Physiology News

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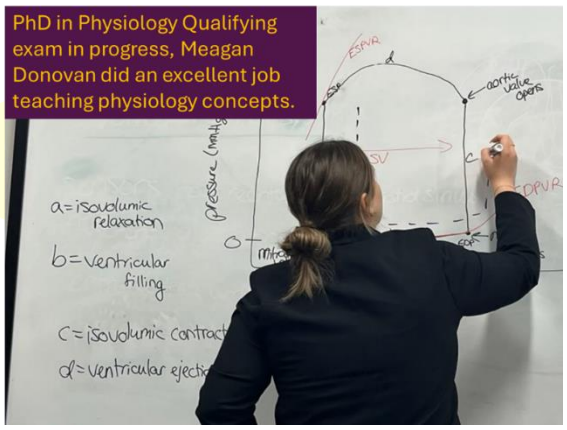
The Physiology family is proud to have a leading female physiologist at the helm. Dr. Patricia Molina made the front cover of the current edition of the “The Physiologist”.

Physiology News

Dear all,

Summer is here and I am sure many of you have friends and family that wonder if you are enjoying your summer months. Few appreciate the fact that our work continues throughout the entire year. No sooner have we finished entering grades, than we are preparing for the new group of students coming to Medical, Nursing, Allied Health, and Dental Schools, or working on summer courses like Tiger Scholars or Scientific Writing. Those of us involved in research transition to focus on our students participating in short term research experiences. This year excellence has been the theme in terms of their performance, enthusiasm, and appreciation for the unique opportunity to learn how knowledge is created.

My message in the previous note from the Chair's corner focused on gratitude and appreciation for the contributions of so many team players that make our success a reality. At times I find myself reflecting on what are the factors that support and energize my commitment to our mission. I am constantly thinking of how to keep us safe, protected, supported, relevant, recognized, and directed to succeed. At times I feel we operate in a yellow submarine that navigates under water, with stealth and resilience never losing our focus. And then my thoughts turn to how we manage and what we can do to continuously make things better. Everyone's efforts in achieving our mission are critical and can sometimes produce fatigue, stress, and anxiety. *I want this to be a message of encouragement for each one of you to think and practice kindness and grace during the upcoming months*. That means respect for different points of view, silence and a smile when what you are thinking of saying is not positive, consideration for what others may be going through that we may not be aware of but that can affect how they feel. The next few months are likely to be filled with negative and destructive messaging and language coming to us through social media, the press, and mundane interactions. Let us make it our goal to use kindness and grace as a soothing balm that will shield us from negativity, protect our personal and collective wellbeing, and serve to invigorate our daily interactions.



PhD in Physiology Qualifying exam in progress, Meagan Donovan did an excellent job teaching physiology concepts.

We have much to be proud of! Our trainees continue to excel, those here and those who have moved on to their next professional development phase. The School of Medicine graduating class of 2024 recognized Physiology as the best department. Our NIAAA T35 got refunded, and the submission of grants continues to be robust. As we enjoy the rest of the summer sun, heat, rain, peaches, and creole tomatoes, keep your spirits up! You are what makes Physiology, tick!

Sincerely

Patricia

Inside this edition

Editor, Liz Simon

Excessive alcohol consumption: a modifiable risk factor in the development of dementia

About the author- Sydney M. Vita, PhD is a newly appointed Assistant Professor in the Department of Physiology. Dr. Vita's research is focused on alcohol use and neurodegeneration, particularly with adolescent alcohol use. Dr. Vita is funded for the work by the NIH/NIAAA.

The rising prevalence of dementia, a debilitating neurodegenerative condition characterized by progressive cognitive impairment and functional decline, with Alzheimer's disease being the most common form diagnosed. As the population ages, the burden of dementia continues to intensify, with the number of cases anticipated to reach 82 million worldwide by 2030[1], underscoring the urgency for comprehensive research into its modifiable risk factors. In January 2011, then President Obama enacted the National Plan to Address Alzheimer's Disease, aimed at developing effective prevention and treatment approaches for Alzheimer's disease and related dementias. Alcohol consumption, a widely embraced social practice, has emerged as one of the most significant modifiable risk factor, particularly when it comes to early onset, necessitating a rigorous examination of its impact on cognitive function and the development of dementia[2].

The neurological implications of chronic and excessive alcohol use are well-documented in preclinical research. The primary mechanisms include neurotoxicity, prolonged neuroinflammation, oxidative stress, and associated nutritional deficiencies[1]. Preclinical models show that alcohol administration affects cognitive function, with the nature and severity of the effects correlating with the duration and intensity of the drinking. In the short term, heavy episodic or binge drinking can induce transient cognitive impairments, manifesting as deficits in attention, memory, decision-making, and executive functioning[3]. These acute effects are primarily attributed to the direct neurotoxicity in brain structures involved in cognitive processes, as well as the disruption of neurotransmitter systems. In contrast, the long-term effects of chronic, excessive alcohol use on cognitive function are far more pervasive, leading to substantial structural and functional alterations in the brain culminating in persistent cognitive deficits and an increased risk of dementia[2,4,5].

One of the primary alcohol-induced mechanisms of compromised cognitive health is neurotoxic effects. Alcohol metabolism generates an excess of reactive oxygen species (ROS), leading to oxidative stress within brain tissues. This imbalance results in cellular component damage, including lipid peroxidation, protein modification, and DNA strand breakage, ultimately compromising neuron functionality and promoting cell death[3]. These responses involve the activation of microglia, the brain's resident immune cells, facilitating neuroinflammation linked to neurodegenerative diseases[6]. Chronic neuroinflammation catalyzed by alcohol misuse results in the secretion of pro-inflammatory cytokines and chemokines, causing neurotoxicity that can lead to cognitive impairment and subsequent dementia. Alcohol can also disrupt the neurotransmitter systems vital for learning, memory, and cognitive function by skewing the balance between excitatory and inhibitory neurotransmitters, leading to cognitive decline and memory impairments[7]. Additionally, alcohol dampens the function of the endocannabinoid system, contributing to the neuroplastic alterations that underpin addiction and cognitive decline[8].

Cohort studies have highlighted the age-dependent nature of the risk and the influence of the duration of consumption[7]. Of particular concern is the link between alcohol consumption and the hallmark pathologies of Alzheimer's disease, such as the accumulation of amyloid-beta (Aβ) plaques and the formation of neurofibrillary tangles. Alcohol misuse modulates key pathways involved in Aβ production and tau hyperphosphorylation, thereby potentially exacerbating underlying Alzheimer's pathophysiology[3]. Studies have also explored the interaction between alcohol misuse and genetic predispositions, such as the Apolipoprotein E (ApoE) genotype, linking

hazardous alcohol use to accelerated Alzheimer's disease pathology through mechanisms like oxidative stress and apoptosis[9]

The long-term impact of excessive alcohol use on cognitive function extends beyond the direct effects on the brain. Nutritional deficiencies driven by alcohol consumption, particularly thiamine depletion, play a pivotal role in compromising cognitive health. Thiamine is essential for glucose metabolism, oxidative stress regulation, and the maintenance of nervous system integrity. Chronic alcohol consumers are at risk of developing Wernicke-Korsakoff syndrome, a type of dementia characterized by severe cognitive impairment and memory loss, as a direct result of thiamine deficiency[2,3,10]. Alcohol-induced liver injury, a common consequence of chronic alcohol consumption, can further exacerbate cognitive impairments by dysregulating systemic inflammatory processes, contributing to the neuroinflammatory cascade implicated in Alzheimer's pathogenesis [2,3,10]. Finally, it is important to take into account the psychosocial consequences, including social isolation and comorbid mental health issues, which can compound the cognitive challenges faced by individuals with alcohol use disorder[2].

While heavy, excessive drinking has been consistently linked to cognitive impairments and an increased risk of dementia, the impact of moderate alcohol consumption remains a subject of ongoing debate[3]. Some epidemiological studies have suggested that light to moderate consumption may confer protective benefits, possibly through mechanisms such as enhanced acetylcholine release and reduced cardiovascular risk factors, while other investigations have not found a significant association at all, underscoring the complexity of the link between alcohol use and cognitive performance[2,4,6,10]. However, it is crucial to note that these purported benefits are often outweighed by the risks associated with alcohol consumption, particularly in the context of dementia. Furthermore, the definition of "moderate" alcohol consumption has varied across studies and populations, complicating the interpretation of research findings, especially when combined with individual factors such as genetics, age, sex, metabolic differences, and overall health status[4,6,10]. Such confounds highlight the need for more empirical studies, including randomized controlled trials, to better delineate alcohol's direct effects on dementia progression. While disentangling the effects of alcohol from these other lifestyle and environmental factors in a clinical setting may be extremely challenging, addressing methodological inconsistencies across studies could be highly impactful. Large-scale surveys, global modeling studies, and investigations into sex-specific factors and genetic predisposition could provide valuable insights and inform targeted interventions aimed at mitigating the alcohol attributable burden of dementia. In addition, collaborative, integrative multi-disciplinary approaches involving diverse expertise could accelerate a comprehensive understanding of the neurobiological mechanisms underlying alcohol's impact on dementia pathology.

In conclusion, while certain risk factors for dementia, such as age and genetics, cannot be addressed, excessive alcohol use stands as a factor that can be targeted through preventative measures and lifestyle modifications. By implementing evidence-based strategies, promoting public awareness, enacting effective policies, and fostering continued research, we can take significant strides towards mitigating the burden of alcohol-related dementia and preserving cognitive health and promoting overall well-being.

Citations

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Physiology News

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Promotions

Dr. Andrea Jones, PhD is promoted to Senior Staff Scientist in the Gilpin Lab.

Dr. Sydney Vita was promoted to Assistant Professor in Physiology.

Recognition

Stephanie Lee won travel awards and presented at the Research on Alcohol and HIV Satellite Meeting and Sex & Gender Satellite Meeting during the Research Society on Alcohol Conference in Minneapolis, MN in June 2024.

Taylor Fitzpatrick-Schmidt was appointed an American Physiological Society Graduate Student Ambassador for 2024-2026, including travel support for the next two APS meetings in Baltimore, MD and Minneapolis, MN.

The **LSUHSC PREP** welcomed 4 new Scholars on June 1, 2024. Pictured from left to right: Alyssa Negron, BS, Graduate of Caldwell University/Caldwell, NJ in Biology will train with Peter Winsauer, PhD in Pharmacology. Trinity Martin, BS, Graduate of Loyola University New Orleans in Cell and Molecular Biology will train with **Scott Edwards**; Deja Holmes, BS, Graduate of Prairie View A&M University/Prairie View, TX in Biology will train with Amelia Jernigan, MD in OB/GYN; and Tendayi Mpofu, BS, Graduate of Xavier University of Louisiana/New Orleans in Neuroscience Pre-Med will train with Jorgelina Calandria, PhD in Neurology and Neuroscience

Grants

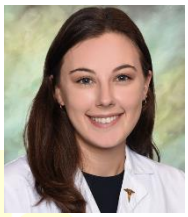
Stephanie Lee- NIH/NIAAA F30 NRSA proposal (Sponsors: Edwards, Gilpin, Molina)

Sydney Vita- 1K01AA031516-01, "Adolescent alcohol exposure exacerbates rmTBI associated BBB disruption and dementia risk".

Liz Simon and Noelle Moreau. Molecular regulation of skeletal muscle function in children with cerebral palsy: implication for therapeutic targets. LSUHSC Wide Intramural Program.

New Faces

Katherine Copenhaver graduated with a BS in Biology from Davidson College. Katherine is a new MD/PhD student in the department and is excited to join the lab of Dr. Rajani Maiya. On the weekends, Katherine enjoys gardening and going for runs in City Park.



Kaitlin Couvillion graduated with a BS in Microbiology from LSU, Baton Rouge. Kaitlin is an MD/PhD student in the Simon lab.

Loren Johnson graduated with a BS in Biology from Louisiana Tech University. Loren is the newest Research Associate of Dr. Elizabeth Avegno. Loren enjoys spending time with her daughter.

Thomas Kyllo defended his PhD in the Neuroscience Center here at LSU in June 2024. Tommy got a Master's in Public Health and Tropical Medicine from Tulane university in 2019 and a BS in Biology from High Point University in 2017. Tommy is appointed as a Postdoctoral Fellow under Dr. Wills in Cell biology and Anatomy and Dr. Gilpin is a Co-mentor/PI.

Jamie McMichael joined as the newest research associate in Dr. Robert Siggins' lab. Jamie is a graduate of Mississippi State University. Jamie has a dog and a cat; and enjoys taking the dog to parks and letting her explore. Jamie

is an avid nature lover and, on the weekends, visits the Audubon Nature Institute with friends.

The Edwards Lab welcomed ENDURE Scholar **Andrew Bruce** and PREP Scholar **Trinity Martin** to investigate the neurobiology of alcohol use disorder and related co-morbidities.

Professional services

Laury Byerley organized two meetings Cultivating Health in a Changing World. Cardiovascular Health and Well-being DPG Symposium, April 11-14, 2024, Tucson, AZ and in May 21-23, 2024, Ottawa, CA for the 43rd National Nutrient Databank Conference.

Scott Edwards was appointed to Dr. Peter DeBlieux's Standardized Patient Working Group and Dr. Janet Southerland's LSUHSC Hunger-Free Campus Taskforce.

Scott Edwards reviewed for the *NIH/NIDA Targeting Inflammasomes in HIV and Substance Use* study section.

Taylor Fitzpatrick-Schmidt reviewed applications for the APS William Galey Professional Skills Award Committee.

Eden Gallegos was selected for the LSUHSC QEP 2024-2025 committee as the graduate student representative along with Linh Ha.

Publications

Bazan HA, Bhattacharjee S, Reid MM, Jun B, Polk C, Strain M, St. Pierre LA, Desai N, Daly PW, **Cucinello-Ragland JA, Edwards S**, Recio J, Alvarez-Builla J, Cai JJ, Bazan NG. Transcriptomic signature, bioactivity, and safety of a non-hepatotoxic analgesic generating AM404 in the mid-brain PAG region. Scientific Reports 2024 14(1):11103.

Fitzpatrick-Schmidt T, Leonardi C, Norlin C, Beiter K, Stuke LE, Brown T, Marr A, Greiffenstein P, Schoen J, Hunt JP, **Smith A**. Global health experience among general surgery residents: Experiences, attitudes, and barriers. The American Journal of Surgery 2024 doi: 10.1016/j.amjsurg.2024.05.001.

Fitzpatrick-Schmidt T, **Edwards S.** Within and Beyond the Binary: Sex and Gender Differences in Pain and Alcohol Use Disorder. Current Addiction Reports 2024 11:68-80.

Fitzpatrick-Schmidt T, Oral E, Welsh DA, **Molina PE, Ferguson TF, Edwards S.** Moderate-to-severe cognitive impairment is associated with both recent and chronic alcohol misuse in people with HIV: The New Orleans Alcohol Use in HIV (NOAH) Study. Alcohol: Clinical and Experimental Research 2024 48(7):1405-1416.

Gallegos EM, Reed T, Deville P, Platt B, Leonardi C, Bellfi L, Dufrene J, Chaudhary S, Hunt J, Stuke L, Greiffenstein P, Schoen J, Marr A, Paramesh A, **Smith AA**. Does the use of double hormone replacement therapy for trauma patient organ donors improve organ recovery for transplant. World J Transplant 2024; 14(2): 89825 [DOI: 10.5500/wjt.v14.i2.89825]

Smith AM, Ray TJ, Hulitt AA, **Vita SM**, Warrington JP, Santos CDSE, Grayson BE. High-fat diet consumption negatively influences closed-head traumatic brain injury in a pediatric rodent model. Exp Neurol. 2024 Jul 13:114888. doi: 10.1016/j.expneurol.2024.114888. Epub

Xin Shi, Kevin J Simms, Thomas J Ewing, Yuan-Ping Lin, Yi-Ling Chen, John N Melvan, **Robert W Siggins**, Ping Zhang. The bone marrow endothelial progenitor cell response to septic infection. Frontiers in Immunology, 2024. PMID: 38665923.

Presentations

Lauri Byerley presented an abstract "Protein's Effect on the Gut Microbiota and Its Metabolites: Our Virtual/Remote Recruitment Efforts" at the American Society of Nutrition meeting in Chicago, IL, June 29-July 2nd.

Scott Edwards presented a talk titled *The Importance of Interprofessional Education in Developing Collaboration-Ready Biomedical Scientists for Translational Research* at the American Physiological Society Summit in Long Beach, CA in April 2024.

Scott Edwards presented two talks at the 2024 Research Society on Alcohol meeting in April 2024 in Minneapolis, MN: *Preclinical Research on Pain & Alcohol Interactions and Pain* and *Negative Affect in Relation to Alcohol Use Disorder Risk in People with HIV*.

Physiology News

Scott Edwards presented a talk titled *Intersection of Pain and Alcohol Use Disorder Risk* at the University of Virginia Brain Symposium in May 2024 in Charlottesville, VA

Taylor Fitzpatrick-Schmidt was selected to present her research at the 2024 NIH Pain Consortium Symposium on Advances in Pain Research in May 2024 in Bethesda, MD.

Robert Siggins presented a talk "Alcohol's Unseen Harm: Fueling Immunosenescence & SASP in HIV+ Individuals at the Research Society on Alcohol meeting in April 2024 in Minneapolis, MN

Liz Simon chaired the symposium Mitochondrial adaptations: basic mechanism in alcohol-associated end organ injury and gave a talk "Alcohol-mediated mitochondrial adaptations in the skeletal muscle." Research Society on Alcohol meeting in April 2024 in Minneapolis, MN

Sydney Vita presented a talk titled "Neurodegenerative consequences of blood-brain barrier injury" in the Spring 2024 Physiology Seminar Series.

Posters

Gallegos EM, **Simon L, Molina P**. Chronic binge alcohol alters hepatic expression of metabolic genes in SIV-infected female rhesus macaques. Annual Meeting of the Research Society of Alcoholism. Poster presentation. Minneapolis, MN. June 2024.

Gallegos EM, Molina P, Simon L. Ethanol increases cholesterol and decreases ATP in HepaRG spheroids. Annual Meeting of the Research Society of Alcoholism. Poster presentation. Minneapolis, MN. June 2024.

PM McTernan, RW Siggins, H-Y Lin, **PE Molina** and DA Welsh**.** High Alcohol Use Increases Caspase 1 Activation in Senescent CD8+ T Cells in People With HIV. June 2024. *Poster*. Minneapolis, Minnesota.

Notable Events

The NIH/NIAAA T35 Medical Student Alcohol Research Internship program began in June with seven new T35 Fellows. Technical seminars were provided by **Eden Gallegos, Dr. Sydney Vita, Dr. Patrick McTernan, Nicholas Harris, Taylor Fitzpatrick-Schmidt, and Stephanie Lee**, and research seminars were provided by **Dr. Stefany Primeaux, Dr. Janos Paloczi, Dr. Liz Simon,** and Dr. Michael Salling.

Department of Physiology alum **Dr. Danielle Levit** was awarded an R01 from the NIH/NIA. Proud of Dr. Levitt's great achievement.

Department of Physiology alum **Dr. Adrienne McGinn** started a new position as Research Proposal Development Officer at Tulane University School of Medicine.

Xavier Chapa-Dubocq, Nicholas Harris, Liz Simon and Keishla Rodriguez-Graciani completed the 5K RSA MarkWood Run. Nick clocked 26 minutes, Xavier and Keishla 29, and Simon 34.

Patrick McTernan welcomed a new family member -**Luna** (picture attached)!

Courtesy- Nicholas Harris