BIOGRAPHICAL SKETCH

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NAME: Ryan Peter Vetreno

POSITION TITLE: Assistant 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
St. Thomas Aquinas College	B.S.	12/2001	Psychology
Radford University	M.A.	05/2006	Clinical Psychology
Binghamton University – SUNY	Ph.D.	01/2011	Behavioral Neuroscience
University of North Carolina at Chapel Hill	Postdoctoral	01/2016	Pharmacology

A. Personal Statement

My training is in psychology, behavioral neuroscience, and pharmacology, with a concentration on long-term alterations to adult neurobiology following adolescent binge ethanol exposure. My research focuses on elucidating the mechanisms underlying basal forebrain pathology associated with adolescent binge drinking. I discovered that AIE treatment increases expression of Toll-like receptors (TLRs), the receptor for advanced glycation end products (RAGE), the cytokine-like TLR/RAGE agonist high-mobility group box 1 (HMGB1), and multiple proinflammatory signaling molecules in the adolescent brain that persist into adulthood. I also discovered that AIE causes persistent reductions of basal forebrain cholinergic neurons that is accompanied by impaired cognition that persists into adulthood. I have replicated these findings in post-mortem human alcoholic tissue samples. The AIE-induced reduction of basal forebrain cholinergic neurons was initially interpreted as indicative of cell death. However, total forebrain neuron numbers do not change and we discovered that the AIE reduction of cholinergic neurons is reversible following the conclusion of AIE suggesting ***persistent epigenetic silencing of the cholinergic phenotype that can be restored***. Indeed, I discovered that AIE increases gene silencing markers (e.g., H3K9me2) at ChAT and TrkA cholinergic gene promoters, and decreases basal forebrain cholinergic neurons, which are both reversible. It is unknown if cholinergic phenotypic silencing is due to proinflammatory signaling. My current research focuses on identifying neuroimmune involvement in epigenetic silencing of cholinergic phenotype as well as contributions of dysfunctional basal forebrain cholinergic system and altered brain functional connectivity in adulthood.

B. Research Support:

R01 AG 072894 Vetreno (PI) 9/1/20 – 8/31/25
NIH/NIA
Adolescent alcohol in 5xFAD mouse model accelerates neuroinflammation and Alzheimer's disease pathology across aging
Role: PI

U01 AA 020023 Crews (PI) 9/1/20 – 8/31/25
NIH/NIAAA
Component 5/8 and 7/8 NADIA U01: Effects of adolescent alcohol on adult brain neurocircuitry
Role: Co-PI

K01 AA 025713 Vetreno (PI) 9/1/18 – 8/31/23
NIH/NIAAA

HMGB1 and innate immune involvement in adult neuropathology following adolescent alcohol exposure
Role: PI

R21/R33 Crews, Hendershot (PI) Pending
NIH/NIAAA
Translational alcohol response batteries to define mechanisms of tolerance
Role: Co-investigator

R01 Vetreno (PI) Pending
NIH/NIAAA
Microglial proinflammatory epigenetic reprogramming regulates neuronal phenotype
The proposed studies on microglial proinflammatory phenotype and brain region-specific AIE pathology explores novel epigenetic and neuronal plasticity mechanisms that have broad neuroscience and therapeutic implications.
Role: PI

Citations:

1. **Vetreno, R.P.**, Bohnsack, J.P., Kusumo, H., Liu, W., Pandey, S.C., & Crews, F.T. (2020). Neuroimmune and epigenetic involvement in adolescent binge ethanol-induced loss of basal forebrain cholinergic neurons: Restoration with voluntary exercise. *Addict Biol*, PMID: 30779268.
2. Crews, F.T., Fisher, R., Deason, C., & **Vetreno, R.P.** (2021). Loss of basal forebrain cholinergic neurons following adolescent binge ethanol exposure: Recovery with the cholinesterase inhibitor galantamine. *Front Behav Neurosci*, PMID: 33716687.
3. Crews, F.T., & **Vetreno, R.P.** (2022). Cholinergic REST-G9a gene repression through HMGB1-TLR4 neuroimmune signaling regulates basal forebrain cholinergic neuron phenotype. *Front Mol Neurosci*, PMID: 36072299.
4. Macht, V., **Vetreno, R.P.**, & Crews, F.T. (2022). Cholinergic and neuroimmune signaling interact to impact adult hippocampal neurogenesis and alcohol pathology across development. *Front Pharmacol*, PMID: 35308225.

C. Positions, Scientific Appointments, and Honors

Positions

2018 - Present Assistant Professor, Bowles Center for Alcohol Studies, Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, NC
2016 - 2018 Research Associate, Bowles Center for Alcohol Studies, University of North Carolina School of Medicine, Chapel Hill, NC
2011 - 2016 Postdoctoral Fellow, Bowles Center for Alcohol Studies, University of North Carolina School of Medicine, Chapel Hill, NC

Honors

2023 Young Investigator Award, NIAAA Meeting “Alcoholism and Stress: A Framework for Future Treatment Strategies”, Volterra, Italy
2018 ISBRA Young Investigator Travel Award Recipient
2016 ISBRA/ESBRA Young Investigator Travel Award Recipient
2014 Gordon Research Conference Travel Award, “Alcohol & the Nervous System”
2014 Research Society on Alcoholism Memorial Award
2013 Early Career Investigator Conference Award, Society on Neuroimmune Pharmacology
2013 NIAAA Trainee Workshop Travel Award
2012 Society for Neuroscience Early Career Investigator Travel Award
2012 – 2015 National Institutes of Health Loan Repayment Award, NIAAA (Pediatric)
2011 NIAAA Trainee Workshop Travel Award
2011 Distinguished Dissertation Award, Binghamton University
2006 Graduate Research Thesis Award, Radford University
2005 Department of Psychology Research Award, Radford University

D. Contributions to Science

1. Adolescent binge drinking is a risk factor for development of AUD later in life. I discovered that adolescent intermittent ethanol (AIE), which models human adolescent binge drinking, induces proinflammatory neuroimmune signaling molecules throughout the adolescent brain that persist into adulthood. This discovery is of particular import to health as neuroimmune induction in the brain is associated with most, if not all, neurodegenerative disorders. Further, I discovered upregulation of neuroimmune markers in post-mortem human AUD brain that contribute to neurodegeneration.
    a. Macht, V., **Vetreno, R.P.**, Elchert, N., & Crews, F.T. (2021). Galantamine prevents and reverses neuroimmune induction and loss of adult hippocampal neurogenesis following adolescent alcohol exposure. *J Neuroinflammation*, PMID: 34530858.
    b. **Vetreno, R.P.**, Qin, L., Coleman, L.G., & Crews, F.T. (2021). Increased Toll-like receptor-MyD88-NFkB-proinflammatory neuroimmune signaling in the orbitofrontal cortex of human alcohol use disorder. *ACER*, PMID: 34415075.
    c. Qin, L., Zou, J., Barnett, A., **Vetreno, R.P.**, Crews, F.T., & Coleman, L.G. (2021). TRAIL mediates neuronal death in AUD: A link between neuroinflammation and neurodegeneration. *Int J Mol Sci*, PMID: 33806288.
    d. Qin, L., **Vetreno, R.P.** & Crews, F.T. (2023). NADPH oxidase and endoplasmic reticulum stress is associated with neuronal degeneration in the orbitofrontal cortex of individuals with alcohol use disorder. *Addict Biol*, PMID: 36577732.

2. Adolescent binge ethanol exposure and proinflammatory neuroimmune signaling drive loss of basal forebrain cholinergic neurons and hippocampal neurogenesis. I discovered that blockade of neuroimmune signaling can prevent adolescent binge ethanol-induced loss of basal forebrain cholinergic neurons and hippocampal neurogenesis. Further, I discovered a loss of basal forebrain cholinergic neuron markers in the post-mortem human AUD brain. I recently discovered that the AIE-induced loss of basal forebrain cholinergic neuron markers involves epigenetic silencing of cholinergic genes, resulting in a loss of the cholinergic phenotype, and not cell death, that can be recovered later in life. These discoveries identified a novel neuroplastic process of reversible loss of neuronal phenotype.
    a. **Vetreno, R.P.**, Bohnsack, J.P., Kusumo, H., Liu, W., Pandey, S.C., & Crews, F.T. (2020). Neuroimmune and epigenetic involvement in adolescent binge ethanol-induced loss of basal forebrain cholinergic neurons: Restoration with voluntary exercise. *Addict Biol*, PMID: 30779268.
    b. Crews, F.T., Fisher, R., Deason, C., & **Vetreno, R.P.** (2021). Loss of basal forebrain cholinergic neurons following adolescent binge ethanol exposure: Recovery with the cholinesterase inhibitor galantamine. *Front Behav Neurosci*, PMID: 33716687.
    c. Crews, F.T., & **Vetreno, R.P.** (2022). Cholinergic REST-G9a gene repression through HMGB1-TLR4 neuroimmune signaling regulates basal forebrain cholinergic neuron phenotype. *Front Mol Neurosci*, PMID: 36072299.
    d. Macht, V., **Vetreno, R.P.**, & Crews, F.T. (2022). Cholinergic and neuroimmune signaling interact to impact adult hippocampal neurogenesis and alcohol pathology across development. *Front Pharmacology*, PMID: 35308225.

3. Adolescence is a critical period of brain refinement as well as a time of experimentation with drugs of abuse, including alcohol, that could impact maturation. We discovered that adolescent intermittent ethanol (AIE), which models human binge drinking, leads to persistent alterations in cortical thickness, loss of hippocampal neurogenesis, and diminished serotonergic phenotype markers as well as other neuropathology that persists well into adulthood. These effects are accompanied by impaired behavioral flexibility, diminished object recognition memory, and increased anxiety-like behaviors in adulthood. Together, these data reveal that adolescent binge drinking alters brain development that persists into adulthood.
    a. Coleman, L.G Jr., Crews, F.T., & **Vetreno, R.P.** (2021). The persistent impact of adolescent binge alcohol on adult brain structural, cellular, and behavioral pathology: A role for the neuroimmune system and epigenetics. *Int Rev Neurobiol*, PMID: 34696871.
    b. Macht, V., **Vetreno, R.P.**, Elchert, N., & Crews, F.T. (2021). Galantamine prevents and reverses neuroimmune induction and loss of adult hippocampal neurogenesis following adolescent alcohol exposure. *J Neuroinflammation*, PMID: 34530858.
    c. **Vetreno, R.P.**, Massey, V., & Crews, F.T. (2021). Long-lasting microbial dysbiosis and altered enteric neurotransmitters in adult rats following adolescent binge ethanol exposure. *Addict Biol*, PMID: 31880056.

d. Dannenhoffer, C.A., Gómez, A., Macht, V.A., Jawad, R., Sutherland, E.B., **Vetreno, R.P.**, Crews, F.T., Boettiger, C.A., & Robinson, D.L. (2022). Impact of adolescent intermittent ethanol exposure on interneurons and their surrounding perineuronal nets in adulthood. *ACER*, PMID: 35307830.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/myncbi/ryan.vetreno.1/bibliography/public/