Syracuse University

Neuroscience and Health Behavior Research Day 2026

April 10, 2026

Collegian Hotel and Suites

1060 E. Genesee Street, Syracuse, NY 13210

Co-sponsored by:
The Interdisciplinary Neuroscience Program
The Center for Health Behavior Research & Innovation

Program Committee:
Jessica MacDonald (Biology)
Joseph Ditre (Center for Health Behavior Research & Innovation; Psychology)
James Hewett (Biology)
Jialiu Zeng (Biomedical and Chemical Engineering)

Program Agenda

Time	Activity
8:00 am -9:00 am	Registration Desk opens and continental breakfast
9:00 am -9:10 am	Welcome Jessica MacDonald, Executive Director, Neuroscience Program Joseph Ditre, Director, Center for Health Behavior Research & Innovation
9:15 am - 10:10am	Keynote Address **Karla Kaun,** Associate Professor, Department of Neuroscience, Brown University Presentation Title: Neuromelecular mechanisms underlying approach-avoidance conflict in alcohol self administration.
10:15 am - 10:45 am	Invited Faculty Speaker **Sarah Karalunas,** Cobb-Jones Endowed Professor and Chair of Psychology, College of Arts & Sciences Presentation Title: Staying in control: developing mechanisms of cognitive and emotion regulation in ADHD.
10:45 am - 11:00 am	Break
11:00 am - 11:30 am	Invited Faculty Speaker **Yalian Pei,** Assistant Professor, Department of Communication Sciences and Disorders, College of Arts & Sciences Presentation Title: Reading after Mild Traumatic Brain Injury.
11:30 am - 12:30 pm	Selected poster abstract oral presentations
12:30 pm - 1:30 pm	Lunch and Poster set up
1:30 pm - 2:30 pm	Poster Session
2:30 pm -2:45 pm	Break
2:45 pm -3:15 pm	Invited Faculty Speaker **Jayson Smith,** Assistant Professor, Department of Biology, College of Arts & Sciences Presentation Title: Deciphering mechanisms of neuronal terminal differentiation & function: From worms to humans.
3:15 pm - 3:45 pm	Invited Faculty Speaker **Jialiu Zeng,** Assistant Professor, Department of Biomedical and Chemical Engineering, College of Engineering and Computer Science Presentation title: Alpha-synuclein driven neurodegeneration in Parkinson's disease: Mechanisms and engineered therapies.
3:45 pm - 4:00 pm	Closing remarks

Keynote Address

Dr. Karla Kaun

Associate Professor, Department of Neuroscience, Brown University

Neuromolecular mechanisms underlying approach-avoidance conflict in alcohol self-administration

Invited Presentations

Sarah Karalunas

Cobb-Jones Endowed Professor and Chair of Psychology, College of Arts & Sciences, Syracuse University

Staying in control: developing mechanisms of cognitive and emotion regulation in ADHD

Yalian Pei

Assistant Professor, Department of Communication Sciences and Disorders, College of Arts & Sciences, Syracuse University

Reading after Mild Traumatic Brain Injury

Jayson Smith

Assistant Professor, Department of Biology, College of Arts & Sciences, Syracuse University

Deciphering mechanisms of neuronal terminal differentiation & function: From worms to humans

Jialiu Zeng

Assistant Professor, Department of Biomedical and Chemical Engineering, College of Engineering and Computer Science, Syracuse University

Alpha-synuclein driven neurodegeneration in Parkinson's disease: Mechanisms and engineered therapies

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Poster Presentations

1. #1 or #2? Describing early auditory brainstem response waves in extremely and very preterm infants.

Faith Whitebread, Stefania Arduini, and Beth Prieve
Communication Sciences & Disorders; Syracuse University

Background and objectives: Auditory brainstem response (ABR) is an excellent metric to track auditory brainstem development using absolute and interwave latencies. Reports of Wave I latencies in early literature (1980's and 1990's) from preterm infants are highly variable; it seems likely that Wave II was labeled as Wave I, and the amplitude of Wave I was a measure of the I-II complex, confounding measures of interwave latencies. With the rise of clinical diagnostic use of ABR in the 1990's, Waves I, III, and V became popular, resulting in a dearth of information on Waves II and IV in current literature. Moreover, data reported in prior literature were collected 40 years ago, and characteristics of those preterm infants are dramatically different than infants born preterm today. Therefore, defining Waves I and II, in addition to Waves III, IV, and V, are critical for studying brainstem maturation. It is imperative that brainstem maturation be studied in the current preterm population, which includes extremely and very preterm infants, and that the cadre of canonical ABR measures be considered. The goal of the current study is to (1) define whether the presence/absence of early waves change with age; (2) describe the changes in ABR latencies and amplitudes with particular attention to Waves I and II; (3) investigate whether ABR latencies and amplitudes vary as a function of gestational age at birth.

Methods: 119 preterm infants were tested at 33, 35, 48-52 and 62-66 weeks gestational age (WGA) at Crouse Hospital and the Pediatric Audiology Laboratory in Syracuse, NY. Gestational ages for infants at birth ranged from 23 to 32 weeks. Middle-ear status was assessed via Wideband Acoustic Immittance (WAI). ABRs were recorded in response to condensation and rarefaction clicks presented at 27.7/second at an intensity of 70 dB nHL. ABRs from infants having abnormal middle ear status were excluded from ABR analysis. ABR waveform latencies and amplitudes were evaluated independently by research team members. Strict rules were in place to judge replicability of waves. Replicable condensation waveforms were averaged, and wave latencies and amplitudes were determined for ipsilateral Waves I-VI.

Results: Based on agreement of wave latencies and amplitudes by team members, Wave II was judged to be present more often than Wave I for infants tested at 33 and 35 WGA. At older test ages, Waves I and II were more equally observable. Grand averages of ABR responses for each test time indicated Wave I increased in amplitude and all wave latencies decreased with increasing test age. Wave II was robust and observable for all test ages.

Conclusion: Wave II is a more robust measure of peripheral neural functioning than Wave I in infants born extremely and very preterm. Wave II, rather than Wave I, which are both modeled to be arising from the auditory neurons before synapse with the cochlear nucleus, should be considered for study-ing development of brainstem conduction in time in this population. [Research supported by NIH-NIDCD R01DC011777].

2. Anxiety but not Depression or Pain is Related to Perceived Cognitive Difficulties among Women with Chiari Malformation

Katie O'Leary, Karlee Patrick, Ashlana S Prashad, Ryn Hirst, Grant Ripley, Emily Rabinowitz
Psychology Department; Syracuse University

Introduction: Perceived cognitive difficulties are a predominant complaint among women with Chiari Malformation (CM). However, a specific neuropsychological profile for people with CM remains challenging due to the complex interactions between cognition, psychiatric symptoms, pain, and surgical treatment for CM. The current study aims to explore the unique impact of psychiatric and pain variables on self-reported cognitive difficulties as well as to determine the extent to which surgical status impacts these relationships.

Method: Females with Chiari malformation (N=95) completed the Cognitive Difficulties Scale, a 39-item scale that captures perceived difficulties in the domains of attention and concentration, praxis, prospective memory, speech, people's names, and temporal orientation. Participants also completed the DASS-21 which assessed depression, anxiety, and stress as well as the brief pain inventory which measured pain interference and pain intensity. Self-reported sociodemographic and medical characteristics were also recorded.

Results: In a multivariate regression model, level of anxiety (b=1.79, SE=.40, p<.01) but not depression, pain interference, or pain intensity, predicted total cognitive difficulties. An exploratory analysis found that there was a interaction between anxiety level and surgical history to address Chiari in predicting total cognitive difficulties (b=-1.69, SE=.66, p=.01) such that individuals who had not undergone surgical treatment tended to have a stronger relationship between anxiety and cognitive difficulties compared to those who had undergone surgery.

Discussion: Anxiety emerged a unique predictor of cognitive difficulties when accounting for depression and pain, suggesting that the cognitive profile of people with CM may be heavily influenced by factors related to anxiety such as executive dysfunction, inhibitory processes, and hyperarousal. Moreover, individuals without a history of surgery had a stronger relationship between anxiety symptoms and cognitive difficulties, which may be related to increased psychosomatic anxiety as well as neuropsychiatric characteristics related to the presentation of CM and surgical treatment.

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3. Associations between Sleep Hygiene, Insomnia, and Dysfunctional Sleep Beliefs among Adults with Chiari Malformation

Ashlana S. Prashad, Katie O'Leary, Ryn Hirst, Grant Ripley, Emily Rabinowitz
Exercise Science; Syracuse University

Introduction: Chiari malformation (CM) occurs when the cerebellum extends into the spinal canal, blocking the flow of cerebral spinal fluid (CSF). Patients with CM have a higher prevalence of insomnia. Less is known about the psychological and behavioral factors contributing to insomnia in CM patients.

Method: This study utilized data from 108 Individuals with CM (N=108), who completed the Dysfunctional beliefs and Attitudes about Sleep (DBAS-16), Insomnia Severity Index (ISI), and Sleep Hygiene Index (SHI). The DBAS-16 contains 16 questions assessing sleep related beliefs and attitudes. Hierarchical regression analyses were used to

examine the unique variance explained by adding sleep hygiene into the model predicting insomnia from dysfunctional beliefs and attitudes.

Results: Higher DBAS scores were positively correlated with ISI scores (r = .68, p < .01), and poorer sleep hygiene was positively correlated with ISI scores (r = .39, p < .01). Regression analyses indicated that DBAS explained 46.3% of the variance in ISI (R^2 = .46, p < .01). Adding SHI in the second step significantly improved the model (ΔR^2 = .05, p <.01), and both DBAS (b = 0.14, p < .01) and SHI (b = 0.20, p < .01) were significant predictors in the final model. When reversed, SHI alone explained 15.4% of ISI variance (R^2 = .15, p < .001), and adding DBAS explained an additional 36% (ΔR^2 = .36, p < .001). Overall, both sleep hygiene and sleep-related beliefs were associated with insomnia severity, but dysfunctional sleep beliefs accounted for more unique variance.

Discussion: Both dysfunctional beliefs about sleep and poor sleep hygiene were associated with greater insomnia severity. However, beliefs about sleep appeared to be the stronger unique contributor to insomnia. Findings highlight the potential value of cognitive interventions targeting dysfunctional sleep beliefs.

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4. Anxiety Sensitivity and Alcohol Use in College Students: Moderating Effects of Drinking Refusal Self-Efficacy

Mariya Churina & Michelle J. Zaso
Psychology Department; Syracuse University

College drinking continues to present considerable negative academic, health, and social consequences. Understanding factors that might mitigate college drinking risk is crucial for improving intervention and treatment. One risk factor that appears linked with alcohol use is anxiety sensitivity, which is conceptualized as the tendency to fear anxiety-related sensations due to the belief that they may lead to harmful consequences. Higher anxiety sensitivity has been related to problematic alcohol use among college students specifically, perhaps due to drinking to cope with distressing internal sensations. In contrast, drinking refusal self-efficacy may serve as a protective factor, defined as confidence in one's ability to refuse alcohol. However, to our knowledge, research has yet to explore how anxiety sensitivity and drinking refusal self-efficacy interplay to predict college student drinking. This study tested whether associations between anxiety sensitivity and alcohol outcomes differ as a function of drinking refusal self-efficacy among college students. Methods: Participants were undergraduate students enrolled in introductory psychology courses at Syracuse University who completed an online survey for research participation credit (SONA) as part of a larger project. Secondary data analyses were conducted on asubsample of participants who reported any alcohol use in the past year and passed various attention checks throughout the survey (n = 271; M age = 18.97; SD = 1.52; 57% women; 63.2% White; 13.4% Asian; 12.6% Black or African American; and 1.5% American Indian or Alaska Native). Participantscompleted assessments on anxiety sensitivity, drinking refusal self-efficacy, alcohol consumption, and alcohol problems. Linear regressions in SPSS, Version 29.0.2.0 tested whether anxiety sensitivity, drinking refusal self-efficacy, or their interaction related to alcohol consumption or alcohol problems as separate outcomes, controlling for gender. Both outcomes were winsorized to minimize the influence of univariate outliers, and assumptions of linear regression were verified prior to analyses. Predictors were centered prior to calculating product terms, and simple effects were computed to interpret the pattern of any significant interactions identified. Results: Models demonstrated a significant interaction of anxiety sensitivity with drinking refusal self-efficacy on alcohol problems ($\beta = -.12$, $p = .04$). Specifically, greater levels of anxiety sensitivity related to more alcohol problems among students with relatively lower levels of drinking refusal self-efficacy ($\beta = .30$, $p < .001$) but not among students with relatively higher levels of drinking refusal

self-efficacy (β = .10, p = .26). In contrast, models did not support an interaction of anxiety sensitivity with drinking refusal self-efficacy on alcohol consumption (β = .08, p = .17). Discussion: Findings suggest that heightened drinking refusal self-efficacy might help to buffer associations of anxiety sensitivity with problematic alcohol outcomes. As such, this study highlights drinking refusal self-efficacy as a potential target for interventions aimed at reducing alcohol problems. Efforts to bolster students' confidence in their ability to refuse alcohol might ultimately reduce some of the many harms of college student drinking.

5. Dietary metabolites selectively modify phenotypes of a vpr-1/VAPB mutant

Isabel L. Ross, David Greenstein, Sarah E. Hall
Biology Department; Syracuse University

ALS8 is a dominant familial form of the neurodegenerative disease Amyotrophic lateral sclerosis, associated with a P56S mutation in the N terminal MSP domain of the VAMP-associated protein B (VAPB). Under physiological conditions, VAPB acts as a tethering protein at mitochondria-associated ER membranes to promote lipid transfer and calcium homeostasis between the two organelles. In addition, the MSP domain can be cleaved and secreted to signal cell non-autonomously to other tissues. The P56S mutation disrupts both the intracellular tethering function and extracellular signaling function of VAPB; however, how this global disturbance leads specifically to the upper and lower motor neuron death characteristic of ALS is not well understood. The functions of VAP family proteins are conserved between mammals and nematodes. In C. elegans, VPR-1 is the sole orthologue of the VAP protein family. We demonstrate that a vpr-1 deletion mutant exhibits systemic dysfunction including maternal effect sterility, chemotaxis defects, and a locomotion defect that recapitulates the motor symptoms that define ALS. Furthermore, we show that these phenotypes occur in a diet-dependent manner, with animals raised on the nutritionally minimal E. coli OP50 diet exhibiting far more severe phenotypes than animals fed the E. coli NA22, HT115, or HB101 diets. Interestingly, rescue of vpr-1 phenotypes was diet-specific, suggesting that each E. coli strain provided specific metabolites to modify vpr-1 phenotypes. To identify a candidate set of metabolites that may be responsible for the differential vpr-1 phenotypes, we analyzed a previously published dataset for the metabolic profile of E. coli OP50, HB101, and MG1655 strains. We have identified a set of candidate metabolites from specific diets that correlate with less severe phenotypes in vpr-1 mutants and are currently testing whether they are sufficient to improve VPR-1 function. Further, we are investigating the role of these metabolites in the regulation of mitochondrial morphology and function under these different dietary conditions. Together, our results will enhance our understanding of the mechanisms underlying ALS8 pathology and may give insight into potential therapeutic approaches.

6. Associations Between Psychological Distress and Benzodiazepine Use and Misuse among U.S. Veterans

Joshua M. Soh, Victoria E. Carlin, Joon K. Nam, Joseph W. Ditre
Psychology Department; Syracuse University

Introduction: Psychological distress, defined as a generalized state of emotional suffering characterized by depressive and anxiety symptoms, is common among U.S. military veterans. The use of benzodiazepines, which are central nervous system depressants often used to treat symptoms of anxiety, post-traumatic stress disorder, and insomnia, is also prevalent in this population despite ongoing concerns regarding dependence, misuse, and potential adverse mental health outcomes. Although benzodiazepines may provide short-term symptom relief, both their use and misuse may contribute to increases in symptoms of psychological distress. As such, this study examines the relationship between psychological distress and BZD use and misuse among a representative sample of U.S. military veterans.

Method: Drawing from the 2021-2024 National Survey on Drug Use and Health (NSDUH), general linear models were employed to test associations between psychological distress (Kessler-6 Psychological Distress Scale) and past-year BZD use (yes/no) and misuse (yes/no).

Results: A general linear model revealed that veterans with past-year BZD use had higher psychological distress scores ($F(1, 50) = 23.39$, $p < .001$), when compared to those with no past-year use (M BZD use = 6.42, SE = 0.40; M no BZD use = 4.38, SE = 0.14). Veterans with past-year BZD misuse reported higher psychological distress scores ($F(1, 50) = 7.15$, $p = .01$), compared to those with no past-year misuse (M BZD misuse = 7.58, SE = 1.11; M no BZD misuse = 4.56, SE = 0.14).

Discussion: Past-year BZD use and misuse were associated with elevated psychological distress among U.S. veterans, underscoring the importance of careful monitoring of BZD use patterns in the context of distress symptoms. Longitudinal research is needed to establish temporal precedence and to examine trajectories of BZD use and distress over time.

7. Behavioral Inhibition in Preschoolers Who Stutter: A Comparative Study Using Behavioral Measures

Jessica Singh & Victoria Tumanova, Ph.D.
Communication Sciences & Disorders; Syracuse University

Stuttering is a multifactorial neurodevelopmental disorder that results in disruptions in the fluency of speech. In preschool aged children, temperament is a contributing factor to the development of stuttering. Although it does not cause stuttering, it can affect how stuttering progresses after its onset. The present study investigated a temperamental trait called behavioral inhibition (BI), which is a correlate of shyness. Three research questions were answered: (1) Are preschool-age children who stutter more likely to show a higher degree of BI than typically fluent preschool-age children?, (2) Does the degree of behavioral inhibition influence the frequency of stuttering moments during conversational speech in preschool age children who stutter?, (3) Does BI predict mean length utterance (MLU) and subordination index (SI) in conversation? Participants were 49 children between ages three and five. There were 25 children who stutter (CWS) and 24 children who do not stutter (CWNS). After a play-based conversation with an unfamiliar examiner, the degree of BI was assessed by measuring the latency to the 6th spontaneous comment. Additionally, MLU and SI were analyzed using the Systematic Analysis of Language Transcripts (SALT) software. For CWS, frequency of stuttered utterances was calculated as well. Although most comparisons showed no statistical significance, there were emerging trends observed. First, there was a trend that CWNS has a higher mean latency to the 6th spontaneous comment compared to CWS. Second, the data showed a trend of a higher frequency of stuttered utterances in CWS who had a higher degree of BI. Third, higher BI was significantly associated with lower MLU for all children. Findings suggest that temperament plays a significant role in the development of a child's linguistic complexity.

8. Co-Occurring Hallucinogen Use and Mental Health Symptoms Among U.S. Veterans

Emerson J. Hoagland, Grant H. Ripley, Joseph W. Ditre, Dessa Bergen-Cico
Psychology Department; Syracuse University

Introduction: Mental health concerns, including depression and psychological distress, remain highly prevalent among U.S. military veterans and are associated with elevated functional impairment, suicide risk, and barriers to care. Public discourse increasingly suggests the potential therapeutic effects of psychedelic substances in treating mental illness.

However, population-level data examining associations between psychedelic use and mental health burden among U.S. military veterans remain limited. The present study examined associations between past-year hallucinogen use and past-year major depressive episode (MDE) and serious psychological distress (SPD) among veterans.

Method: Data were drawn from the National Survey on Drug Use and Health (2021-2024). Analyses were subset to (N = 9,172) U.S. military veterans and employed survey weights to produce nationally representative estimates. Past-year hallucinogen use was assessed using an NSDUH-provided binary (yes/no) variable. MDE was defined using DSM-5 criteria for MDE with items regarding depressed mood or loss of interest lasting at least two weeks, accompanied by ☒5 additional depression symptoms (e.g., changes in sleep, appetite, energy, concentration, feelings of worthlessness, etc.) and related psychosocial impairment. SPD was assessed using the Kessler K6 scale (score ⩾ 13). Design-based F tests were used to evaluate associations between SPD, MDE, and hallucinogen use.

Results: Veterans who reported past-year hallucinogen use demonstrated substantially higher prevalence of MDE (31.99%) compared to those who did not report hallucinogen use (6.34%; $p < .001$). Elevated prevalence was similarly observed for SPD (35.67% vs. 8.82%; $p < .001$).

Conclusion: Hallucinogen use was disproportionately concentrated among veterans experiencing heightened psychological distress and past-year MDE. Although cross-sectional data preclude causal inference, findings suggest that psychedelic use may occur within the context of heightened mental health burden. Thus, additional research may clarify whether use reflects self-directed coping, recreational patterns among veterans experiencing symptoms of depression or distress, or emerging interest in alternative therapeutic approaches.

9. Does the Exposure of BPA, or its Analogs, Increase Seizure Susceptibility in Zebrafish Larvae?

Kylie Kahng, Ravie Grewal, James Lilienfiled, Katherine Lewis and Intisar Haddad
Biology Department; Syracuse University

For my project, I propose to investigate if exposure to Bisphenol A (BPA), or its analogs increases seizure susceptibility. Every day, people are exposed to environmental chemicals that may have long-term health effects. BPA, a chemical commonly used in plastics and food packaging, has been linked to neurological changes, including increased seizure susceptibility. Due to growing health concerns, BPA has been replaced with structural analogs like Bisphenol F (BPF), yet little is known about how these substitutes affect seizure likelihood. Given its chemical similarity to BPA, BPF may have comparable or even more persistent effects on the risk of seizures. This study aims to determine whether embryonic exposure to BPF increases seizure susceptibility using a zebrafish model, which will be exposed to PTZ (pentylenetetrazol) to induce seizure-like activity, since seizures are rare in fish and humans. Zebrafish provide an ideal system for my study due to their transparent embryos, rapid development, and genetic similarity to humans. By comparing seizure activity in BPF-exposed and control larvae, this research will help determine whether BPF poses a seizure risk. Understanding the impact of BPF on seizure risk is essential, as human exposure to BPA alternatives is increasing. Findings from this research will contribute to a broader understanding of how this environmental contaminant influences seizure likelihood and may inform future regulations on BPA replacements.

10. Differential patterns of audiovisual integration in autistic and neurotypical adults: A mismatch negativity study

Xiaoxiao Chen, Jarryd Osborne, Elia F Soto, Danielle Lynch, Hunter J Pyke, Sarah F Alamarie, & Natalie Russo
Psychology Department; Syracuse University

Real-world perception requires integrating information across modalities, yet how brains process semantically incongruent bimodal inputs remains unclear. This study examined early multisensory processing in cognitively able autistic (n = 16; mean age = 22.56 years old) and neurotypical (n = 22, mean age = 19.78 years old) adults using EEG in a modified bimodal oddball task. Mismatch negativity (MMN), a negative-going ERP, offers a window into preattentive change detection and can reveal whether multisensory integration differences emerge at early, automatic processing stages. Participants viewed and heard meaningful animal pairings simultaneously: a standard ("meow-cat," 70%) and three deviants (10% each): meow-frog (visual deviant), ribbit-cat (auditory deviant), and ribbit-frog (audiovisual deviant yet semantically congruent). Mean amplitudes of difference waves (deviant − standard) quantified auditory, visual, and audiovisual mismatch responses, and fractional latencies characterized temporal dynamics. Both groups showed similar patterns for auditory and visual deviants. The autistic group exhibited attenuated visual MMN (mean = -0.98 uv) amplitude relative to neurotypical participants (mean = -1.44 uv). Temporal analyses indicated visual dominance (Colavita-like effect) across groups, with auditory difference waves peaking later in an N2-like window in 200 - 300 ms. Critically, neurotypical participants showed a clear audiovisual MMN, whereas autistic participants showed no reliable audiovisual MMN (t = -2.28, p = .028). Subsequent N400 analysis revealed semantic processing in neurotypical but not autistic participants, highlighting differential sensory integration mechanisms. Neurotypical adults' responses were driven by both stimulus frequency and cross-modal semantic relationships, whereas autistic participants showed sensitivity primarily to audiovisual semantic incongruence.

11. Disrupted cholesterol homeostasis as potential therapeutic target for Rett syndrome

Nasim Khatibi, Mayara C. Ribeiro, & Jessica L. MacDonald
Biology Department; Syracuse University

Rett syndrome (RTT) is a severe progressive neurodevelopmental disorder that is caused by mutations in the gene methyl-CpG-binding protein 2 (MECP2). After 6-18 months of relatively normal development, RTT patients undergo a rapid regression and develop a broad series of phenotypes. The symptoms include intellectual disability, loss of speech and muscle tone, abnormal breathing, and severe motor deficits with repetitive hand movements. RTT is the second leading cause of intellectual disability in girls, yet there is currently no cure. Further, while RTT is a neurological disorder, it also affects the peripheral nervous system and multiple organs and tissues. Effective interventions will thus likely require a combinatorial approach, targeting multiple nodes within the interactomes of the myriad cellular pathways disrupted downstream of MeCP2.

Among the metabolic disruptions observed in Mecp2-mutant mouse (hemizygous null male and heterozygous female) are disruptions in cholesterol homeostasis. Cholesterol is essential for proper brain function; however, it cannot cross the blood-brain-barrier and must be synthesized in situ, by astrocytes. CYP46A1, a brain-specific cholesterol homeostasis enzyme, is expressed by neurons and catabolizes cholesterol to 24S-hydroxycholesterol, allowing it to diffuse across the blood-brain-barrier for turnover. Cholesterol homeostasis in the brain thus involves a complex interplay between neurons and astrocytes that must be very tightly regulated; either insufficient or excess neuronal cholesterol impairs memory formation and synaptic plasticity and contributes to multiple neurological conditions.

We found that Cyp46a1 is downregulated in the Mecp2-mutant cortex but rescued with vitamin D supplementation, both in vivo and in vitro. We are thus investigating the hypotheses that reduced Cyp46a1 expression in the Mecp2-mutant cortex contributes to RTT pathophysiology, is caused by both cell autonomous and non-cell-autonomous disruptions, and that restoration of homeostasis to this pathway could provide a partial therapeutic approach. We have found that down-regulation of Cyp46a1 expression leads to reduced neuronal size, recapitulating the phenotype of Mecp2-null neurons, and we have identified downregulation in the expression of the key rate-limiting cholesterol synthesis enzyme HMGCR in both the brain and liver of Mecp2 Het mice at symptomatic stages. Ongoing studies are investigating whether CYP46A1 activating drugs increase the neuronal size and complexity of Mecp2-null neurons in vitro and could provide a novel therapeutic approach. Together, these studies address a major gap in knowledge on the mechanisms of cholesterol homeostasis disruptions in RTT brain, and they are essential to determine the therapeutic potential of CYP46A1 modulation.

12. Dual-Task Cost During Balance Perturbations Relates to Gait Variability in Overground Walking*

Sami Carnahan, Anthony Zhang, Tony Lalta, Jesse Goldstein, Reese Michaels, Yaejin Moon
Exercise Science; Syracuse University
*Selected for Oral Presentation

Growing evidence shows that greater declines in walking speed during simultaneous cognitive tasks are linked to higher fall risk. This cognitive-motor interference is typically assessed using a dual-task approach quantifying motor performance changes under cognitive load (dual-task cost, DTC). However, most studies have focused on steady-state walking rather than balance perturbations, which are more directly related to fall risk. PURPOSE: To examine correlations between DTC in perturbation trials and unperturbed overground walking outcomes. METHODS: Twenty healthy young adults (10 females, Age = 22.0 ± 1.5 yrs) completed overground walking and treadmill-based perturbation trials with and without cognitive tasks (e.g., word generation, subtraction). In the overground test, participants walked 25 ft at a comfortable pace on an electronic walkway (GAITRite) measuring spatiotemporal parameters. They then performed balance loss trials on an instrumented perturbation treadmill (BalanceTutor) while experiencing random perturbations in four directions (right, left, forward, backward) at 27 cm/s (lateral) and 48 cm/s (forward/backward). A built-in force plate recorded center of pressure (COP) data, including path length, medio-lateral (ML) and anterior-posterior (AP) ranges, symmetry index, and jerk. DTC was calculated as [100 × (dual-task - single-task)/single-task], and Spearman correlations were computed between DTC values from overground walking and perturbation outcomes. RESULTS: DTC of COP outcomes from perturbation trials were more strongly and consistently related to DTC of gait variability (step-to-step fluctuations) than to average gait measures. Right-side perturbations showed the most associations, including correlations between AP and ML COP ranges and variability measures (e.g., step length, step time, stride velocity variability), as well as between variability metrics and path length (ρ = 0.482-0.843, $p \leq 0.03$). Additional associations included a positive correlation between AP range and step time average (ρ = 0.598, $p < 0.01$) and a negative correlation between AP range and stride velocity average (ρ = -0.474, $p = 0.04$). Left-side perturbations demonstrated associations primarily involving step time variability, including positive correlations with path length (ρ = 0.551, $p = 0.01$) and jerk (ρ = 0.590, $p < 0.01$), as well as associations with symmetry index, including a positive correlation with double support time average (ρ = 0.581, $p < 0.01$) and a negative correlation with single support time average (ρ = -0.461, $p = 0.04$). Forward perturbations showed positive correlations between step length variability and path length (ρ = 0.527) and AP range (ρ = 0.585). Backward perturbations showed positive correlations between step length variability and symmetry index (ρ = 0.656, $p < 0.01$), stride velocity variability and

symmetry index (ρ = 0.542, p = 0.02) and inflection (ρ = 0.508, p = 0.02). CONCLUSION: Gait variability, rather than average gait performance, is more closely associated with balance recovery ability in dual-task scenarios. SIGNIFICANCE: Gait variability under cognitive load may be a novel intervention target to reduce fall risk during cognitively demanding activities.

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13. Dissecting Inflammatory and Metabolic Drivers of Neurodegeneration in Secondary Progressive Multiple Sclerosis

Tanver Riyed, Kriti Kalary, Jialiu Zeng & Chih Hung Lo
Biomedical & Chemical Engineering; Syracuse University

Secondary Progressive Multiple Sclerosis (SPMS) remains a therapeutically intractable neurodegenerative condition, largely characterized by persistent, compartmentalized neuroinflammation. While the inflammatory drivers of the disease are well-documented, the role of metabolic dysfunction remains poorly understood. In the progressive phase, demyelinated axons face a shift toward sustained bioenergetic failure and weakened cellular homeostasis. This collapse renders neurons vulnerable to ionic stress, while concurrent dysfunction of the lysosomal-autophagy axis and mitochondrial impairment further diminish the clearance of damaged organelles and myelin-derived debris. To dissect the molecular basis of this metabolic-inflammatory interface, we performed integrative transcriptomic analysis via data mining of the progressive MS brain tissue dataset (GSE131282). Bulk RNA sequencing analysis using Gene Ontology (GO) and Gene Set Enrichment Analysis (GSEA) revealed that SPMS is characterized by a robust immune and inflammatory transcriptional profile, featuring elevated NF-κB and interferon signaling. Key regulators of oxidative phosphorylation and lysosomal acidification were significantly downregulated in SPMS samples, suggesting a close association between persistent neuroinflammation and the reinforcement of metabolic and lysosomal failure. Comparative analysis further differentiated the progressive subtypes. While SPMS maintains high inflammatory signature, PPMS exhibits a more isolated mitochondrial and autophagy-lysosomal profile. These computational signatures were corroborated in an experimental autoimmune encephalomyelitis (EAE) animal model, where Western blot and immunostaining analyses confirmed a significant downregulation of mitochondrial respiratory, lysosomal, and autophagy markers alongside persistent upregulation of inflammatory signaling. Collectively, these findings define the metabolic-inflammatory axis as a primary driver of SPMS chronicity and establish a rational basis for therapeutic strategies that prioritize bioenergetic resilience alongside the resolution of chronic neuroinflammation.

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14. Ethanol-induced Dysregulation of Src Kinase in Mouse and Human Embryonic Neurodevelopment

Joslyn Doupe, Mohammad Badrul Anam, Brian Howell & Eric Olson
SUNY Upstate Medical University

Fetal alcohol syndrome (FAS) is the leading cause of preventable intellectual disability in humans and is characterized by disrupted brain development and postnatal cognitive impairments. The pathology of FAS is complex and includes disruptions of signaling pathways involved in neuronal proliferation, migration, differentiation, and apoptosis. However, it is unclear whether there are common biochemical mechanisms that initiate this diverse pathology. Prior work from our laboratory established that just 15 minutes of ethanol exposure in doses ranging from 100 to 400mg/dl causes a rapid increase in tyrosine phosphorylation of multiple proteins, both in cultured mouse neurons and in the fetal mouse brain after maternal dosing. Pharmacological intervention revealed that Src Family Kinase (SFK) activity was critical for the hyperphosphorylation. Phosphoantibody array data revealed phosphorylation targets in several neurodevelopmental

signaling pathways suggesting that multiple cellular pathologies could be initiated by this SFK mediated hyperphosphorylation. To determine whether this SFK activation mechanisms could contribute to FAS we asked whether ethanol can trigger a similar response in human embryonic cortical neurons. Using cultured cerebral organoids, generated from human iPSCs (Kolf2.1/J), we find that 15 minute exposure to 400 mg/dl ethanol causes a ~2.5-fold increase in phosphotyrosine immunosignal in 50 DIV and older organoids. The highest response is observed in regions of the organoids enriched in Dcx+ immature neurons. The phosphorylation response is completely blocked with PP2, a selective inhibitor of SFKs but not with the inactive control compound PP3. We then used a genetic approach to determine which of the three SFKs expressed in cortical neurons is activated by EtOH. We exposed genetically deficient Src mouse embryos to 400mg/dl ethanol. The phosphotyrosine immunosignal in Src deficient embryos was not increased following ethanol exposure indicating Src is uniquely required for ethanol induced hyperphosphorylation. These initial results suggest that human cortical neurons, like mouse cortical neurons, are vulnerable to ethanol induced SFK hyperactivation and that Src hyperactivity may result in the consequent disruption of multiple developmentally important signaling pathways.

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15. Examining the Impact of Sex Differences on the Relationship Between Sensory Features and Adaptive Behavior in Individuals with Autism

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Sensory differences are core features of Autism Spectrum Disorder (ASD) that can significantly impact an individual's daily life and behavior; however, less is understood about how sensory features may differ by sex. The present study assesses sex as a moderator in the relationship between sensory features and adaptive behavior in autistic individuals using existing data. Thirty- nine individuals with autism, ages 11 to 17 years (F= 13, M= 26), completed the Vineland Adaptive Behavior Scales (Vineland-II) and the Sensory Profile Self-Questionnaire (SP2) to compare the relationship between sensory avoiding as well as sensory sensitivity related behaviors and adaptive behaviors as a function of sex. It was hypothesized that sex would moderate the relationship between sensory features and adaptive behavior, with females showing a stronger association between sensory differences and lower adaptive behavior compared to males. Correlation analyses did not indicate a significant relationship between sensory differences and adaptive behavior for either sex. Additionally, moderation analyses revealed that sex did not significantly moderate the relationship between sensory features and adaptive behavior (p> .05). Due to the relatively small sample size and heterogeneity of the participants in this study, future research should utilize larger and more diverse samples to clarify these findings and examine factors that may contribute to sex differences in sensory processing, adaptive functioning, and autism diagnosis.

16. Investigating Aberrant Neuroinflammation and Downstream Signaling Pathways in the Neurodevelopmental Disorder Rett Syndrome

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Rett Syndrome (RTT) is an X-linked neurodevelopmental disorder which affects approximately 1in 10,000 live female births. This disorder is caused by mutations in the transcriptional regulatorMECP2. When functioning normally, the MECP2 gene is able to code for the proper production of the MECP2 protein which can either suppress or activate the transcription of downstream target genes. There is currently no cure for RTT, however, there are possible partial

therapeutic strategies through the alteration of these downstream pathways. The NF-kB pathway is included in this list of targets. Vitamin D supplementation has an effect on the NF-kB pathway as it stops the pathway from being activated. However, NF-kB pathway attenuation only provides significant phenotypic amelioration with the male mouse model. Therefore, we investigated the possible compensation of the NF-kB pathway with another inflammasome component, Alpk1, in female MeCP2 loss-of-function mice. Within the vitamin D homeostasis pathway, there are different enzymes affected by supplementation, such as Cyp27b1 and Cyp24a1. Additionally, cholesterol homeostasis gene Cyp46a1 is affected by MeCP2 loss-of-function. We investigated the effect of NF-kB genetic attenuation on these different genes to determine if the NF-kB pathway converges with and modulates the vitamin D homeostasis pathway and cholesterol biosynthesis pathway.

17. Foraging Connections: Optimal Foraging in Letter Fluency

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The letter fluency task is the timed listing of words that begin with a specific letter (e.g., words starting with T). Participants often list words in phonologically related clusters (e.g., tank, task, tap) and occasionally switch clusters (e.g., tap, thud). This process has been likened to patch switching in animal foraging. Optimal performance requires switching clusters in a manner that maximizes the rate of retrieving words, known as the marginal value theorem. Previous work has found evidence for this in semantic fluency. The current study tests whether people adhere to the marginal value theorem in letter fluency and whether executive functioning is associated with optimal performance. Three letter cues (T, N, and J) and one semantic cue (animals) were administered. Results are consistent with optimal search in N and J, but not T or animals. These findings provide mixed support that people search optimally during letter fluency.

18. Investigating the Influence of Transcriptional Co-regulator Cited2 and Maternal Folic Acid Supplementation on Neocortical Development

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Neocortical development is highly regulated by transcriptional and epigenetic regulators that, when disrupted, can result in neurodevelopmental disorders (NDDs). One such epigenetic co-regulator is CITED2, which modifies histone acetylation through its interaction with the histone acetyltransferases CBP/P300, causing an increase in transcription of certain genes. When Cited2 is knocked out globally, it is embryonic lethal and causes neural tube defects. Importantly, neural tube defects in the global knockout are largely prevented by maternal folic acid supplementation, indicating that environmental factors can modify neurodevelopmental disruptions caused by Cited2 loss-of-function. To study the role of CITED2 in neocortical development, we use a conditional knockout (cKO) model where Cited2 is knocked out only in the forebrain. In the cortex, Cited2 is primarily expressed embryonically in the intermediate progenitor cells (IPCs) of the subventricular zone and post mitotically in the callosal projection neurons of layers II/III. In the cKO mouse, fewer IPCs proliferate in the subventricular zone at E15.5, resulting in fewer callosal projection neurons in layers II/III, ultimately leading to reduced cortical thickness, particularly in the superficial layers. RNA-sequencing data found cilia-related genes to be downregulated and neurogenesis-related genes upregulated in the cKO. This may suggest a disruption in cilia function causing precocious exit from the cell cycle and premature generation of neurons, which would explain the reduction in proliferating IPCs and superficial layer thickness observed in cKO mice. At P3, the reduced somatosensory cortex thickness in cKO mice is rescued by maternal folic acid supplementation. To determine if this is caused by increased IPC proliferation in cKO embryos whose dams were given folic acid supplemented food compared

to those given a folic acid sufficient diet, we are labeling proliferating progenitors in E15.5 cKO and WT embryos with and without maternal folic acid supplementation.These studies will continue to provide insight into how environmental factors tip the balance between typical and atypical development.

19. Gender Differences in Motives for Alcohol Abstinence Among College Students

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Introduction: Alcohol use among college students is a major public health concern linked to academic problems, injuries, assaults, and alcohol use disorder. Recent research suggests that rates of alcohol abstinence might be increasing on college campuses, perhaps due to greater awareness of these alcohol-related consequences and/or students' shifts toward use of other substances, such as marijuana. Reviews and qualitative research suggest that individuals may abstain from alcohol due to religious or moral beliefs, family influence, personal lifestyle choices, and concerns about health or negative consequences. However, the reasons that college students choose to abstain from alcohol remain understudied, particularly whether different groups of students report different reasons for abstaining. The goal of this study was to examine whether college students' reasons for not drinking alcohol differ by gender. We hypothesized that women would be more likely to report safety concerns, value-based motives, and healthrelated reasons for not drinking, whereas men would be more likely to report situational or performance-related reasons for not drinking.

Method: This secondary data analysis project used data from an ongoing cross-sectional study of undergraduate students enrolled in PSY 205 at Syracuse University. Eligible participants had never consumed alcohol or had not done so within the past year. Participants who reported a gender identity other than woman or man (due to small group sizes) or who failed survey attention checks were excluded. The final sample included 41 students (28 women, 13 men), with a mean age of 18.44 years (SD = .91), of which 74% were first-year students. Participants completed survey measures assessing reasons for not drinking alcohol, and independent-samples t-tests were conducted to examine gender differences in reported reasons for not drinking.

Results: Findings showed that, contrary to our hypotheses, most reasons for drinking were not significantly different by gender. Women (M = 1.35, SD = .79) were not significantly more likely than men (M = 1.32, SD = .57) to endorse risks or negative effects of alcohol as a reason for not drinking (t(39) = .10, p = .92, Cohen's d = .03). Similarly, men (M = 2.00, SD = 1.08) were not significantly more likely than women (M = 1.75, SD = 1.32) to report not wanting to disappoint family or friends (t(39) = -.59, p = .56, Cohen's d = -.20). There was also no significant gender difference for being happy without drinking between men (M = 2.15, SD = .90) and women (M = 2.07, SD = 1.15; t(39) = -.23, p = .82, Cohen's d = -.08).

Discussion: These findings suggest that motives for alcohol abstinence may not differ substantially by gender, at least within this sample. It is also possible that this secondary data analysis study was not sufficiently powered to detect meaningful gender differences due to the small sample size and unequal gender distribution. Future research should use larger and more diverse samples as well as examine a broader range of reasons for not drinking to better understand why subgroups of college students choose to abstain from alcohol.

20. Lysosome-acidifying nanoparticles restore lysosomal acidification and mitigate Aβ42 oligomer-induced neurotoxicity in cellular and mouse models of Alzheimer's disease

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Lysosomal dysfunction is an early and central event in Alzheimer's disease (AD), which is characterized by the accumulation of amyloid-β oligomers (AβO) that disrupt lysosomal acidification, proteolytic activity, and autophagic flux. Aβ has been shown to associate with lysosomal V-ATPase subunits, suggesting that its accumulation may disrupt proton pump function and further compromise lysosomal integrity. Whether restoring lysosomal acidification is sufficient to reverse the Aβ-induced pathology remains unresolved. We hypothesized that AβO impair neuronal function through disruption of lysosomal pH and autophagic flux, and hence targeted lysosomal re-acidification to rescue these defects. Using SH-SY5Y neurons, we first examined the effects of AβO on lysosomal functions. AβO exposure induced lysosomal alkalinization, reduced cathepsin activities, and impaired autophagic flux, as well as decreased neuronal viability. Mitochondrial fragmentation, increased ROS (MitoSOX), loss of membrane potential (TMRE) indicated mitochondrial dysfunction downstream to lysosomal impairment. Treatment with lysosome-acidifying nanoparticles (AcNPs), restored lysosomal acidification, cathepsin activity, and enhanced autophagic function, reversed mitochondrial fragmentation and restored network integrity leading to recovery of lysosome-mitochondria activities, resulting in improved cell survival. This demonstrates that lysosomal pH dysregulation is a key mediator of AβO-induced toxicity and represents a direct therapeutic target. Using APPNL-G-F knocked-in mouse model, we performed longitudinal analyses at 2, 4, 6, and 8 months of age to characterize progressive lysosomal dysfunction. With aging, there is reduced expression of lysosomal VATPase subunits including ATP6V1A, ATP6V1H, ATP6V1C1 and increased accumulation of p62, indicating impaired autophagic flux. Behavioral testing demonstrated age-dependent cognitive decline without significant locomotor deficits. Hippocampal administration of AcNPs improved autophagic functions and significantly rescued spatial memory performance.Collectively, these results establish lysosomal acidification failure as a potential driver of Aβinduced neurotoxicity and establish lysosomal re-acidification as a potential therapeutic strategy in AD and identify lysosome-targeted nanotherapeutics as a promising approach to restore cellular homeostasis and cognitive functions.

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21. How Violations of Expectation Influence Subjective Time

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Expectation can shape time judment. Recent work suggests that when an stimuli matches what a person expects, it is often judged as lasting longer (Birngruber, Schröter, Schütt, & Ulrich, 2018., Utegaliyev & von Castell, 2024), consistent with principle proseccing proposing that expected stimuli are processed more efficiently and therefore feel temporally expanded (Matthews & Meck, 2016). Much of this work, however, has relied on neutral stimuli. Building on this, we asked whether outcomes that are better or worse than expected might also bias subjective time. Such outcomes not only violate expectation, but may also carry value. To our knowledge, only one previous study has examined this question, using monetary stimuli (Toren, Aberg, & Paz, 2020). Here, we extended this question to an auditory paradigm.

Participants completed a prospective temporal bisection task in which they first predicted which sound they expected to hear, then listened to the sound, and finally judged whether its duration was short or long. The stimuli were a relatively neutral tone and a band-pass-filtered white noise intended to be less pleasant than the tone, presented at durations

ranging from 575 to 975 ms in 50-ms steps. Participants adjusted the listening volume to a comfortable level before the task. Responses were analyzed using a trial-level probit generalized linear mixed model (GLMM), from which point of subjective equality (PSE) estimates were derived. Bootstrap confidence intervals were used to assess the matched-minus-mismatched contrast.

Across two independent samples, a university participant sample (SONA) and an in-person Amazon participant sample, matched outcomes were judged as longer than mismatched outcomes. This pattern was consistent across datasets: bootstrap confidence intervals for the matched-minus-mismatched contrast excluded zero in both the SONA sample (95% CI [-22.12, -2.87]) and the Amazon sample (95% CI [-31.77, -5.52]). These findings indicate that the subjective expansion of time for expectancy-confirming events generalizes beyond previously studied neutral paradigms.

These findings support the idea that expectation fulfillment can bias perceived duration. More broadly, the results suggest that subjective time is shaped not only by physical stimulus properties, but also by whether incoming events confirm or violate prior expectations.

22. Lysosome-Targeting Acidic Nanoparticles Restore Blood-Brain Barrier Integrity under Neuroinflammatory Stress

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Neuroinflammation-driven blood-brain barrier (BBB) dysfunction is a central feature of many neurological disorders. Tumor necrosis factor (TNF) is a key pro-inflammatory cytokine that disrupts neurovascular unit (NVU) integrity by destabilizing tight junctions and increasing BBB permeability. However, the underlying cellular mechanisms linking TNF-induced inflammation to barrier dysfunction, as well as effective strategies to restore BBB integrity, remain incompletely understood. In this study, we establish a multicellular transwell BBB model composed of brain microvascular endothelial cells, astrocytes, pericytes, and neurons to recapitulate TNF-induced neuroinflammatory barrier dysfunction. Barrier integrity is assessed through transendothelial electrical resistance and sodium fluorescein permeability assays, while tight junction remodeling is evaluated via immunofluorescence analysis of claudin-5, ZO-1, and occludin. We identify lysosomal dysfunction as a previously underappreciated mechanism contributing to TNF-induced BBB impairment in NVU cells. To target this pathway, we introduce a novel class of acidic nanoparticles based on polyethylene(tetrafluorosuccinate-co-succinate) (PEFSU), designed to restore intracellular pH homeostasis. Treatment with PEFSU nanoparticles rescues lysosomal function and significantly improves BBB integrity under TNF-induced inflammatory conditions. Trans-BBB transport and NVU cellular interactions are further examined within the transwell system, and nanoparticle safety is confirmed through MTT dose-response assays. Together, this work establishes a physiologically relevant in vitro platform for studying TNF-mediated neuroinflammation and BBB dysfunction, and demonstrates a novel therapeutic strategy using pH-modulating nanoparticles to restore barrier integrity. These findings provide a foundation for targeting lysosomal dysfunction in neuroinflammation-associated brain disorders.

23. Kratom and Prescription Opioid Use among U.S. Veterans: A Nationally Representative Analysis of the 2021-2023 NSDUH*

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Aims. Kratom contains alkaloids with μ-opioid receptor activity, as well as dopaminergic and serotonergic effects. Kratom use in the United States is increasing, often in relation to pain relief and prescription opioid withdrawal. Many individuals report using kratom as either a substitute for opioids or to reduce opioid use, whereas others use kratom concurrently with opioids, which raises the potential for toxicity. U.S. military veterans have elevated rates of chronic pain, prescription opioid use (POU), misuse (POM), and prescription opioid use disorder (POUD). While these patterns mirror known motivators of kratom use in the general population, very limited research has examined kratom use among veterans, who are likely at increased risk for kratom-opioid interaction-related harms.

Methods. Using weighted 2021-2023 NSDUH survey data from 6,981 veterans, we: 1) estimated the national prevalence of kratom use; 2) used logistic regression to test whether past-year kratom use was associated with odds of POU, POM, and POUD compared with no kratom use.

Results. Approximately 2% of veterans reported lifetime kratom use, and approximately 1% reported past-year use. Veterans with past-year kratom use had markedly higher odds of POU (OR = 3.7, p < .01), POM (OR = 9.8, p < .001), and POUD (OR = 20.5, p < .001).

Conclusions. The current results indicate that veterans who used kratom in the past year had approximately 4 times the odds of prescription opioid use, approximately 10 times the odds of prescription opioid misuse, and more than 20 times the odds of prescription opioid use disorder compared with veterans who did not use kratom. Further research is needed to identify whether these patterns reflect prescription opioid substitution, supplementation, or both. This and future work may inform clinical screening and harm reduction strategies for veterans.

24. Maternal Folic Acid Supplementation improves disrupted neocortical development in a forebrain-specific Cited2 knockout

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Neurodevelopment relies heavily on temporally and spatially restricted transcription factors and epigenetic regulators. Disrupting this regulation can impact neocortical form and function, causing neurodevelopmental disorders. One such transcriptional regulator in the neocortex is CITED2, a transcriptional coregulator that interacts with histone acetyltransferases CBP/P300 to promote histone acetylation and increase transcription of target genes. In mice, Cited2 is highly expressed by intermediate progenitor cells of the subventricular zone at E15.5 and postnatally in cortical layer II/III callosal projection neurons. Forebrain-specific Cited2 conditional knock out (Cited2f/f;Emx1-Cre+/-; cKO) causes atypical behavioral and neocortical phenotypes that are common in rodent models of neurodevelopmental disorders. Specifically, we have identified reduced progenitor cell proliferation and, consequently, fewer post-mitotic callosal projection neurons of layer II/III compared to wildtype littermates. Additionally, we have found reduced and disorganized interhemispheric connectivity and atypical behavioral phenotypes in Cited2 cKOs, including reduced ultrasonic vocalizations when separated from the dam, increased rearing, and sensitization to acoustic startle. Importantly, neural tube closure defects in the embryonic lethal global Cited2 knockout are largely prevented by maternal folic acid supplementation, indicating that environmental factors, including maternal diet, can modify neurodevelopmental disruptions caused by Cited2 loss-of-function. We hypothesize that maternal folic acid supplementation will also prevent the neocortical phenotypes in Cited2 cKO mice. We have found that Cited2 cKO mice whose dams were fed a folic acid sufficient diet (2 mg/kg folic acid) have reduced somatosensory cortex thickness

compared to WT littermates, but a supplemented maternal diet (10 mg/kg folic acid) prevents this reduction. We are investigating whether maternal folic acid supplementation rescues behavioral alterations in Cited2 cKOs, and identifying transcriptional and epigenetic alterations in intermediate progenitor cells that underpin this phenotypic rescue. These studies have the potential to provide novel insight into how environmental factors can tip the balance between typical and atypical neurodevelopment.

25. Menstrual Cycle Hormones Influence Antidepressant Dynamics: A Computational Model

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Background: Psychiatric prescribing follows a one size fits all approach, ignoring the hormonal fluctuations many people experience during the menstrual cycle. This standard approach assumes that everyone's body remains stable biologically, even though hormone levels change consistently throughout each cycle phase. Changes in estradiol (E2) and progesterone (P4) can affect how drugs are absorbed, processed, and cleared from the body. These hormonal fluctuations may influence how medications are processed, altering their effects. Patients often report that their medications work differently at different points in their cycle. The gap in research may lead to less effective treatment or increased side effects. Menstrual cycle effects are not accounted for in standard models.
Methods: A combined pharmacokinetic (PK)-pharmacodynamic (PD)-endocrine model was created to simulate hormone-related variability. The model equations were solved numerically using Python. The hormone profiles for each phase were based on values that were reported in the literature, so the model reflects realistic physiological fluctuations. Drug absorption was modeled using a one-compartment system with first-order kinetics. Key parameters, such as bioavailability and distribution, were held constant to isolate the effects of hormone fluctuations on the drug effectiveness across cycle phases. Protein binding and metabolism were adjusted based on the hormone levels. Drug clearance followed Michaelis-Menten kinetics, which was influenced by hormone levels. The enzyme activity varied depending on the E2 and P4 levels. The liver clearance was modeled using a well-stirred framework. Hormone levels for each menstrual phase were incorporated as the dynamic inputs of the simulation. SERT occupancy was modeled as a function of unbound drug concentration to represent serotonin transporter inhibition. The serotonin dynamics were modeled with hormone-dependent effects. Mood was modeled based on serotonin and hormone levels to represent the hormone-dependent behavioral effects. The simulations tracked a 24-hour period after a single 25mg dose.
Results: A 24-hour PK-PD-endocrine profile was captured using the model of a hypothetical scenario of a 26-year-old on 25mg of Sertraline, tracking the 25mg oral dose through all four-cycle phases. Although overall plasma concentrations stayed stable, the unbound drug, SERT occupancy, serotonin dynamics, and mood showed clear differences related to hormonal changes. The late follicular and mid-luteal phases showed the largest changes matching up with the peak E2 and P4 levels that were observed.
Conclusion: These results suggest that menstrual cycle related hormone shifts can influence medication response and may impact how medications work. Considering hormonal variability and integrating these hormonal factors into prescribing can help create stable effectiveness and enhance treatment reliability and outcomes.

26. Risk of Depression Across the Female Lifespan: Insights from 64 million Electronic Health Records

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Background/Objective: Women experience higher rates of depression than men, but how risk varies across lifespan, particularly during distinct hormonal and reproductive phases remains incompletely understood. Periods such as adolescence, pregnancy, and perimenopause are hypothesized to increase vulnerability, yet large-scale, longitudinal data capturing these patterns are limited.
Methods/Results: We analyzed de-identified health records of over 64 million women from the TriNetX Research Network to assess depression diagnoses and antidepressant prescriptions across the lifespan. Incidence rates (new cases per 1,000 person-years) were calculated in 5-year age strata from 2005-2025. Adolescents (10-19) had the highest incidence, with 35 new diagnoses and 50 initiating antidepressants per 1,000 person-years. Rates declined after 20 and plateaued near 40. Prescription rates rose again during perimenopause (40-55). These findings indicate adolescence and perimenopause as key periods of heightened depression onset and treatment initiation in women.
Conclusion: Depression risk in women is not uniform across the lifespan, with heightened risk during adolescence and perimenopause, likely reflecting hormonal fluctuations and psychosocial stressors. Large-scale real-world EHR data provided unprecedented insight, informing targeted prevention, monitoring, and intervention strategies.

27. Mismatch Negativity and Neurodevelopmental Outcomes in Children Born Preterm

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Premature birth is a leading factor contributing to neurodevelopmental disorders, including autism and cognitive disabilities. Early detection measures can help children access services earlier, even before behavioral traits manifest. Event-related potentials (ERPs), measured though electroencephalography (EEG), are objective and non-invasive methods to study brain activity in children born preterm. The mismatch negativity (MMN), measured by the difference in neural response to alternating frequent and rare stimuli, has been associated with cognitive abilities in preterm children, but its relation to autistic traits remains underexplored. The present study examined whether speech evoked MMN amplitude and latency in children born preterm between 5 and 6 years of age predicts cognitive abilities and autistic traits. Twenty-one school-aged children born preterm completed a passive auditory oddball paradigm with alternating standard /da/ (80%) and deviant /ba/ (20%) syllables. Caregivers completed the Social Communication Questionnaire, Current version (SCQ-C) to measure autistic traits, and the Stanford-Binet, Fifth Edition was administered to assess cognitive abilities. Results indicated that MMN mean amplitude significantly predicted cognitive abilities and marginally predicted autistic traits, whereas MMN fractional area latency was not a significant predictor of either. The relationship between cognitive abilities and autistic traits was also explored, indicating no significant correlations between SCQ-C total scores and FSIQ or NVIQ. These results, which warrant replication, suggest that MMN amplitude may provide preliminary insight into neural mechanisms underlying cognitive and neurodevelopmental differences in preterm children. Long-term, this work may inform early identification and intervention strategies for children born preterm who are at elevated risk for cognitive delays or neurodevelopmental disorders.

28. Mnk1-Dependent Protein Synthesis in Myelin Sheath Growth

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Central nervous system myelin sheaths are multilayered membranes produced by oligodendrocytes that wrap axons. These sheaths enable rapid signal transmission and scale in size with axon diameter, a relationship critical for coordinating signaling speeds across neural networks. Oligodendrocyte cultures on synthetic axons (microfibers) that isolate diameter as the sole experimental variable have demonstrated that axon diameter is sufficient to instruct sheath growth. Despite this functional importance, the molecular mechanism by which oligodendrocytes translate this physical cue into myelin sheath growth remains poorly understood.
Preliminary phosphoproteomic data revealed oligodendrocytes myelinating large diameter microfibers have enhanced activation of Mnk1, a kinase that directly phosphorylates and activates translation initiation factor eIF4E for protein synthesis. Previous work has shown that indirect activation of eIF4E regulates myelin sheath length. Further, protein synthesis within myelin sheaths has been proposed to enable on-demand sheath growth. Together, this has led to our hypothesis that Mnk1-dependent protein synthesis promotes myelin sheath growth.
We investigated whether Mnk1 regulates myelin sheath growth using oligodendrocyte microfiber cultures. Inhibiting Mnk1 activity in early oligodendrocytes reduced levels of MBP, one of the most abundant structural myelin proteins. Mnk1 inhibition during early myelination resulted in sheath fragmentation and impaired myelin formation, while inhibition in mature oligodendrocytes did not significantly alter sheath lengths. These findings establish Mnk1 as a critical regulator of early myelin formation. We are now establishing the subcellular localization of Mnk1 and identifying which proteins require Mnk1-dependent synthesis during myelin sheath formation to further define how translation regulation drives proper myelin architecture.

29. Navigation of Drosophila Larvae in Taste Enviornments

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Drosophila larva is a powerful model organism that allows us to understand how patterns of neural activity encode behaviors. To navigate its environments, larvae undergo biased random walks, by interspersing forward runs with reorienting turns. The navigational strategies have already been identified in gradients of odors, light, wind, CO2, but little is known how animals navigate gradients of different tastants, where prior experience may modify the perception of and behavior to novel presentations of tastants. We've adopted an experimental procedure in which we design two taste choice assays-checkerboard and gradient surfaces. By generating these surfaces of simple sugars we quantify navigational behaviors in these taste enviornments through machine vision. By pre-exposing larvae to a different tastant prior to releasing them onto an established taste enviornment, we can quantify how their experience can modulate navigational strategies.

30. Multiplexed imaging reveals lysosomal protein diversity across brain cells

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Lysosomes are membrane-bound acidic organelles that are crucial for protein degradation. Once viewed as a homogeneous population, lysosomes are now recognized to exhibit diversity in function and protein composition, reflecting intrinsic heterogeneity. While lysosome heterogeneity has been reported in peripheral cell types, its role in the

brain remains largely unexplored. To profile lysosomal protein composition and investigate lysosome heterogeneity in brain cells, we performed spatial proteomics using iterative indirect immunofluorescence imaging (4i), a cyclic fluorescence staining and elution method that supports multiple rounds of primary and secondary antibody labeling on the same sample. We applied this approach to human and mouse neurons, astrocytes, and microglia using 10 antibodies. We show that there is an excellent signal-to-noise ratio of fluorescent images acquired using 4i and that cell integrity was preserved after multiple rounds of staining and elution, which is confirmed by the brightfield images. Importantly, we observed significant differences in lysosomal protein expression across cell types. Together, these results demonstrate the effectiveness and reliability of applying multiplexed imaging to understand organelle diversity in brain cells.

31. Neural Correlates of Working Memory Subprocesses in Children with and without ADHD

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Working memory impairments are common in ADHD but most clinical studies do not consider within-group heterogeneity. Further, clinical studies often rely on neuropsychological assessments not aligned with modern cognitive theory, limiting understanding of mechanisms and potential for intervention. The current study utilized a well-characterized sample of school-aged children (n = 227, nADHD = 101) to examine differences in working memory performance and its neural correlates during a change detection task that aligns with controlled attention theories of working memory. Time-frequency analysis and cluster-based permutation tests investigated group differences in event-related synchronization and desynchronization (ERS/ERD) associated with alertness, encoding, and maintenance. Additional analyses addressed within-group heterogeneity by comparing Low and High Capacity ADHD groups. Children with ADHD had worse accuracy and higher reaction time variability (RTSD) compared to TD children, particularly on high load trials (Group*Load p = .026). Accuracy differences were driven by Low Capacity ADHD children, whereas elevated RTSD characterized both ADHD subgroups. The High Capacity ADHD group showed distinct beta and gamma ERD clusters during alerting, encoding, and maintenance compared to TD children (all p < .025), potentially related to neural preparation for change. Results support controlled attention models of working memory impairment in ADHD and suggest even ADHD children with normative performance may achieve it in different ways than their typically-developing peers.

32. Predicted Transcriptomic Dysregulation in Individuals Living with Alzheimer's Disease

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Background
The postmortem state of the brain tissue poses significant challenges and considerations for gene-expression analysis, such as the confounding effects from agonal factors. Studying RNA levels in living individuals via imputation of brain-regional gene-expression levels circumvents some of the major issues plaguing postmortem brain analyses. To fill this gap, we developed the Brain Gene Expression and Network Imputation Engine (BrainGENIE), which is a method for predicting gene-expression levels in the brain from peripheral blood that goes beyond assessing monotonic relationships of genes expressed in both tissues. In this study, we aim to use BrainGENIE-imputed gene expression to identify genes and gene-sets that are differentially expressed in the brains of living individuals with AD, and to improve our understanding of similarities and differences across brain regions showing AD-associated gene-expression changes.

Methods
In each of eight blood transcriptomic studies of AD, we used BrainGENIE to impute brain-regional gene-expression profiles across 10 brain regions, including amygdala, anterior cingulate cortex, cerebellum, dorsolateral prefrontal cortex (DLPFC), hippocampus, hypothalamus, caudate nucleus, nucleus accumbens, putamen, and substantia nigra. For each brain region, we identified AD-associated gene-expression changes by pooling imputed data from 777 AD cases and 779 cognitively unimpaired comparisons.

Results
We identified genes that were significantly differentially expressed (FDR-p < 0.05) in AD cases in nine brain regions (except for substantia nigra), with the number of genes ranging from six to 705. For cerebellum and DLPFC, differential gene-expression effect sizes estimated from imputed gene-expression profiles were significantly correlated with those estimated from directly measured gene-expression profiles (Spearman's r = 0.351, p = 3.5e-180; Spearman's r = 0.281, p = 1.5e-144; respectively). Among the AD-associated genes identified in directly measured brain data, we found two genes in cerebellum and six genes in DLPFC that were significantly replicated in the BrainGENIE-imputed data (FDR-p < 0.05).
Across 10 imputed brain regions, we found a total of 493 distinctly up-regulated and 326 distinctly down-regulated Reactome pathways in AD cases (FDR-p < 0.05). We found two up-regulated pathways shared between those identified from imputed and directly measured DLPFC gene-expression profiles (Fisher's exact test, Bonf-p = 0.015). We found an overlap of 24 down-regulated pathways between imputed and directly measured gene-expression profiles, including 12 in DLPFC (Fisher's exact test, Bonf-p = 6.4e-08) and 12 in cerebellum (Fisher's exact test, Bonf-p = 7.6e-12).

Conclusion
Our study demonstrated that BrainGENIE-imputed brain-regional gene-expression profiles of AD could parallel transcriptomic changes in the postmortem brain to some extent, and could help identify previously undetectable patterns of transcriptome abnormality in the brains of people actively suffering from AD.

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33. Pain Catastrophizing as a Distinct Predictor of Pain Interference among Veterans

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Introduction:
Pain catastrophizing, defined as a cognitive distortion that magnifies threat of pain, is a strong predictor of pain interference. However, the construct of pain catastrophizing has been criticized for potentially reflecting underlying psychopathology rather than a distinct pain-specific process. The present study examined whether pain catastrophizing uniquely predicts pain interference after accounting for symptoms of PTSD, depression, and anxiety. Clarifying this distinction is critical for understanding whether the Pain Catastrophizing Scale (PCS) captures a construct that is meaningfully distinct from general psychological distress or if the measure is conceptually and statistically redundant with psychopathology
Method:
A sample of 266 veterans were recruited using Prolific, an online research panel service. Participants completed measures assessing pain interference (PEG scale from the Graded Chronic Pain Scale), PTSD symptoms (PCL), depression symptoms (PHQ), anxiety symptoms (GAD-2), and pain catastrophizing. A hierarchical linear regression

analysis was conducted to evaluate the unique association between catastrophizing and pain interference over and above psychological symptoms.
Results:
A total of 157 veterans, 55% male average age 47 years, completed the study. Both PTSD symptoms (b = 0.80, SE = 0.30, p = .01) and depression symptoms (b = 1.28, SE = 0.35, p < .01) but not anxiety symptoms (b=.17, SE=.34, p=.60) were independently associated with pain interference. A hierarchical regression found that pain catastrophizing was uniquely associated with pain interference (b=4.39, SE=.65, p<.01) and explained an additional 17% of variance in pain interference above and beyond mental health symptoms (F(1,152)=46.15, p<.01).
Discussion:
Pain catastrophizing explains unique and clinically meaningful variance in pain interference beyond general psychological distress. These findings support catastrophizing as a distinct cognitive mechanism and suggest that interventions targeting maladaptive pain-related cognitions may improve functional outcomes among veterans with chronic pain.

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34. Quantifying Mechanosensory Responses with Optogenetics in the Drosophila Larva*

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The Drosophila melanogaster larvae are small, crawling animals with a brain composed of roughly 10,000 neurons. In response to unfavorable changes in odor and light, larvae modulate their turn rate and turn size, but in response to a sudden onset of vibration larvae engage a much richer behavioral repertoire: turns,but also pauses (startle response) and reverse crawl (strong avoidance response), which we never see in response to light or odor. The frequency and intensity of vibration determine the speed at which each decision is made.The same sensory neurons that mediate response to vibration also mediate larval anemotaxis, navigation in response to wind. Although these behaviors have been studied using natural mechanosensory stimuli, relatively little work has been done to reproduce similar responses through optogenetic stimulation.
Here we optogenetically deliver vibrational stimuli through the activation of mechanosensory chordotonal neurons, quantify responses across a range of temporal patterns, and compare them to responses to natural vibration. We address the extent to which optogenetic activation of mechanosensory neurons can recover the behavioral repertoire to natural stimuli and whether distinct activation patterns can drive known behaviors.

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35. Pupil Dilation in Moral and Non-Moral Decisions

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Dual-process theories in moral cognition attribute moral judgment and decision-making to both intuitive and deliberative processes, with emotional arousal believed to drive intuitive responses. Pupil dilation, as a measure of autonomic and emotional arousal, can be used to examine emotional arousal during decision-making. Moral dilemmas elicit greater emotional arousal than non-moral decisions, such as consumer decisions. It has also been suggested that personal moral dilemmas elicit greater arousal than impersonal ones. These dilemmas are presented as hypothetical thought experiments in which participants must weigh competing moral outcomes. In personal dilemmas such as the footbridge problem, an individual must choose whether to physically push someone off a bridge to stop a trolley and save five others, a decision involving direct physical contact with the victim. In impersonal dilemmas such as the trolley

problem, an individual must choose whether to pull a lever that diverts a trolley from five people to one, a decision that is more indirect. Emotional processing is argued to be more strongly engaged in personal dilemmas because direct physical action makes the harm more emotionally salient. A pilot study demonstrated the feasibility of measuring pupil dilation using the Tobii Pro Spark eye-tracker, though it suggested that stimuli must have sufficient emotional intensity to elicit a differentiable pupillary response between different stimuli.

Using this eye-tracker, Syracuse University student participants made choices about both moral and consumer problems in a within-subjects design. Presentation format (vignette vs. matrix) was varied as a between-subjects variable, though this was not the primary focus of analysis for this poster. Pupillary response was quantified as deviation from a baseline prior to stimulus presentation. Moral dilemma trials showed greater peak pupil dilation than consumer choice trials; however, this difference was not statistically significant. Contrary to predictions, overall mean pupil dilation was significantly greater for consumer than moral trials ($p = .022$). No significant difference was found between personal and impersonal moral dilemmas, inconsistent with predictions based on prior research. These results may be partially explained by the fact that pupil dilation is not only a measure of autonomic arousal, but also reflects cognitive load, as indicated by net constriction rather than dilation. The lower mean pupil dilation during moral trials may indicate that pupillary responses in this context reflect cognitive load rather than emotional arousal, since consumer choices are familiar and routine decisions that are unlikely to have substantial cognitive demands. In sum, these findings highlight the difficulty of isolating emotional arousal from cognitive load using pupillometry alone, and future research should incorporate independent measures of both constructs.

36. Reducing the Need for Cueing: The Impact of tDCS on Sentence Comprehension in Aphasia

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Introduction

Transcranial direct current stimulation (tDCS) has mixed results when paired with speech and language treatment, but often enhances aphasia treatment outcomes (e.g., Fridriksson et al., 2018). Many aphasia studies have investigated tDCS's effect on language task accuracy, but none have specifically examined its effects on treatment cueing. Although not involving aphasia, Pergolizzi and Chua (2017) found that healthy college-age students who received active tDCS were able to use cueing more effectively than those who received sham stimulation in a memory task. This study examined frequency and effectiveness of treatment cues during tDCS paired with behavioral sentence comprehension treatment in a double-blinded, randomized clinical trial.

Methods

Twenty-two participants with mild to moderate Aphasia, at least 6 months post-stroke, were randomly assigned to active or sham tDCS. In the active condition, 2 mA of current was administered for 20 minutes while the participant received 60 minutes of attention-focused language treatment (similar to Peach et al., 2019). The sham condition was identical except that current was ramped up to 2 mA for 30 seconds (to simulate the sensation of tDCS), then reduced to 0 mA. Electrode placement was identical across conditions (anode electrode on left dorsolateral prefrontal cortex, cathode electrode on right supraorbital region). Participants each received ten of these sessions, progressing through five sentence comprehension treatment tasks that increased in difficulty. In our treatment protocol, participants received cues from the clinician when their initial response was inaccurate. Cue types were predetermined for each treatment item, but only provided when needed, allowing us to assess their reliance on cues in treatment. Accuracy of

initial and subsequent responses (after receiving the cue) were recorded. We compared the number of cues administered between conditions using nonparametric statistical methods.

Results

Participants who underwent active tDCS needed fewer treatment cues than those who received sham tDCS (see Figure 1). When separating cue frequency by treatment task type, cueing frequency was significantly lower for the active (M = 2.90 SD = 2.46) tDCS condition as compared to sham (M = 3.62 SD = 2.72) in one of the most difficult treatment tasks, but the difference was not significant for the others. This pattern was consistent across two of the three cue types. Although participants receiving active tDCS did not need as many cues as those in the sham condition, success of using cues did not differ across the treatment conditions.

Conclusions

Our findings suggest that active tDCS administered to prefrontal brain regions during sentence comprehension treatment may reduce the number of cues needed to successfully complete treatment tasks. This finding could have important clinical implications in personalizing therapy and provides evidence in stroke and Aphasia beyond what has been found in healthy controls (Pergolizzi and Chua, 2017). Therapy could become more efficient if fewer cues are needed for success, allowing participants to achieve more in each session. Results showing this effect in one of the most difficult tasks suggest potential for maximizing gains in treatment by progressing through therapy more quickly and perhaps advancing to harder tasks earlier than typical.

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Figure 1. Number of cues administered in each tDCS condition. Error bars show standard error. *p < .05

37. Recent Alcohol Use Moderates the Relationship between Psychological Distress and Daytime Sleepiness among Military-Connected Students

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Recent Alcohol Use Moderates the Relationship between Psychological Distress and Daytime Sleepiness among Military-Connected Students

Pulley, T., Rabinowitz, E., Ripley, G., Huang, Q., Maisto, S., & Ditre, J.W. (2026, April 9).

Introduction: Sleep difficulties are prevalent among college students and especially among veteran and military-connected students (VMCS), who face unique stressors related to military service and campus life. Alcohol use is common in both military and university settings, and many students use it as a sleep aid, especially when dealing with

symptoms of psychological distress. However, alcohol use disrupts sleep quality and contributes to next-day fatigue. Research has shown that psychological distress is strongly linked to both alcohol use and sleep problems, although little research has examined how these factors jointly relate to sleep among VMCS. This study examined associations between recent alcohol use and daytime tiredness among student veterans, and whether alcohol use moderates the relationship between psychological distress and daytime sleepiness.

Methods: Data were drawn from the National College Health Assessment (NCHA)-IIIb, which comprised Fall 2023 through Spring 2025. Negative binomial regression models examined associations between recent alcohol use (past two weeks) and daytime tiredness. All models were adjusted for age, sex, and psychological distress. An interaction model tested whether associations between psychological distress and sleep symptoms differed by recent alcohol use.

Results: After adjustment, recent alcohol use was no longer independently associated with daytime tiredness (χ^2=.34, p=.56). However, the interaction indicated that past two-week alcohol use augmented the relationship between psychological distress and daytime sleepiness (IRR=1.01, SE=.003; p=.03).

Conclusions: Past two-week alcohol use was linked to a stronger positive association between psychological distress and daytime sleepiness. Findings suggest that addressing alcohol use may be a salient target for improving daytime sleepiness, especially in individuals with psychological distress. Integrated campus interventions targeting coping, mental health, and alcohol use may reduce sleep-related impairment in this population. Longitudinal research may be needed to clarify the directionality of these relationships.

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38. STI1 domains coordinate partitioning of UBQLN2 into stress-induced condensates

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UBQLN2 is a ubiquitin-binding shuttle protein that undergoes phase separation in vitro and localizes to stress-induced cellular condensates including stress granules. The central region of UBQLN2 contains two chaperone- and substrate-binding STI1 domains (STI1-I, STI1-II) and disordered linkers; the individual contributions of these domains and linkers to cellular condensate partitioning remain poorly characterized. Here we use live-cell imaging and immunofluorescence experiments to systematically examine domain requirements for UBQLN2 puncta formation in cultured human cells. We show that in vitro phase separation propensity largely correlates with puncta formation in transfected cells. Importantly, STI1-II and UBA domains are each required for baseline puncta formation in cells, but not STI1-I. In contrast, both STI1 domains are required for heat stress-induced puncta formation. Removal of STI1-II abrogates this stress response, and STI1-I deletion substantially attenuates it. Using N-terminal truncation constructs, we demonstrate that STI1-I strongly promotes both phase separation and puncta formation in the absence of the N-terminal region containing the UBL domain. Together, our findings demonstrate that the two STI1 domains of UBQLN2 have distinct roles in puncta formation and condensate partitioning, with STI1-II essential under all conditions.

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39. Structural remodeling of tau aggregation by BBB-penetrating small molecules and peptides to mitigate neurotoxicity in tauopathies*

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*Selected for Oral Presentation

Pathological aggregation of tau into paired helical filaments (PHFs) and neurofibrillary tangles (NFTs) is a defining hallmark of Alzheimer's disease (AD) and related tauopathies. Increasing evidence suggests that distinct conformational states within the tau aggregation pathway differentially contribute to toxicity, highlighting the need for therapeutic

strategies that remodel, rather than simply inhibit, tau aggregation. Here, we developed an integrated computational and experimental pipeline to identify structural modulators of tau aggregation, including both blood-brain barrier (BBB)-penetrating small molecules and peptides. Using molecular docking and molecular dynamics simulations on the cryo-EM structure of AD-derived tau PHFs (PDB: 5O3L), we identified multiple binding sites, including previously uncharacterized pockets, that can be targeted to alter fibril stability and inter-protofilament interactions. Both small molecules and peptides exhibited distinct interaction patterns across these sites, suggesting complementary mechanisms of tau remodeling. Experimental validation demonstrated consistent modulation of tau aggregation across both modalities. Thioflavin-T kinetics revealed altered aggregation profiles, while fluorescence resonance energy transfer (FRET) and tau puncta analysis showed reduced tau-tau interactions and intracellular aggregation. Scanning electron microscopy (SEM) further confirmed structural remodeling of fibrillar assemblies. In peptide-specific analyses, a lead candidate demonstrated strong binding affinity and pronounced modulation on aggregation dynamics. Together, these results support a model in which both BBB-penetrating small molecules and peptides act as structural remodelers of tau, targeting multiple conformational states within the aggregation pathway. Ongoing studies aim to further characterize these mechanisms and evaluate in vivo efficacy in mouse models of tauopathy.

40. Quenching variability of Drosophila larval behavior using multi-sensory stimulation

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The larvae of the common fruit fly (Drosophila melanogaster) are small, crawling animals that have a nervous system comprised of approximately 10,000 neurons. To navigate their environment, larvae execute computations that modify their behavioral outputs based on temporal changes in sensory input—for instance, by increasing their turn rate when detecting rising levels of aversive stimuli. However, the behavior of individual larva can vary when subjected to the same stimulus, revealing intrinsic variability in the neural computations underlying behavior.
To investigate this variability, we delivered increases and decreases in fictive odor concentration by optogenetically activating CO_2 (Gr21a) and odor (Or42a) receptor neurons, alone and in combination with increases in visual stimulation. Individual analyses revealed substantial variability: while some animals selectively responded to uni-sensory stimulation, combining light and CO_2 reliably amplified behavioral responses, suggesting downstream integration that boosts weakly encoded sensory signals. In contrast, combining a decrease in attractive odor with an increase in light did not significantly amplify responses, implying that odor-light and CO_2-light combinations may be processed by distinct pathways.

41. Targeting Tau-Microtubule-End Binding Protein Axis as a Therapeutic Strategy in Alzheimer's Disease

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Abstract: Tau pathology and microtubule (MT) disruption are well-established hallmarks of Alzheimer' disease (AD) and related tauopathies. Although the role of hyperphosphorylated tau and its dissociation from microtubules has been extensively studied, the broader landscape of other MT-associated proteins remains largely unexplored. Among these, the end-binding (EB) protein family, which comprises MT plus-end-tracking proteins, has emerged as a critical regulator of MT dynamics and stability. EB proteins modulate microtubule polymerization, interact with various MT-associated proteins, and influence cytoskeletal organization in neuronal cells. Notably, EB1 interacts directly with tau, conferring a protective effect on microtubule integrity by stabilizing the MT network against tau-mediated disruption In contrast, EB3 represents particularly compelling target due to its predominant expression in the central nervous system and study

also revealed that pathological tau can sequester EB3 from microtubule plus-ends by binding to EB3 either via tau's MT binding site or proline-rich domain, thereby suppressing EB3 function in MT elongation and stability. The goal of this study is to monitor the dynamic interactions among all components within the tau-MT-EB axis. To achieve this, we have established fluorescence resonance energy transfer (FRET) biosensor systems in HEK 293 cells to monitor these interactions. FRET spectroscopy enables the capture of real-time, proximity-based interactions between individual protein pairs within a living cellular context. By using FRET, significant interactions have already been observed across multiple protein pairs: tau-tau, tau-EB1, tau-EB3, tubulin-EB1, and tubulin-EB3. These initial findings indicate that tau, tubulin, EB1, and EB3 form a dynamic and interconnected system in which each component is in close spatial proximity to the others. Importantly, the results suggest that disruption of any single interaction within this axis, such as the loss of tau-tubulin or tau-EB1/3 binding, may cause structural and functional consequences across the entire axis, potentially amplifying microtubule instability in neurodegeneration. Hence, our future studies will employ various tau inhibitors, microtubule destabilizers, and EB protein inhibitors to elucidate potential underlying disease mechanisms in AD using these cellular models. Our long-term goal is to implement high-throughput screening to identify novel blood-brain barrier penetrating small molecules that modulate pathological tau-MT-EB interactions. This study explores a new therapeutic approach within the tau-MT-EB axis to develop interventions for AD.

42. Teacher-Caregiver Vineland-3 Response Variation in Neurotypical Children

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The Vineland-3 is a caregiver and teacher-reported assessment designed to evaluate adaptive behavior. Research examining reporter differences is limited and has focused on autistic populations, demonstrating the need for broader investigation.

We collected caregiver and teacher responses on the Vineland-3 for 54 neurotypical children (4-5 years). The Vineland-3 provides scores across four adaptive domains (Communication, Daily Living Skills, Socialization, Motor Skills) and two maladaptive domains (Externalized Behaviors, Internalized Behaviors). Corroborating previous studies, teachers averaged higher scores for adaptive behaviors and caregivers for maladaptive behaviors. Using the Wilcoxon signed-rank test, Motor Skills and Externalized Behaviors had significantly different scores between respondents ($p=0.001$ and 0.012, respectively). Over 30% of participants in each domain had reporter differences that surpassed limits of concern set by the Vineland-3 manual (8 points for adaptive domains, 3 points for maladaptive domains). ANOVA tests reveal significant variation in teacher-caregiver discrepancy scores across subgroups for four demographic variables: household income of the participant, difficulty living on that income, caregiver employment status, and receipt of public welfare since the child's birth. This pattern held for caregiver-only analyses but not teacher-only analyses, suggesting family financial circumstances shape caregiver perceptions. These findings highlight the need to consider respondent perspective and financial situation to best interpret Vineland-3 results.

43. The Impact of Cortisol on Gene Expression and the Differentiation of iPSC-derived Neural Progenitor Cells to Neurons

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The balance between excitatory and inhibitory neurons (E/I) in the human brain is tightly regulated, though the mechanisms underlying this regulation remain unclear. Schizophrenia, a neurodevelopmental disorder, is marked by disruptions in E/I balance across multiple brain regions, and stress has been linked to the emergence of schizophrenia symptoms. This study aims to examine how cortisol impacts gene expression and the development of inhibitory and excitatory neurons differentiated from induced pluripotent stem cell (iPSC)-derived neural progenitor cells (NPCs). We hypothesized that treatment of neural progenitor cells (NPCs) with cortisol alters the resulting ratio of excitatory to inhibitory neurons differentiated from these cells. iPSCs were differentiated into neural progenitor cells and then into neurons using a commercial kit, and different cortisol concentrations were applied at different stages of cell development. RNA was isolated from NPCs 24-48 hours after treatment, and immunofluorescence staining was performed on the differentiated neurons to identify excitatory and inhibitory neurons. NPCs did not respond to cortisol, resulting in no response in gene expression, and additionally, there was an insignificant change in the E/I ratio. These findings suggest that applying cortisol at the NPC stage may not be the appropriate developmental stage to observe these effects.

44. Targeting TNFR1 signaling alleviates obesity-induced metabolic and cognitive dysfunction through the body-brain axis

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Obesity affects approximately 40.3% of adults in the United States, representing nearly 100 million individuals. It is characterized by chronic peripheral inflammation that disrupts metabolic homeostasis and contributes to neuroinflammation and neurodegeneration through body-brain interactions. A central mediator of this inflammatory axis is tumor necrosis factor receptor 1 (TNFR1) signaling. Zafirlukast (ZAF) directly binds to TNFR1 and inhibits TNF-induced NF-κB activation by disrupting receptor functional dimers. Here, we investigated whether targeting TNFR1 with ZAF could mitigate obesity-associated peripheral inflammation, metabolic dysfunction, and cognitive impairment. Using mice fed a high-fat diet (HFD) for 5 months as a model of obesity, we administered ZAF intraperitoneally (2.5 mg/kg) twice a week for 4 weeks and evaluated metabolic and behavioral outcomes. ZAF treatment significantly improved glucose tolerance and insulin sensitivity in HFD-fed mice, indicating restoration of metabolic homeostasis. Behaviorally, ZAF reduced anxiety-like phenotypes, as demonstrated by improved performance in the open field maze and elevated plus maze, along with decreased freezing behavior. In parallel, ZAF enhanced cognitive function, as evidenced by improved spatial working memory in the Y-maze. Importantly, ZAF reduced neuronal necroptosis in the brain, suggesting that suppression of peripheral TNFR1-driven inflammation attenuates downstream neurodegenerative processes. Consistent with this, the observed improvements in behavioral and cognitive outcomes indicate functional recovery of brain activity. Together, these findings demonstrate that ZAF ameliorates HFD-induced metabolic dysfunction and cognitive impairment by modulating the peripheral inflammation-brain axis. Targeting TNFR1 signaling may therefore represent a promising therapeutic strategy for obesity-associated metabolic and neurocognitive deficits.

45. The Impact of Maternal Self-Reported Depression and Anxiety on Child Difficulties

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Introduction: Chiari Malformation (CM) is a congenital condition characterized by the descension of the cerebellum, causing a disruption in cerebrospinal fluid (CSF) flow. More commonly diagnosed in women, CM presents in early-mid adulthood, coinciding with reproductive years. Consequently, women with CM may struggle with additional physical and mental health difficulties that may impact their child's mental health. This study examined the relationship between maternal self-reported symptoms and overall child difficulties.
Method: Women with CM who had children aged 11-17 completed self-report measures of depression and anxiety using the Depression, Anxiety, and Stress Scale (DASS-21), pain intensity using the Brief Pain Inventory (BPI), and maternal-ratings of child mental health using the Strengths and Difficulties Questionnaire (SDQ). Bivariate correlations were used to assess the relationship between maternal symptom indicators (i.e., depression, pain interference) and child mental health (i.e., scores on the SDQ).
Results: Maternal ratings of overall child difficulties as measured on the total SDQ score were positively correlated with maternal self-report ratings of anxiety ($r = .48$, $p = .01$) and stress ($r = .43$, $p = .02$). Maternal ratings of child emotional difficulties were also positively correlated with maternal self-reported anxiety ($r = .46$, $p = .01$). However, maternal rating of child hyperactivity and peer issues were not associated with maternal self-report symptoms.
Discussion: There was a positive association between maternal self-report ratings of anxiety and stress and child overall difficulties as well as child emotional difficulties. These results suggest that in families where a parent has a chronic illness such as CM, maternal mental health symptoms may impact child functioning. Future research should evaluate potential targets for interventions to support parents with chronic illness and their families.

46. The navigation of Drosophila larvae in taste environment

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Drosophila larva is a powerful model organism that allows us to understand how patterns of neural activity encode behaviors. To navigate its environments, larvae undergo biased random walks, by interspersing forward runs with reorienting turns. The navigational strategies have already been identified in gradients of odors, light, wind, CO_2, but little is known how animals navigate gradients of different tastants, where prior experience may modify the perception of and behavior to novel presentations of tastants. We've adopted an experimental procedure in which we design two taste choice assays-checkerboard and gradient surfaces. By generating these surfaces of simple sugars we quantify navigational behaviors in these taste environments through machine vision. By pre-exposing larvae to a different tastant prior to releasing them onto an established taste environment, we can quantify how their experience can modulate navigational strategies.

47. The Impact of Traumatic Event Exposure on PTSD, Depression, and Anxiety among Veterans.

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Background: Psychiatric disorders including post-traumatic stress disorder (PTSD), depression, and anxiety are highly common and debilitating conditions among veterans. Exposure to potentially traumatic events (PTEs) such as active combat, blast exposure, close calls, and witnessing injury or death during military service may be a significant risk factor

for the development and maintenance of psychiatric conditions. This analysis sought to examine the extent to which individuals with PTE exposure related to military service had different levels of psychiatric symptoms.

Method: A sample of 266 veterans were recruited using Prolific, an online research panel service. Participants completed the Primary Care PTSD Screen for DSM-5 (PC-PCL-5), Patient Health Questionnaire-2 (PHQ-2), and the Generalized Anxiety Disorder-2 (GAD-2). Exposure to potentially traumatic events (PTEs) was assessed using self-report of exposure to traumatic events such as combat or enemy fire, blast exposure, close calls, witnessing injury or death, or exposure to civilian suffering. Only PTE exposures incurred during military service were included in this analysis. Independent sample t-tests were used to examine differences in levels of PTSD, depression, and anxiety symptoms among veterans, with and without PTE exposure.

Results: Respondents were 62% male, average age of 47, and 43% reported exposure to PTEs. Independent sample t tests revealed significant group differences in levels of PTSD ($t(174)=-3.51$, $p<.01$), depression ($t(264)=-4.65$, $p<.01$), and anxiety ($t(264)=-4.00$, $p<.01$) such that individuals with PTE exposure reported more psychological symptoms than those without PTE exposure.

Conclusions: Exposure to PTE during military service is associated with elevated symptoms of PTSD, depression, and anxiety, as measured by self-reported screening questionnaires. These findings stress the importance of screening veterans who have exposure to PTEs and tailoring interventions to address different military service experiences. Future research is necessary to determine how to best match military intervention to individual needs among veterans.

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48. The Role of Social Support in Cigarette Smoking Reduction among Individuals With and Without HIV

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Cigarette smoking rates amongst individuals living with HIV (PWH) significantly outnumber smoking rates amongst the general population. Despite the field's attempts to create smoking cessation interventions specifically for PWH and this population's high motivation to quit, cessation rates remain low. In order to develop an intervention that will have a lasting effect on PWH, we must explore different routes leading to cessation, like smoking reduction. This study investigated how social support may influence smoking reduction in PWH and people living without HIV (PWOH). Secondary data was obtained from a primary study that assessed the role of abstinence-induced cognitive dysfunction in maintaining smoking behavior among PWH. Participants were eligible regardless of HIV status if they self-reported smoking at least five cigarettes per day. The procedures included a cognitive testing session and six standard individual behavioral counseling sessions for smoking cessation. All participants were provided nicotine patches. During Week 12, the end of treatment (EOT), social support and smoking reduction were measured. To measure social support participants completed the Partner Interaction Questionnaire. To measure smoking reduction, participants self-reported the amount of cigarettes smoked per day (CPD) between intake and their target quit day, then between their target quit day and EOT. A mean difference score was calculated between the two periods. This score was used to define smoking reduction. Generalized linear models were used to assess the relationship between smoking reduction and positive and negative social support across PWH and PWOH. Results showed a decrease in cigarettes smoked per day for both PWH and PWOH. Neither negative nor positive social support was significantly associated with cigarette reduction, although positive partner support was nearly significant ($p = .080$ at $p = .05$ level). The interaction effect of HIV status and positive partner support was significant, indicating that the effect of positive partner support on smoking reduction

differed across PWH and PWOH. In PWOH, higher levels of positive support were associated with greater smoking reduction, whereas for PWH, higher levels of positive support were associated with lesser reduction of CPD. Findings suggest that those who seek smoking abstinence can reduce their smoking throughout treatment, and that positive social support may function differently among PWH

49. The role of tunneling nanotubes (TNTs) in neuron-glia trafficking of pathological tau species and lysosomes

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Alzheimer's disease (AD) and related tauopathies are neurodegenerative diseases characterized by the spread of pathological tau species in the brain. Pathological tau exacerbates cell stress and ultimately leads to neuroinflammation and progressive neuronal death through various mechanisms, such as lysosomal dysfunction. Mechanisms of tau spreading and disease propagation are promising routes to target neurodegeneration in tauopathies. Intercellular trafficking pathways, such as through tunneling nanotubes (TNTs), are potential routes of pathology spreading, as they have been shown to traffic intrinsically disordered proteins and organelles. In this study, we examined whether TNTs, which are actin-based cytoplasmic bridges, facilitate the transfer of pathological tau between neurons and glial cells. Using mouse cell lines to express TauP301L-GFP and LysoTracker staining, we evaluated TNT formation and intercellular trafficking of tau and lysosomes. Tau expression enhanced TNT formation, with tau-burdened neurons forming more TNTs when co-cultured with healthy astrocytes. We observed the transfer of tau between cells through these pathways, along with the exchange of lysosomes, indicating cooperative movement of both protein aggregates and organelles between cells. Modulation of lysosomal acidification impacted TNT formation, suggesting a link between lysosomal function and intercellular trafficking. Together, these results show that intercellular exchange aid in tau propagation to surrounding cells may exacerbate neurodegeneration in AD and related tauopathies.

50. Tracking neurons in freely moving animal

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A brain can be considered a function with inputs and outputs, and muscle contractions and body motions are typical outputs of animal brains. Thus, to fully decode the brain function it is essential to be capable of monitor the brain activity while the animal is in motion, ideally in single neuron level imaging resolution. However, real-time imaging of moving brain has been a challenge for decades, due to the motion-blur and the deformation of the brain during motion. We built a two-photon tracking microscopy system which firstly forms a cylindrical scan pattern around a single neuron, then applies the Kalman filter on the target neuron to extract the motion information. Then the microscope "follows" the surrounding neurons by moving galvanometric mirrors, piezo objective and a XYZ stage. A27h motor neurons in Drosophila larva are imaged to demonstrate the signal wave travel as the larva moves.