius (mNTS) inhibits gastric tone and motility by reducing local GABA activity. Am J Physiol Gastrointest Liver Physiol. 2010 Aug;299(2):G494-506.

Complete List of Published Work in MyBibliography:

https://www.ncbi.nlm.nih.gov/sites/myncbi/melissa.herman.1/bibliography/43552900/public/?sort=date&direction=descending

D. Research Support - Ongoing Research Support

1F31DA053064 NIH/NIDA	PI: Zhu	4/1/2021 - 3/31/2024

Impact of electronic nicotine vapor on mouse mesolimbic CRFR1 circuitry and motivated behavior
Role: Sponsor/Mentor

Brain & Behavior Research Foundation PI: Herman 1/15/2020 - 1/14/2022
Central Amygdala circuitry underlying potential therapeutic effects of Psilocybin in the brain.
Role: PI

R01AA026858 PI: Herman 7/01/19 - 6/30/24
NIH/NIAAA
The role of a nucleus tractus solitarius-central amygdala circuit in alcohol-induced plasticity and drinking behavior
Role: PI

5 P60 AA11605 Co-PDs: Kash/Morrow 12/01/2017 - 11/30/2022
NIH/NIAAA
Molecular and Circuit Pathogenesis in Alcoholism - Research Component 4 –
GABAergic Corticolimbic Circuit Mechanisms of Ethanol Dependence - Morrow/Herman (co-PIs)
Role: Research Component Co-PI