BIOGRAPHICAL SKETCH

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NAME: Mary-Louise Risher

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

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
George Mason University, Fairfax, VA	B.S.	05/2022	Applied Biology
University of Georgia, Augusta, GA	Ph.D.	12/2010	Neuropharmacology
Duke University, Durham, NC	Postdoc	03/2016	Addiction Neuroscience and Glia

A. Personal Statement

As a graduate student I trained under the mentorship of two renowned behavioral neuropharmacologists and neurotoxicologists; Dr. Alvin Terry and the late Dr. Jerry Buccafusco. I combined behavioral techniques and cell culture, and biochemical measures that I developed in the laboratory to assess behavioral impairment and changes in mitochondrial function following exposure to various pharmacological compounds and commercially available pesticides (PMID: 21799050). However, the dissociated neuronal cell cultures lacked the circuitry necessary to make inferences about neuronal network function; therefore, to fill this gap, I joined the laboratory of Dr. Scott Swartzwelder (Duke University) for my postdoctoral training. I learned the basics of slice electrophysiology to delineate ethanol's neurotoxic effects on neuronal network function and continued to refine my expertise in rodent models of behavior.

Towards the end of my postdoctoral training, I began to pursue the role of astrocyte-driven neuronal dysfunction as a potential mechanism underlying how ethanol can promote synaptic deficits and cognitive impairment. In collaboration with Dr. Cagla Eroglu (Duke), I determined that adolescent intermittent ethanol (AIE) promotes the upregulation of astrocyte-secreted factors, leading to aberrant synaptic remodeling, and behavioral impairment that persists into adulthood. This work led to multiple grants and promotion to Assistant Research Professor at Duke University. In 2018, I began my tenure track position at the Joan C. Edwards School of Medicine, Marshall University. We combine AAV approaches, fiber photometrics, IHC, high resolution imaging, and behavioral tasks to understand how cell-level functional changes, in response to AIE and across adolescent development, influence performance in a multitude of behavioral tasks. Our overarching goal is to identify non-neuronal therapeutic targets to alleviate long-term cognitive dysfunction. We have determined that extracellular matrix proteins, the tripartite synapse, and astrocyte signaling are profoundly impacted by AIE in male and female rats and that these deficits persist into adulthood. More recent work demonstrates that recovery of astrocyte function can rescue these behavioral deficits (BioRvix, Coulter et al., 2025, '*Adolescent Ethanol Exposure Disrupts Astrocyte-Synaptic Structural and Functional Coupling in the Male Hippocampus')* and that a history of binge ethanol exposure in mice exacerbates behavioral recovery from blast traumatic brain injury (bTBI) in adulthood (PMID: 40123100).

As a note, my publication history reflects my maiden name (Middlemore) and I have been publishing under my married name (Risher M-L) since 2010.

Ongoing and recently completed projects that I would like to highlight include:

Highlighted Prior and Ongoing Research

NSF-2242771 Risher (Research Lead) 06/01/2023-05/31/2028
RII Track 1: West Virginia Network for Functional Neuroscience and Transcriptomics (WV-NFNT)
This project investigates how ethanol exposure disrupts PAP-synaptic coupling and synaptic structure in selective subregions of the orbital frontal cortex and the role of astrocyte heterogeneity.

R21AA030086 Risher (PI) 03/15/2023-02/28/2025
NIH/NIAAA
Title: Effects of adolescent ethanol exposure on astrocyte-neuronal crosstalk.
The overall objective of this study is to elucidate how ethanol disrupts functional crosstalk between synapses and peripheral astrocyte processes and subsequent gliotransmitter release.

VA Merit Award IBX005403A Risher (PI) 07/01/2021-06/30/2026
Department of Veterans Affairs (BLR&D)
Title: Long-term effects of binge drinking on astrocyte-synaptic interactions
This project will determine the temporal relationship between CIE-induced PAP-synaptic decoupling and synaptic morphology. It will also assess changes in K^+ homeostasis in astrocytes and determine the behavioral consequences of astrocyte dysregulation.

Examples of past support

WVCTSI Pilot Grant 2U54GM104942 Risher (PI) 01/01/2024-12/31/2024
West Virginia Clinical and Translational Science Institute Open Competition Pilot Grants Program
Title: The role of astrocytes in the convergence of alcohol-induced and age-related cognitive decline
This project investigates how lifetime EtOH use and aging converge to disrupt astrocyte-neuronal interactions and impair cognition. Our central hypothesis is that continued EtOH use throughout the lifespan exacerbates the aging process through accelerated impairment of astrocyte-neuronal crosstalk that manifests as worsening cognitive decline.

Career Development Award 1IK2BX002505 Risher (PI) 01/01/2016-12/31/2020
Department of Veterans Affairs (BLR&D)
The Glial Mechanisms of Ethanol-Induced Damage: Plasticity and Pathology
The goal of this study is to use a rat model of chronic intermittent ethanol exposure and novel cellular approaches to unravel the mechanisms of brain injury and dysfunction that occur after repeated binge alcohol use, implicating astrocytes as potential targets for innovative therapeutic strategies.

NARSAD Young Investigator Award: 25432 Risher (PI) 01/01/2017-12/31/2018
Brain and Behavior Research Foundation
The Role of the Synaptogenic Receptor α2δ-1 in the Development of Addiction
A number of astrocyte secreted factors interact with the neuronal synaptogenic α2δ-1 voltage-gated accessory receptor subunit. The goal of this study is to determine the role that α2δ-1 plays in the development of addiction and response to reward.

Neurobiology of Adolescent Drinking in Adulthood (NADIA): 5U01AA019925-08
Risher (Consultant) Swartzwelder (PI) 09/01/2010-07/31/2018
National Institute on Alcohol Abuse and Alcoholism
Title: Adolescent Alcohol Effects on Learning and Hippocampal Function
The goal of this study is to understand the enduring effects of AIE on learning and hippocampal function in adulthood. This component focused on the hippocampal cholinergic input from Ch1-2 and the effects of AIE on memory-related hippocampal function. This award also focused on the cholinergic approaches that may be effective in reversing AIE-related behavioral deficits.

B.Positions, Scientific Appointments, and Honors

2004-2010 **Graduate Student** at the University of Georgia (Clinical and Experimental Therapeutics) under the guidance of Dr. Alvin V. Terry Jr.

2011-2016	**Postdoctoral Research Associate** in the Department of Psychiatry and Behavioral Sciences (Division of Addiction), Duke University Medical Center, Durham, NC and Durham VA Medical Center, Durham, NC.
2015-2018	**Research Physiologist** at the Durham VA Medical Center, Durham, NC.
2016-2018	**Assistant Professor** in the Department of Psychiatry and Behavioral Sciences (Division of Addiction), Duke University Medical Center, Durham, NC.
2018-2021	**Adjunct Assistant Professor** in the Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC.
2018-2024	**Tenure track Assistant Professor** in the Department of Biomedical Sciences at the Joan C. Edwards School of Medicine, Marshall University, Huntington, WV.
2018-present	**Research Physiologist** at the Hershel 'Woody' Williams Veterans Affairs Medical Center, Huntington, WV.
2024-present	**Tenured Associate Professor** in the Department of Biomedical Sciences at the Joan C. Edwards School of Medicine, Marshall University, Huntington, WV.

Other Experience

2021-present	Joan C. Edwards School of Medicine Academic Standards Committee
2021-present	Joan C. Edwards School of Medicine Institutional Biosafety Committee
2021-present	Joan C. Edwards School of Medicine Vivarium Space Committee
2017-2018	Neuroimmunology and Glia Group Spring Symposium Committee (Duke)
2016-2018	Duke BioCoRE faculty affiliate
2016-2018	Duke Institute for Brain Sciences – faculty member
2012-2018	Durham VA Institutional Animal Care and Use Committee (IACUC)

2021-present	Frontiers in Pharmacology – manuscript peer revier
2021-present	International Journal of Molecular Sciences – manuscript peer review
2020-present	Cells – manuscript peer review
2018-present	Molecular Neurobiology – manuscript peer review
2014-present	Alcoholism: Clinical and Experimental Therapeutics – manuscript peer review
2013-present	Psychopharmacology – manuscript peer review
2012-present	Pharmacology, Biochemistry and Behavior – manuscript peer review

2025	NIH Study Section (SEP, ZRG1 ICN- L (94))
2023-present	NIH S10 Study Section
2023-present	Veterans Affairs BLR&D Study Section (NURA)
2022-present	KY-INBRE – Pilot Grant Study Section
2021	NIH Study Section (Ad hoc – NAL)
2014-present	Alzheimer's Association Trainee Grant Reviewer

Memberships

2015 - 2018	Triangle Society for Neuroscience Chapter
2011 - present	Member, Research Society on Alcoholism
2005 - present	Member, Society of Neuroscience

Awards and Honors

2023	Joan C. Edwards School of Medicine 'Dean's Award for Excellence in Research'
2020	32nd Annual Conference of the International Society for Environmental Epidemiology Travel Award
2017	Duke University Department of Psychiatry Addiction Division Travel Award
2016	Duke University Department of Psychiatry Addiction Division Travel Award
2013	Veterans Affairs Research Week, Young Investigator Award
2010	Medical College of Georgia, Pharmacology and Toxicology Graduate Student Symposium Award (Oral Presentation) University of Georgia, 2nd Annual Scientific Research Day (Poster Presentation)
2010	
2009	

	Medical College of Georgia, Pharmacology and Toxicology Graduate Student Symposium Award (Oral Presentation)
2017	Duke University Department of Psychiatry Addiction Division Travel Award
2016	Duke University Department of Psychiatry Addiction Division Travel Award
2013	Veterans Affairs Research Week, Young Investigator Award
2010	Medical College of Georgia, Pharmacology and Toxicology Graduate
2010	Student Symposium Award (Oral Presentation) University of Georgia, 2nd Annual Scientific Research Day (Poster Presentation)
2009	Medical College of Georgia, Pharmacology and Toxicology Graduate Student Symposium Award (Oral Presentation)

C. Contributions to Science

https://www.ncbi.nlm.nih.gov/myncbi/mary-louise.risher.1/bibliography/public/

As I transitioned into an independent faculty position, I began to investigate if astrocytes play a role in the effects of repeated ethanol exposure on neuronal structure/function. This combined work resulted in two high-profile publications in the alcohol field that garnered a great deal of media attention and became the focus of my first two independent grants (Career Development Award from the U.S. Veterans Affairs and the prestigious Young Investigator Award from the Brain and Behavior Research Foundation). My work demonstrated that rats exposed to repeated EtOH exposure during late-stage brain development show persistent changes in neuronal number, structure, and function, and that the timing of these changes corresponds with the dysregulation of the glial signaling proteins are involved in regulating synaptogenesis. Our most recent publication is in BioRvix (titled: *Adolescent Ethanol Exposure Disrupts Astrocyte-Synaptic Structural and Functional Coupling in the Male Hippocampus*) and has been submitted for peer review. This most recent work involves the use of viruses, chemogenetics, and fiberphotometry that allow us to assess how EtOH disrupts astrocyte-synaptic interactions during behavior. In this manuscript, we demonstrated that structural and functional astrocyte-synaptic decoupling occurs in response to EtOH and that we can rescue deficits in contextual fear conditioning through chemogenetic recovery of astrocyte function. Ongoing work includes *ex-vivo* assessment of Ca2+ and glutamate signaling and *in-vivo* assessment of gliotransmitter release in awake behaving rats.

1. Coulter, O.R, Walker, C.D, **Risher, M-L**. Astrocyte-specific Ca^{2+} activity: mechanisms of action, experimental tools, and roles in ethanol-induced dysfunction. Review. Biochemistry and Cell Biology. Accepted. 2023.
2. C.D. Walker, H.G. Sexton, J. Hyde, B. Greene, **M-L Risher**. Diverging effects of adolescent ethanol exposure on tripartite synaptic development across prefrontal cortex subregions. Cells. Oct 2022; 11(19):3111. DOI: 10.3390/cells11193111.
3. Testen A, Ali M, Sexton HG, Hodges S, Dubester K, Reissner KJ, Swartzwelder HS, **Risher M-L**. Region Specific Differences in Morphometric Features and Synaptic Colocalization of Astrocytes During Development. Neuroscience. 2019 Feb 21;400:98-109. doi: 10.1016/j.neuroscience.2018.12.044. *Artwork selected for the cover of this issue.
4. **Risher ML,** Sexton HG, Risher WC, Wilson WA, Fleming RL, Madison RD, Moore SD, Eroglu, Swartzwelder HS. Adolescent Intermittent Alcohol Exposure: Dysregulation of thrombospondins and synapse formation are associated with decreased neuronal density in the adult hippocampus. Alcoholism: Clinical and Experimental Research. 2015 Dec; 39(12):2403-13. PMID:26537975
   ** This research was featured in the NIAAA Spectrum Newsletter (Volume 7, Issue 3, September 2015).*
5. **Risher M-L**, Fleming R.L., Risher W.C., Miller K.M., Klein R.C., Wills T.A., Acheson S.K., Moore S.D., Wilson W.A., Eroglu C. Swartzwelder H.S. Adolescent Intermittent Alcohol Exposure: Persistence of Structural and Functional Hippocampal Abnormalities into Adulthood. Alcoholism: Clinical and Experimental Research. 2015. June;39(6):989-97. PMID:25916839
   **Interviews were conducted with a number of media outlets. 139 media outlets published articles relating to this research including: AAAS, U.S. News and World Report and the Wall Street Journal.*

Ethanol: effects on learning, memory and behavior: As a post-doctoral research associate I turned my attention to alcohol. This felt like a natural transition for me given my background in behavioral neurotoxicology and neuropharmacology. I began my postdoc career assessing the behavioral effects of intermittent ethanol exposure on learning and memory processes in the adolescent rat. We discovered that intermittent ethanol exposure disrupts behavioral efficiency in the water maze task, working memory in the spatial-temporal object recognition task, and working memory after acute EtOH exposure in the radial arm maze. More recently, we

have investigated the impact of adolescent unpredictable stress on anxiety, novelty seeking, and voluntary ethanol consumption and the potential attenuating effects of rosiglitazone (PARRγ agonist). More recent work is focused on understanding the role of astrocytes in regulating behavior.

6. Y. H. Xu, H.G. Sexton, A. N. Henderson-Redmond, C. Harris, J.D. Huber, **M-L. Risher**. The impact of adolescent drinking on traumatic brain injury-induced cognitive deficits and alcohol preference in adulthood. Alcoholism: Clinical and Experimental Research. 2025. May;49(5):1013-1027. DOI: 10.1111/acer.70027.
7. HG Sexton, NA Olszewski, **M-L Risher**. Rosiglitazone attenuates task specific anxiety-like behavior and novelty seeking in a model of chronic adolescent unpredictable stress. Jan 2022. Frontiers in Behavioral Neuroscience. 2022 Feb 11;16:830310. PMID**:** 35221947**.** DOI: 10.3389/fnbeh.2022.830310
8. Miller KM, **Risher ML**, Acheson SK, Darlow M, Sexton HG, Schramm-Sapyta N, Swartzwelder HS. Behavioral inefficiency on a risky decision-making task in adulthood after adolescent intermittent ethanol exposure in rats. Scientific Reports. 2017 Jul 5;7(1):4680. doi: 10.1038/s41598-017-04704-7.
9. Swartzwelder HS, Acheson SK, Miller KM, Sexton, HG, Liu, W, Crews, FT and **Risher M-L**. Adolescent Intermittent Alcohol Exposure: Deficits in Object Recognition Memory and Forebrain Cholinergic Markers. PlosOne. 2015. Nov 3;10(11):e0140042. PMID:26529506
10. **Mary-Louise Risher**, Rebekah L. Fleming, Nathalie Boutros, Svetlana Semenova, Wilkie A. Wilson, Edward D. Levin, Athina Markou, Harry S. Swartzwelder, and Shawn K. Acheson. Long-Term Effects of Chronic Intermittent Ethanol Exposure in Adolescent and Adult Rats: Radial-Arm Maze Performance and Operant Food Reinforced Responding. Plos One. 2013. May. 8(5):1-14. PMID:23675442

Ethanol and GABA: To complement the behavioral findings that we elucidated in the laboratory we began exploring the effects of ethanol on neuronal function using hippocampal slice electrophysiology. These data revealed changes in tonic inhibition and GABAA receptor expression in the hippocampus following adolescent ethanol exposure that was not replicable following adult ethanol exposure. Further work demonstrated enduring changes in K^+ conductance.

11. Qiang Li, Rebekah L. Fleming, Shawn K. Acheson, Roger A. Madison, Scott D. Moore, **Mary-Louise Risher**, Wilkie A. Wilson and H.S. Swarztwelder. Long-term modulation of A-type K^+ conductances in hippocampal CA1 interneurons in rats exposed to ethanol during adolescence or adulthood. Alcoholism: Clinical and Experimental Therapeutics. 2013. Dec. 37(12): 2074-85. PMID:23889304
12. Fleming, Rebekah, Li, Qiang**, Risher, Mary-Louise**; Sexton, Hannah; Moore, Scott; Wilson, Wilkie; Acheson, Shawn; Swartzwelder, H. Binge-pattern ethanol exposure during adolescence, but not adulthood, causes persistent changes in GABAA receptor-mediated tonic inhibition in dentate granule cells. Alcoholism: Clinical and Experimental Research. 2013. Jul. 37(7), 1154-60. PMID:23413887

Organophosphates: During graduate school, it was well known that acute, high-level exposure to chlorpyrifos could result in severe cholinergic crisis. However, the implications of chronic, low-level exposure were unknown. I began to explore the effect of this pesticide on performance in the 5-choice serial reaction time task and found deficits in sustained attention and increased impulsivity in our rat model. Another part of my project was to assess changes in cholinergic receptor expression; however, I really wanted to understand more of the underlying mechanisms. After a lengthy literature search, I hypothesized that axonal transport is impaired after chlorpyrifos exposure. I then designed, implemented, and completed a project showing that chlorpyrifos could impair mitochondrial axonal transport in cultured cortical neurons in a dose-dependent manner. Due to these publications, my mentor gained great attention from the EPA and was invited to join a panel that would ultimately influence the regulation of chlorpyrifos use within the US.

13. **Middlemore-Risher ML**, Adam B-L, Lambert NA, Terry AV Jr. Effects of chlorpyrifos and chlorpyrifos-oxon on the dynamics and movement of mitochondria in rat cortical neurons. Journal of Pharmacology and Experimental Therapeutics. 2011. Nov. 339(2):341-9. PMID:21799050
14. **Middlemore-Risher ML**, Buccafusco JJ, Terry AV Jr. Repeated exposures to low-level chlorpyrifos results in impairments in sustained attention and increased impulsivity in rats. Neurotoxicology and Teratology. 2010 Mar 26. 32(4):415-24. PMID:20350597
15. Terry AV Jr, Gearhart DA, Beck WD, Truan JN**, Middlemore ML**, Williamson LN, Bartlett MG, Prendergast MA, Sickles DW, Buccafusco JJ. Chronic Intermittent Exposure to CPF in Rats: Protracted Effects on Axonal Transport, Neurotrophin Receptors, Cholinergic Markers and Information Processing. Journal of Pharmacology and Experimental Therapeutics. 2007. Sept. 322(3) 1117-28. PMID: 1754853