BIOGRAPHICAL SKETCH

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NAME: Herman, Melissa A.

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

POSITION TITLE: Associate 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

Research Focus: I have an active and dynamic research program focused on the neurophysiological changes associated with alcohol and drug exposure that explores how neuroadaptations at the circuit, network, and systems level contribute to behaviors associated with adverse clinical outcomes, such as drug or alcohol dependence. Since establishing my lab in the department of Pharmacology and the Bowles Center for Alcohol Studies (BCAS) at the University of North Carolina at Chapel Hill, I have published >20 papers on brain region- and circuit-specific effects of alcohol and drug exposure on neuronal activity and behavior. I have a broad background in neurophysiology and neuropharmacology and have been trained as a multidisciplinary scientist. My primary interest is how exposure to drugs of abuse and/or psychiatric conditions disrupt neuronal networks via both intrinsic and extrinsic forms of plasticity and how pathological network alterations contribute to the development of clinical conditions such as drug addiction or psychiatric disorders like anxiety and depression.
Mentorship and Training: Through sustained interactions with the BCAS, the Biological and Behavioral Science Program Pharmacology and Neuroscience curricula, the Postbaccalaureate Research Education Program (PREP), and the Seeding Postdoctoral Innovators in Research and Education (SPIRE) program, my laboratory nurtures and maintains a diverse training environment. I prioritize mentorship, and have dedicated time and resources to the professional development of prior and current trainees. My trainees are encouraged to develop innovative research projects and have received independent funding from both NIDA and NIAAA.
Leadership and Collaborative Science: As a member of the Bowles Center for Alcohol Studies, I have extensive experience in collaborative team science and the benefits of bringing a multidisciplinary focus to complex research questions. My lab has established experience in electrophysiological, circuit mapping, and fiber photometry techniques and maintains active collaborative studies with my colleagues in the Bowles Center for Alcohol Studies, in the Pharmacology department, as well as in the larger UNC research community.

<u>Ongoing and recently completed projects I would like to highlight include:</u>
Herman (PI)
01/15/2020 – 01/14/2022
Central Amygdala circuitry underlying potential therapeutic effects of Psilocybin in the brain.
NARSAD Young Investigator Award, Brain & Behavior Research Foundation

R01 AA026858
Herman (PI)
7/01/19 - 6/30/24

The role of a nucleus tractus solitarius-central amygdala circuit in alcohol-induced plasticity and drinking behavior

Publications:

1. Schmitz GP, Chiu YT, Konig GM, Kostenis E, Roth BL, **Herman MA.** Psychedelic compounds directly excite 5-HT2A Layer 5 Pyramidal Neurons in the Prefrontal Cortex through a 5-HT2A Gq-mediated activation mechanism. bioRxiv 2022.11.15.516655; doi: https://doi.org/10.1101/2022.11.15.516655
2. DP Effinger DP, SG Quadir SG, Ramage MC, Cone MG, **MA Herman MA**. Sex-Specific Effects of Psychedelic Drug Exposure on Central Amygdala Reactivity and Behavioral Responding. bioRxiv 2022.04.28.489882; doi: https://doi.org/10.1101/2022.04.28.489882
3. 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. 2022 Jan;27(1):e13067. PMCID: PMC8636550
4. Lee SH, Broadwater MA, Ban W, Wang TW, Kim HJ, Dumas JS, Vetreno RP, **Herman MA**, Morrow AL, Besheer J, Kash TL, Robinson DL, Crews FT, **Shih YY**, "An isotropic EPI database and analytical pipelines for rat brain resting-state fMRI," NeuroImage, 2021; 243:118541. PMCID: PMC8561231.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2022-present	Associate Professor, Department of Pharmacology, Bowles Center for Alcohol Studies The University of North Carolina (Chapel Hill, NC)
2016-2022	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)

Scientific Activities and Professional Memberships

2022-	NIH Review Panelist, ZAA1 DD (04) NIAAA Special Emphasis panel
2020-present	Member, Basic Science Network, Society for Research on Nicotine and Tobacco
2020-present	Program Committee, Society for Research on Nicotine and Tobacco
2019- present	Member, Society for Research on Nicotine and Tobacco
2018	NIH Review Panelist, ZAA1 GG (32) NIAAA Fellowship Review panel
2018	Reviewer, Brain Canada panel, Canada
2013- present	Guest Associate Editor, Frontiers in Psychiatry
2011- present	Member, Research Society on Alcoholism
2005- present	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

Trainee Awards

2022	F32 NRSA postdoctoral training grant, NIAAA (Quadir)
2021	F31 NRSA predoctoral training grant, NIDA (Zhu)

C. Contributions to Science

1. **The effects of ethanol in the central amygdala on inhibitory microcircuitry and affective behavior.** 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 utilize 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. We have extended this work by developing a transgenic rat line with a cre-driver and TdTomato fluorescent reporter under the control of the corticotropin releasing factor 1 receptor 1 (CRF1) promoter and have characterized the functional and properties of CRF1+ CeA cells in these rats as well as the role of CRF1+ cells in affective behavior. 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) Quadir SG, Arleth GM, Jahad JV, Echeveste Sanchez M, Effinger DP, **Herman MA**. Sex differences in affective states and association with voluntary ethanol intake in Sprague-Dawley rats. Psychopharmacology (Berl). 2022 Feb;239(2):589-604. doi: 10.1007/s00213-021-06052-x. Epub 2022 Jan 19. PMID: 35044485
    b) Weera MM, Agoglia AE, Douglass E, Jiang Z, Rajamanickam S, Shackett RS, **Herman MA**, Justice NJ, Gilpin NW..Generation of a CRF1-Cre transgenic rat and the role of central amygdala CRF1 cells in nociception and anxiety-like behavior. Elife. 2022 Apr 7;11:e67822. doi: 10.7554/eLife.67822. PMCID: PMC9033268
    c) 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. 2022 Jan;27(1):e13067. PMCID: PMC8636550
    d) 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. PMCID: PMC8207535

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. We have also extended these studies to examine the impact of nicotine vapor exposure on voluntary drinking and found sex differences in drinking, locomotor, and anxiety-like behavior.

a) Echeveste Sanchez M, Quadir SG, Whindleton CM, Hoffman JL, Faccidomo SP, Guhr Lee TN, Esther CR Jr, Hodge CW, **Herman MA**. The effects of electronic nicotine vapor on voluntary alcohol consumption in female and male C57BL/6 J mice. Drug Alcohol Depend. 2022 Oct 26;241:109676. doi: 10.1016/j.drugalcdep.2022.109676. Online ahead of print. PMID: 36343590
b) 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
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.
d) Grieder TE, **Herman M**, Contet C, Tan LA, Vargas-Perez H, Cohen A, Chwalek M, Maal-Bared G, Freiling J, Schlosburg JE, Clarke L, Crawford E, Koebel P, Canonigo V, Sanna P, Tapper A, Roberto M, Kieffer BL, Sawchecko PE, Koob GF, van der Kooy D & George O. CRF neurons in the ventral tegmental area control the aversive effects of nicotine withdrawal and promote escalation of nicotine intake. Nature Neurosci 2014, 17(12):1751-8. PMC4241147.

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