



UCSanDiego
SCHOOL OF MEDICINE

DEPARTMENT OF PSYCHIATRY

2018 13th Annual Lewis L. Judd Young Investigators Symposium



Monday, April 16, 2018

UC San Diego Medical Education & Telemedicine Building
Auditorium

Keynote Speaker: Jyoti Mishra, Ph.D.

2018 Symposium Program

SYMPOSIUM DIRECTORS:

Igor Grant, M.D., Distinguished Professor, Chair of Psychiatry

Benedetto Romoli, Ph.D., Postdoctoral Scholar, Department of Psychiatry

Neal Swerdlow, M.D., Ph.D., Professor of Psychiatry, Department of Psychiatry

Gregory Light, Ph.D., Professor of Psychiatry, Department of Psychiatry

SYMPOSIUM DESCRIPTION:

This symposium is named after Lewis L. Judd, M.D. who served as the second Chair of the UC San Diego Department of Psychiatry from 1977-2014. During his remarkable tenure, Dr. Judd oversaw the development of the UC San Diego Department of Psychiatry into one of the premier academic departments in the world. While encouraging the strong research portfolio of the Department, Dr. Judd was passionate also about educating the next generation of scholars and clinicians. He wished to create an environment where clinician scholars could interact with basic science trainees and faculty to enhance intellectual cross-fertilization. In this way, best practices in psychiatry and mental health were to be developed. To that end he fostered the development of a specific research training program for M.D.'s, Ph.D.'s, and M.D./Ph.D.'s, as well as research tracks in clinical training programs. To recognize our trainees, he inaugurated in 2005 a research symposium to provide a forum for our trainees to showcase their work and to receive feedback.



This annual research symposium has been an important feature in the academic life of the Department ever since. In recognition of Dr. Judd's foresight and passion for research education, this symposium was named in his honor in 2014.

The half-day event showcases the research of junior faculty, postdoctoral fellows, and trainees, and includes seven oral didactic presentations, a keynote speaker, and a poster session. The Symposium is designed to accomplish two important goals: to serve as a forum in which cutting edge research findings are disseminated to our Department and larger scientific community, and to provide an opportunity for our Departmental family to celebrate the accomplishments of our developing scientists.

2018 Symposium Program

Monday, April 16, 2018

8:30 a.m. Welcome and Opening Remarks:

Igor Grant, MD
Distinguished Professor & Chair
Department of Psychiatry, UC San Diego

Session 1 - Oral Presentations (moderated by Benedetto Romoli, PhD)

8:40 a.m. Amanda Barkley-Levenson, PhD
Evaluating Glyoxalase 1 as a Novel Therapeutic Target for Excessive Ethanol Consumption and Comorbid Disorders

9:00 a.m. Mariam Hussain
Apathy Significantly Predicts Abstinence Self-Efficacy in Methamphetamine Users

9:20 a.m. Jerel Fields, PhD
Cannabinoid Receptor Agonists Reduce Inflammatory Gene Expression and Enhance Mitochondrial Function in Glia Exposed to HIV-relevant Stimuli

9:40 a.m. Kelsey Dickson, PhD
Characterizing Ethnic Disparities in Patterns of Use of Publicly-Funded Developmental Disability Services

10:00 a.m. Break

10:05 a.m. Jorge Urresti, PhD
iPSC-derived Cerebral Organoids Provide Insights into Dysregulated Molecular Pathways in Autism

10:25 a.m. Stephanie Agtarap, PhD
Validating the Rivermead Post-Concussion Symptoms Questionnaire in a Large Sample of Mild TBI Patients: a TRACK-TBI Study

10:45 a.m. Alessandra Porcu, PhD
Photoperiod-induced Neurotransmitter Switching in the Suprachiasmatic Nucleus

Featured Presentation

11:05 a.m. Jyoti Mishra, PhD
Enhancing Neuroplasticity, Cognition and Behaviors in Adolescents with Childhood Trauma using Mobile Technology

Session 2 - Poster Presentations

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

1. Samuel Barnes, PhD
Disrupting Glutamatergic Transmission during Neurodevelopment Impairs Action-outcome Associations and Motivation in Adult Rats
2. Zachary Cope, PhD
Physostigmine Increases Punishment Sensitivity in Mice, a Translational Biomarker for Depression
3. Matthew Klein, MD, PhD;
Hema Kopalle
Probing the Effects of Ketamine on the Habenular-circadian Circuit
4. Molly Kwiatkowski
Inhibiting a Dopamine Synthesis Enzyme, Tyrosine Hydroxylase, Blocks ‘Summer-like’ Photoperiod-induced Mania-like Behavior in Mice
5. I-Chi Lai
Nicotine-induced Neurotransmitter Plasticity in the Substantia Nigra
6. David MacQueen, PhD
Development of an Olfactory 5-Choice Task for mice: Interactions of MK-801 and Nicotine
7. Nandkishore Prakash, MSc
Social Stress Induces Neurotransmitter Plasticity in the Dorsal Raphe Nucleus
8. Dhakshin Ramanathan, MD, PhD
Low Frequency Brain Activity is a Neuromodulatory Target that Tracks Recovery after Stroke
9. Benjamin Roberts
Auditory Discrimination Learning in a Rodent Model of Human Targeted Cognitive Training
10. Ana Sanchez, PhD
Neuronal Network Alterations in Methamphetamine-treated HIV-1/gp120 Transgenic Mice
11. Katelyn Challman
Gender Differences in Trauma Symptomatology, Anxiety, and Relations to Alcohol Craving among Individuals with Comorbid Posttraumatic Stress and Alcohol Use Disorders
12. John Correa, MA
Electronic Cigarette Use among Cancer Patients: Reasons for Use, Beliefs, and Patient-Provider Communication Substance
13. Candace Fanale, PhD
A Moderation Analysis of Personality and Environmental Protective Factors for Problem Drinking: Does Resilience during Teenage Years Predict Less Problem Drinking during Young Adulthood?
14. Natassia Gaznick, MD, PhD
Sex Differences in Serotonin-Mediated Stress Reactivity in Individuals with and without Histories of Alcohol Dependence Substance
15. Elana Hoffman
Environmental Reward, Goal-Directed Activation, and Depressive Symptoms as Predictors of Transdermal Nicotine Patch Adherence in a Randomized Controlled Trial of Behavioral Activation for Smoking

Session 2 - Poster Presentations Continued

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

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| 16. Bryan Messina, PhD | The Impact of Psychological Distress on Pain Volatility in Adults with Chronic Pain and Prescription Opioid Addiction |
| 17. Erin Morgan, PhD | Poor Social Cognition Negatively Influences Methamphetamine Addiction Characteristics |
| 18. Robin Tan, PhD | Neurocognitive Development, Pubertal Status, and Social Expectancies Predict Adolescent Drinking Behaviors |
| 19. Yash Joshi, MD, PhD | A Randomized Clinical Trial Using Auditory-based Computerized Cognitive Training in Patients with Chronic Schizophrenia: Interaction of Anticholinergic Burden with Treatment Effects |
| 20. Zanjbeel Mahmood | Compensatory Cognitive Training for Psychosis: Effects on negative symptom subdomains |
| 21. Juan Molina, MD | History of Cannabis Use Disorder is Associated with Greater Impairment in Neurophysiological, Clinical and Functional Measures in Schizophrenia Patients |
| 22. Emily Treichler, PhD | Dissociation of Performance-Based and Self-Reported Gains Following Cognitive Training in Schizophrenia Patients |
| 23. Christina Wong, PhD | Verbal Memory Performance Under Real and Simulated Hearing Loss Conditions |
| 24. Wendy Zhang | The 40-Hz Auditory Steady-State Response: A Sensitive and Predictive Biomarker of Perceptual Learning During Cognitive Training |
| 25. Griffin Tyree | Hell-weed or Heal-All? A Cost-Effectiveness Model for Adjunctive Smoked Cannabis in the Treatment of Painful Neuropathy |
| 26. Emily Wilhite, MA | Online Dating, Sexual Hookups, and Alcohol Use by Young Women |
| 27. Roger Mercado, MA | The Impact of Attentional Control on Emotional Regulation in Anxiety-Disordered Youth |
| 28. Mercedes Szpunar, MD, PhD | Incidence of Synthetic Oxytocin Administration and Time to Improvement of Depression and Anxiety Symptoms in the UCSD Intensive Outpatient Treatment Program for Postpartum Depression |
| 29. Teresa Lind, PhD | Understanding Emergent Life Events (ELEs) in Evidence-Based Practice Delivery within Children's Mental Health Services |

Session 2 - Poster Presentations Continued

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

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| 30. Willa Marquis, PhD | Predicting Service Utilization in Families of Children with Autism Spectrum Disorder in Community Mental Health Settings across Time |
| 31. Caryn Rubanovich, MS | Physician Communication of Genomic Results in a Diagnostic Odyssey Case Series: A Preliminary Study |
| 32. Cynthia Schairer, PhD | Public Outreach and Community Engagement for Genetically Engineered Mosquitoes: Lessons from Oxitec and MosquitoMate |
| 33. Sonika Ung, PhD | Cultural and Psychological Factors Impact Treatment Adherence and HbA1c in Patients with Type 2 Diabetes |
| 34. Skylar Kelsven | Inflammatory Biomarkers in Early Psychosis |
| 35. Hilary Gould, PhD | Symbolic Play in Autism Spectrum Disorders: Evaluating Two Empirically Supported Treatments in a Randomized Controlled Trial |
| 36. Matthew Herbert, PhD | Acceptance and Commitment Therapy for Veterans with Chronic Pain: Does PTSD Impact Treatment? |
| 37. Eliana Hurwich-Reiss, PhD | Examining Variability in Community Therapist Delivery of Evidence-based Mental Health Intervention Strategies for ASD: Do Child Client Characteristics Matter? |
| 38. Chandra Khalifian, MA | Expanding Intimacy Theory: Vulnerable Disclosures and Partner Responding |
| 39. Tana Luo | Popularity among Peer Role Models: A Moderator of Peer Victimization and Depressive Symptoms |
| 40. Anne Malaktaris, PhD | Chronic Pain and PTSD: A Pilot Study of Cognitive-Based Compassion Training (CBCT®) |
| 41. Chelsey Wilks, MS | Internet-delivered Dialectical Behavior Therapy Skills Training for Suicidal and Heavy Episodic Drinkers: A Randomized Controlled Trial |
| 42. Jessica Carrasco | Stress Correlates in Bipolar I Disorder: An Ecological Momentary Assessment Study |
| 43. Laura Berner, PhD | Altered Aversive Interoceptive Anticipation and Processing in Women Remitted from Bulimia Nervosa: Time-Course and Connectivity Findings |
| 44. Tiffany Brown, PhD | Testing the Dialectical Behavior Therapy Skills Deficit Model in Eating Disorders |

Session 2 - Poster Presentations Continued

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

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| 45. Cara Dochat | Dietary Restraint and Weight Loss in Relation to Disordered Eating in Obese Veterans following a behavioral Weight Loss Intervention |
| 46. Jenna Ellison, MA | Association between Marital Factors and Weight Behaviors in Bariatric Surgery Patients |
| 47. Jason Lavender, PhD | Affective and Neurocognitive Dimensions in a Transdiagnostic Eating Disorder Sample: Examining Measurement Convergence and Associations with Clinical Symptoms |
| 48. Shannon O'Connor, MA | What Drives the Association between Weigh-Conscious Peer Groups and Disordered Eating? Disentangling Genetic and Environmental Selection from Pure Socialization Effects |
| 49. Natalia Orloff, MA | The Role of Food Cravings in Excess Gestational Weight Gain |
| 50. Erin Reilly, PhD | Evaluating Intolerance of Uncertainty as a Predictor of Treatment Response for Individuals with Anorexia Nervosa: A Pilot Investigation |
| 51. Bosi Chen | Atypical Sensorimotor and Language Network Connectivity in Toddlers with Autism Spectrum Disorders |
| 52. Kristen Dwyer, MS | White Matter Connectivity & Social Cognition Across Psychotic Disorders |
| 53. Sean Hatton, PhD | Negative Fateful Life Events in Midlife and Advanced Predicted Brain Aging |
| 54. Jiwan Kohli, MA | Local Gyrfication Abnormalities in Middle-Aged Adults with Autism Spectrum Disorders |
| 55. Alejandro Meruelo, MD, PhD | Neuroimaging Features Predictive of High and Low Performing Adolescent Drinkers versus Nondrinkers |
| 56. Lindsay Olson | Broadly Reduced Intrinsic Functional Connectivity in Girls Compared to Boys with Autism Spectrum Disorders |
| 57. Daniel Stout, PhD | Multimodal Neuroimaging Fusion Reveals Converging Neural Circuitry Across Trauma-Related Disorders |
| 58. Rachel Thayer, MA | Marijuana Use in an Aging Population: Global Brain Structure and Cognitive Function |
| 59. Ni Sun-suslow, MS | The Oxytocin Receptor in Response to Inflammation in Macrophages |
| 60. Jillian Clark, PhD | Relationship between Cognitive Impairment and Functional Capacity in Veterans with a History of Traumatic Brain Injury |

Session 2 - Poster Presentations Continued

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

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| 61. Kelsey Holiday, MS | Hippocampal Volume Independently Predicts Subjective Memory Complaints in Mild Traumatic Brain Injury |
| 62. Victoria Merritt, PhD | Repetitive Mild Traumatic Brain Injury in Military Veterans is Associated with Increased Neuropsychological Intra-Individual Variability |
| 63. Andrew Cawley-Bennett | Factors, Other than Amnesia, that Predict Performance on Tests of News Event Memory |
| 64. Elizabeth Straus, PhD | Risk and Resilience Factors Associated with Posttraumatic Stress Disorder, Alcohol Use Disorder, and Their Comorbidity in U.S. Veterans: Results from the National Health and Resilience in Veterans Study |
| 65. Jessica Tripp, MS | Profiles of PTSD and Moral Injury in Combat Veterans |
| 66. Zhisen Urgolites, PhD | The Medial Temporal Lobe, Conscious Memory, and Experience-dependent Eye Movements |
| 67. Cynthia Schairer, PhD | Stakeholder Attitudes Toward Returning Personal Data Generated by HIV Molecular Epidemiology |
| 68. Johannes Schlachetzki, MD | Defining the cell-specific Epigenetic Landscape Leading to Altered Gene Expression Signatures in HIV-Associated Neurocognitive Disorder |
| 69. Jessica Deslauriers, PhD | The Role of Dopamine D1 Signaling Pathway in COMTval158met-modulated Response to Immune Challenge: A First Study Linking COMTval158met Polymorphism and Inflammation |
| 70. Samantha Friend, MD, PhD | Association Between Inflammation and Alcohol Dependence in PTSD |
| 71. Jordan Kohn, PhD | Synergistic Effects of Cellular Regulation of Inflammation and Cardiometabolic Risk Factors on Cognition in the Elderly |
| 72. Ellen Lee, MD | Demographic, Clinical and Inflammatory Correlates of Sleep in Schizophrenia |
| 73. Jessica Montoya, PhD | Plasma D-dimer Relates to Physical Health and Motor Skills Across the Age Span in HIV |
| 74. Emma Martine Qvale | Amyloid β and HIV Promote a Pro-inflammatory Phenotype in Brain Macrophages that May be Reversed by Cannabinoids |
| 75. Laura Campbell | Physical Activity and Nutrition in Adults with and without HIV/AIDS: Relationships with Successful Cognitive Aging |
| 76. Jennifer Iudicello, PhD | Emotional and Psychosocial functioning are Problematic in HIV and Methamphetamine Dependence and Associated with Significant Functional and Health-related Outcomes |

Session 2 - Poster Presentations Continued

(11:30a.m. – 1:30 p.m., UC San Diego Medical Education & Telemedicine Rooms 141 - 145)

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| 77. Aurelie Lucette, MS | Anxiety Predicts Survival in People Living with HIV Followed for up to 10 Years |
| 78. Emily Paolillo, MS | Depressive Symptoms Are Associated with Cognitive Decline in HIV/AIDS |
| 79. Elizabeth Pasipanodya, PhD | Metabolic Risk Factors as Differential Predictors of Profiles of Cognitive Impairment Among Older HIV+ and HIV- Aging Adults |
| 80. Alexandra Rooney | Depression and Aging with HIV: Associations with Health-related Quality of Life and Positive Psychological Factors |
| 81. Rowan Saloner | Cognitive SuperAging in Persons living with HIV: Demographic, Neuromedical and Everyday Functioning Correlates |
| 82. Micah Savin | The Neurocognitive Implications of Chewing Tobacco Among People Living with HIV in India |
| 83. Megha Amar, PhD | Functional Genomics Approaches Identify Pathways Dysregulated by the 16p11.2 Autism-linked CNV |
| 84. Kevin Chau | Construction and Analysis of Gene and Isoform Co-Expression Networks from the Brain Developmental Transcriptome |
| 85. Jeremy Elman, PhD | Accounting for Genetic Context: Incorporating Interactions between Polygenic Risk Scores for Alzheimer's and Associated Risk Factors and Their Relation to Mild Cognitive Impairment |
| 86. Daniel Gustavson, PhD | Genetic and Environmental Influences on Verbal Fluency in Middle Age: A New Framework |
| 87. Nathaniel Miller, MD, PhD | In Bipolar Patients that Respond to Lithium, Targeted Sequencing of Candidate Genes Reveals Associated Variant in the Promoter of TENM4, NTRK2, and GABRA4 |
| 88. Pan Zhang, PhD | Widespread Transcriptome Dysregulation across Autism, Schizophrenia, and Bipolar Disorder |
| 89. Rory Pritchard | Circuit-specific DNA Modifications Change as Photoperiod-induced Neurotransmitter Plasticity Declines with Aging |
| 90. Mark Sanderson | Genetic and Environmental Architecture of Processing Speed Across Midlife |
| 91. Wei-Ming Watson | Plasma Soluble CD14 is Associated with Apathy in Adults with a History of Methamphetamine Dependence |
| 92. Patricia Moran Losada, PhD | Transcriptional Consequences of 16p11.2 CNV in Patient-derived iPSCs |

POSTER BOARD DIRECTORY

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27-28 & 42: Mood & Anxiety Disorders
29-33: Public Health/Services/CL
35-41: Therapy
43-50: Eating Disorders
51-58: Imaging
59; 69-74: Inflammation
60-66: Neurocognition/TBI/PTSD
67-68; 75-82: HIV
83-92: Molecules and Genes

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2018 Symposium Program

Abstracts for Oral Presentations (IN ORDER OF PRESENTATION)

Evaluating Glyoxalase 1 as a Novel Therapeutic Target for Excessive Ethanol Consumption and Comorbid Disorders

A.M. Barkley-Levenson, PhD, A. Der-Avakian, PhD, A.A. Palmer, PhD

Background: Identifying novel genetic risk factors for alcohol use disorders (AUD) is a critical step in determining new treatment targets with the ultimate goal of developing more pharmacotherapies. Glyoxalase 1 (Glo1) is one such potential target for the treatment of AUD and comorbid psychiatric disorders. Glo1 acts through a GABAergic mechanism and is implicated in ethanol binge-like drinking and anxiety- and depression-like behavior in mouse models.

Methods: To further explore the role of Glo1 in ethanol drinking we used intracranial self-stimulation (ICSS) to assess Glo1's effects on ethanol enhancement of reward sensitivity. Mice were implanted with electrodes targeting the medial forebrain bundle and trained on a discrete-trial current-intensity ICSS procedure. A range of ethanol doses were tested for ability to enhance reward sensitivity or produce aversion, and a Glo1 inhibitor was tested for ability to block reward enhancing effects of ethanol.

Results: Ethanol dose-dependently altered response thresholds in the ICSS procedure, with lower doses decreasing response thresholds (i.e. enhancing reward sensitivity) and higher doses increasing response thresholds (i.e. decreasing reward sensitivity/increasing aversion). Pretreatment with a Glo1 inhibitor blocked the effect of ethanol on response thresholds, indicating that Glo1 inhibition may reduce sensitivity to the rewarding effects of ethanol. When tested alone, a Glo1 inhibitor had no effect on ICSS response threshold, suggesting a low potential for abuse liability.

Conclusions: Glo1 inhibitors may have therapeutic potential for AUD and reducing ethanol intake by blocking the reward enhancing effects of ethanol, while showing limited risk of abuse on their own.

Apathy Significantly Predicts Abstinence Self-Efficacy in Methamphetamine Users

Mariam A. Hussain, BS^{1,2}, Jennifer Iudicello, PhD², Erin Morgan, PhD², Rujvi Kamat, PhD², Robert Heaton, PhD², Igor Grant, MD², & The TMARC Group²

¹San Diego State University/University of California, San Diego Joint Doctoral Program in Clinical Psychology, San Diego, California; ²Department of Psychiatry, University of California, San Diego.

Background: Confidence in one's ability to maintain abstinence (i.e., abstinence self-efficacy) is a strong predictor of treatment outcomes among substance-users. Neurobehavioral factors that may influence abstinence self-efficacy are less established, particularly in methamphetamine (METH) users. This study explored whether apathy, which is highly prevalent during active METH use and periods of abstinence, may influence abstinence self-efficacy in METH users.

Methods: Fifty-eight participants with lifetime METH dependence diagnoses (mean age[SD]=40.7 [11.2]), and no severe psychiatric or neurological disease completed the Methamphetamine Self-Efficacy Scale alongside a comprehensive neurobehavioral evaluation. Apathy was measured using a composite of apathy-related subscales and items from the Frontal Systems Behavioral Scale (FrSBe; Apathy subscale), the Profile of Mood States (POMS; Vigor-Activity subscale), and the Beck Depression Inventory-II (BDI-II; apathy items).

Results: Multivariable linear regression revealed that higher apathy levels were significantly associated with lower METH abstinence self-efficacy ($p < .01$), independent of other potentially relevant factors including comorbid human immunodeficiency virus, lifetime history of major depressive disorder, and cognitive impairment, which did not reach significance ($p > .10$). Longer duration of METH abstinence was also associated with higher METH abstinence self-efficacy ($p < .01$).

Conclusion: Elevated apathy may adversely impact METH abstinence self-efficacy, possibly more so than depression. These findings highlight the importance of addressing apathy to improve abstinence self-efficacy, which may increase the likelihood of successful METH treatment outcome.

Cannabinoid Receptor Agonists Reduce Inflammatory Gene Expression and Enhance Mitochondrial Function in Glia Exposed to HIV-relevant Stimuli

JA Fields¹, M Swinton¹, EM Qvale¹, L Rad¹, I Batki¹, AB Sanchez¹,
F Telese², B Soontornniyomkij¹, I Grant¹, CL Achim¹

¹Department of Psychiatry, ²Department of Medicine, University of California San Diego, San Diego, CA 92093, USA

Background: The endocannabinoid system is emerging as a major factor in brain function via modulation of mitochondrial activity and neuroinflammation. Mitochondrial dysfunction and chronic inflammatory gene expression persist as major players in NeuroHIV. Cannabis is commonly used by HIV+ individuals, and studies with cannabinoid receptor (CB) 1/2 agonists suggest that cannabis can modulate inflammatory responses and buffer mitochondrial activity in the presence of HIV-relevant stimuli. Therefore, we hypothesize that cannabis is neuroprotective during HIV infection by limiting mitochondrial damage and reducing neuroinflammation.

Methods: To test this hypothesis, we 1) performed neuropathological and biochemical analyses of CB1/2 expression and mitochondrial biogenesis protein expression in postmortem brain tissues from HIV-infected decedents that were on ART. In vitro, we 2) investigated CB1/2 receptor agonists effect on primary human astroglial mitochondrial function and immune response to HIV relevant stimuli.

Results: We detected altered CB1/2 expression and distinct cellular localization patterns in frontal cortices of HIV+ brains from cognitively impaired donors compared to cognitively normal controls. We also found deficiencies in mitochondrial biogenesis in these same brain specimens. In vitro, we found that a CB agonist, WIN55,212-2 (WIN), blocked Ab- and IL-1b-mediated reductions in mitochondrial activity and blocked IL-1b-mediated increases in extracellular acidification in astroglial cultures. Furthermore, WIN, blocked Ab- and IL-1b-induced inflammatory gene expression and morphological changes in primary human astroglial cultures.

Conclusions: These data support the hypothesis that CB1/2 agonists block HIV-induced neurotoxicity through mechanisms that buffer mitochondrial function and reduce inflammatory gene expression in astroglial cells.

Characterizing Ethnic Disparities in Patterns of Use of Publicly-Funded
Developmental Disability Services

Kelsey Dickson, PhD, Sarah Rieth, PhD, Ron Plotkin, PhD, Terri Cook-Clark, MSW, LCSW,
Christina Corsello Orahovats, PhD, Lauren Brookman-Frazee, PhD

Background: Ethnic disparities in access to and utilization of indicated services for youth with developmental disabilities (DD) are a critical concern for this population^{1,2,3}. In 2016, based on statewide data documenting significant ethnic disparities in the provision of services for individuals with DD across Regional Centers, the California Department of Developmental Services launched an initiative to reduce disparities in the purchase of service (POS) for Latino clients. The current study uses data from the San Diego Regional Center (SDRC) to examine service use patterns for their clients in San Diego and Imperial Counties to identify at what age disparities emerge and for which qualifying conditions to inform the development of disparity reduction interventions.

Methods: Administrative claims data from fiscal years 2015-2016 were extracted from SDRC POS data for 27,000 clients were used to characterize service utilization patterns from birth to adulthood. Differences were examined by age and qualifying condition (Autism Spectrum Disorder, Intellectual Disability).

Results: Results indicate significantly lower POS for Latino compared to Non-Latino/White clients ($F(3,27,332)=107.47, p<.01$) overall. Follow-up analyses revealed a significant 3-way interaction between ethnicity, age, and disability type. Post-hoc analyses indicated significantly lower POS for Latino clients that emerges between the ages of 14-19 for individuals with ID and ASD. Similar results were observed for individuals with comorbid ASD and ID beginning at age 19. Further analyses examining these disparities by service type will be discussed.

Discussion: These results reveal important patterns of service disparities among individuals with DD including the emergence of disparities for transition age youth that persist throughout the lifespan. These data were used to inform the development of a service navigation intervention targeting clients with ASD and ID as young as age 11 (prior to the emergence to disparities) using a Promotora/Lay Health Worker model to facilitate service engagement.

References/Citations:

1. Harrington, C., & Kang, T. (2008). Disparities in service utilization and expenditures for individuals with developmental disabilities. *Disability and Health Journal*, 1(4), 184-195.
2. Mandell, D. S., Ittenbach, R. F., Levy, S. E., & Pinto-Martin, J. A. (2007). Disparities in diagnoses received prior to a diagnosis of autism spectrum disorder. *Journal of autism and developmental disorders*, 37(9), 1795-1802.
3. Mandell, D. S., Wiggins, L. D., Carpenter, L. A., Daniels, J., DiGuseppi, C., Durkin, M. S., ... & Shattuck, P. T. (2009). Racial/ethnic disparities in the identification of children with autism spectrum disorders. *American journal of public health*, 99(3), 493-498.

iPSC-derived Cerebral Organoids Provide Insights into
Dysregulated Molecular Pathways in Autism

Jorge Urresti, PhD, Patricia Moran Losada, PhD, Pan Zhang, PhD, Megha Amar, PhD,
Priscilla D. Negraes, PhD, Cleber A. Trujillo, PhD, Leon Tejwani, Sarah Romero,
Alysson R. Muotri, PhD, Lilia M. Iakoucheva, PhD

Background: The 16p11.2 copy number variant (CNV) is associated with multiple neurodevelopmental disorders. There is a dosage effect of this CNV, with macrocephaly observed in the deletion carriers, and microcephaly observed in the duplication carriers.

Methods: We generated 3D cultures that model human fetal brain development, i.e. human cerebral organoids, using skin fibroblasts and then iPSCs derived from 16p11.2 deletion (DEL) and duplication (DUP) carriers with autism spectrum disorder (ASD). Transcriptomic profiling (RNA-seq) of iPSCs and organoids at 1 month of development has been carried out. To process the RNA-seq data, we adopted the “long-rna-seq-pipeline” used by the ENCODE Consortium. The size of the organoids was monitored during their maturation, and cell migration was assessed at 1 month of development.

Results: The patients’ head size phenotype was recapitulated in the cerebral organoid models. Transcriptomic profiling of iPSCs identified significant differentially expressed genes with cytoskeletal functions, with the small GTPase RhoA being differentially expressed. Gene co-expression network analyses identified three gene co-expression modules that were strongly associated with 16p11.2 copy number status. The first module containing all 16p11.2 genes was upregulated in DUPs and downregulated in DELs, confirming a strong cis-effect of the CNV. The second module upregulated exclusively in DUPs was enriched in genes involved in cell adhesion and migration. The third module upregulated exclusively in DELs was enriched in genes with histone, nucleosome and chromatin-related functions. This suggests that dosage changes of the same CNV impacts different biological and molecular functions.

Conclusions: Pathways associated with cell migration and adhesion were dysregulated in DUPs, while DELs showed dysregulation of chromatin- and histone-related pathways. This suggests dosage-dependent dysregulation of different molecular pathways by the 16p11.2 CNV. We validated some of the molecular findings by observing a defect in neuronal migration of neural progenitor cells from the DEL and DUP organoids. Importantly, the macro- and microcephaly phenotypes was recapitulated in the cerebral organoids, indicating that they serve as an excellent model for studying neurodevelopmental disorders.

Validating the Rivermead Post-Concussion Symptoms Questionnaire in a
Large Sample of Mild TBI Patients: a TRACK-TBI Study

Agtarap SD, Campbell-Sills L, Jain S, Sun X, Stein M, and TRACK-TBI Investigators

Background: The Rivermead Post-Concussive Symptoms Questionnaire (RPQ) is a well-used measure for Post-Concussive Syndrome (PCS), though questions remain regarding its factor structure and, consequently, the most useful scoring of the scale. The purpose of this study was to determine the optimal structure of the RPQ using data from TRACK-TBI participants who completed the questionnaire at 2-weeks and 3-months post-injury.

Methods: Data were part of a larger, multicenter prospective observational study recruiting patients sustaining mild traumatic brain injury (TBI). RPQ data were collected at 2-weeks (n = 1588) and 3-months (n = 1088) via in-person assessment and phone follow-up, respectively. Random subsamples of data were used from each time point (n = 381, 346) to assess best structural fit using exploratory factor analysis (EFA). The remaining subsamples were used to validate all proposed structures of the RPQ using confirmatory factor analysis (CFA). Finally, we examined psychometric properties of the scale for the entire sample.

Results: Item ratings from EFA and CFA offer strongest support to a 3-factor model with cognitive, somatic, and affective symptom dimensions. However, some features of this model (e.g., cross-loading items; high factor inter-correlations) are prompting us to pursue additional analysis (e.g., bifactor modeling) to clarify whether the 3 proposed factors explain incremental variance in symptom ratings - over and above what can be explained by a single, global PCS factor.

Conclusions: The results of the study provide further validation of the RPQ as well as guidance for optimal scoring, and evidence of symptom structure following mild TBI.

Photoperiod-induced Neurotransmitter Switching in the Suprachiasmatic Nucleus

Alessandra Porcu^{1,2}, Malini Riddle^{1,2}, David K. Welsh^{1,2}, and Davide Dulcis¹

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Background: Light, circadian clocks, and rhythmic behaviors interact to produce a temporal order essential for the survival of living organisms. In mammals, the principal circadian pacemaker in the brain is the suprachiasmatic nucleus (SCN), which receives direct retinal input synchronizing it to the day-night cycle. Disrupted circadian rhythms are associated with impaired cognitive function and mood, and bright light is therapeutic for humans with winter depression. Altering day length (photoperiod) induces changes in neurotransmitter phenotype in the hypothalamic paraventricular nucleus (PVN), leading to depression-like behavior in adult rodents¹. We hypothesize that altering photoperiod also changes neurotransmitter expression in SCN neurons, which then control the activity of PVN neuronal circuits shown to induce depression-like behavior.

Methods: Mice were exposed to 19L:5D (19 hours light, 5 hours dark) or 5L:19D photoperiods for 15 days. Brains were immunohistochemically processed to determine neurotransmitter plasticity in response to photoperiod and investigate whether circadian clock genes can directly affect neurotransmitter identity in the SCN.

Results: In adult mice, we found substantial changes in the number of SCN neurons expressing either vasoactive intestinal polypeptide (VIP) or neuromedin-S (NMS) in response to short (5L:19D) or long days (19L:5D). We also observed altered coexpression ratios of these neuropeptides, consistent with neurotransmitter switching. Moreover, we found that short days increase NMS-expressing projections from the SCN to dopaminergic neurons in the PVN.

Conclusions: Our findings provide new insights into seasonal plasticity of SCN neurons and suggest a potential role for SCN neurotransmitter switching in depressionlike behavior.

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Enhancing Neuroplasticity, Cognition and Behaviors in Adolescents with
Childhood Trauma using Mobile Technology

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Background: Individuals with early childhood trauma are at risk for several mental and physical health problems during their lifetime and pose a huge healthcare and socio-economic burden. It is an imperative to better understand and serve the mental health needs of this vulnerable population.

Methods: In this international project, we investigated whether mobile digital interventions can impart multidimensional mental health benefits in adolescents with childhood trauma. We enrolled 45 adolescents with a history of neglect and trauma, recruited from a Child Welfare Center in India. Study participants underwent neuro-cognitive assessments, including resting state functional MRI measures, cognitive tests of sustained attention and interference processing, and behavioral assessments of attention deficit and hyperactivity. Adolescents were then cluster randomized to digital intervention arms: (i) breath-focused internal attention training, (ii) external attention training with auditory and visual attention exercises, and (iii) a no intervention arm. The intervention period lasted 6 weeks (engagement for ~30 min/day over 30 days). Neural, cognitive and behavioral assessments were repeated at post-intervention and at one-year follow-up.

Results: We found that only internal attention training imparted neural, cognitive and behavioral benefits, including (i) enhanced resting state functional connectivity of the cingulo-opercular network, which is implicated in sustained focus maintenance; (ii) enhanced cognitive functioning in both sustained attention and interference processing tasks; and (iii) reduced hyperactivity ratings. Notably, reductions in hyperactivity were sustained at the one-year follow-up.

Conclusion: Our study demonstrates that a mobile, cost-effective & scalable intervention, which trains internal breath focus can significantly improve mental health in adolescents with trauma.

2018 Symposium Program

Abstracts for Poster Presentations (IN ALPHABETICAL ORDER BY AUTHOR)

Functional Genomics Approaches Identify Pathways Dysregulated by the 16p11.2 Autism-linked CNV

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Background: The 16p11.2 copy number variant is one of the most frequent CNVs involved in neurodevelopmental diseases. It is implicated in multiple psychiatric phenotypes with deletions associated with macrocephaly and duplications associated with microcephaly in patients and mouse models. In our previous study, we observed KCTD13-Cul3-RhoA dysregulation as a potential mechanism contributing towards these phenotypes. To further validate the role of KCTD13-Cul3-RhoA pathway in autism, we have recently created mouse models (KCTD13-HET, KCTD13-KO and Cul3-HET) using CRISPR/Cas9 genome editing technology.

Methods: Advanced genomic, transcriptomic and proteomic approaches (RNAseq, TMT-proteomics, and single-nuclei RNAseq (snRNAseq)) were applied to investigate the impact of KCTD13 and Cul3 mutations on various intracellular molecular pathways in different brain regions and developmental time periods (E17.5, P7 and P35).

Results and Conclusions: The RhoA protein level was consistently upregulated in all mouse models during early development (P7), and this upregulation was cortex-specific. This suggests that trans-effect of Cul3 and KCTD13 mutations may be brain region or neuronal layer specific. The Cul3 mutant mice had lower weight at birth, and this effect was maintained into the adulthood. We confirmed Cul3 reduction and CamK2 upregulation in Cul3 mutant mice by TMT-proteomics. Furthermore, the preliminary snRNAseq data from cortical regions of Cul3 mutant mice suggested a shift in neuronal and non-neuronal populations, with significant decrease in inhibitory neuronal populations in the mutant mice. Interestingly, despite the reduction in the number of RhoA expressing cells, the overall expression level of RhoA was higher in the mutant Cul3 mice compared to WT. This suggests that loss of RhoA-expressing neurons may be compensated by an increase in the level of RhoA expression. The knowledge obtained in this study may provide potential autism drug targets for future therapeutic intervention.

Disrupting Glutamatergic Transmission during Neurodevelopment Impairs
Action-outcome Associations and Motivation in Adult Rats

Samuel A. Barnes, Andre Der-Avakian, Jared W. Young, M.
Margarita Behrens, Mark A. Geyer

Background: Schizophrenia is a neurodevelopmental disorder characterized by a wide spectrum of symptoms. The ability to regularly update current representations of reward value and adjust behavior in response to alterations in reward is required to maintain goal-directed behavior. These processes can be quantified across species using the probabilistic reversal learning (PRL) procedure and are impaired in schizophrenia. Schizophrenia patients also exhibit impairment in a progressive ratio breakpoint (PRBP) task that assesses motivational performance. Our aim was to determine whether neonatal phencyclidine (PCP; NMDA receptor antagonist) treatment produced deficits in rats performing the PRL or PRBP tasks.

Methods: Male and female Wistar rats received PCP (20 mg/kg, s.c., n=24) or saline (0.9% s.c. n=23) on postnatal day (PND) 7, 9, and 11; behavioral testing began on PND 60. Rats were tested in the PRL procedure using an 80:20 reward ratio once daily for 20 days. PRBP was conducted after PRL testing.

Results: Overall PRL performance was impaired in PCP- vs. saline-treated rats; fewer successful reversals were completed. Rats displayed a suppression in both reward and punishment sensitivity and required more trials to reach criterion. PCP-treated rats also exhibited a lower breakpoint in the PRBP task.

Conclusions: Disrupting NMDA receptor transmission during neurodevelopment led to impairments in the ability to correctly utilize response-outcome associations. Impairments in reward sensitivity likely contributed the motivational deficits observed in PCP-treated rats. These findings implicate disrupted NMDA receptor activity during neurodevelopment as a potential mechanism for the impairment in reward sensitivity and motivational abnormalities evident in schizophrenia.

Altered Aversive Interoceptive Anticipation and Processing in Women Remitted from
Bulimia Nervosa: Time-Course and Connectivity Findings

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Background: Out-of-control binge/purge episodes and high levels of emotional instability suggest that individuals with bulimia nervosa (BN) have difficulty maintaining internal homeostasis. Integral to both physiological state regulation and emotion regulation is interoception, or the detection and integration of body signals. No study of BN has examined the neural anticipation of and response to aversive interoceptive state changes, which could impact learning from body-related experience and maintain maladaptive eating behaviors.

Methods: Women remitted from BN (RBN; n=24) and control women (CW; n=25) underwent fMRI during a cued inspiratory breathing load paradigm.

Results: During breathing load anticipation, RBN relative to CW showed increased activation in bilateral mid-insula, left superior frontal gyrus, bilateral putamen, right dorsal anterior cingulate, left posterior cingulate, and right amygdala, along with increased functional connectivity between right insula and right amygdala (pFWE<0.001). Time-course analyses revealed that RBN BOLD responses in interoceptive processing regions showed an aberrant decline over the course of the aversive experience (pFWE<0.001). Exploratory analyses indicated that hyperactivation and hyperconnectivity during breathing load anticipation were associated with past binge eating and purging frequencies (pFWE<0.05).

Conclusions: This study is the first to show that BN is associated with altered neural activation during anticipation and processing of unpleasant body state changes. Exaggerated predictive signals and an aberrant pattern of adjustment over time to aversive states may help explain why individuals with BN engage in behaviors that result in alternating over- and under-shooting of homeostasis (i.e., binge eating and purging) and could serve as novel, brain-based treatment targets.

Testing the Dialectical Behavior Therapy Skills Deficit Model in Eating Disorders

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Jason M. Lavender, PhD, Walter H. Kaye, MD

Background: Dialectical behavior therapy (DBT) has demonstrated initial efficacy for the treatment of eating disorders (EDs). However, no studies have examined potential mechanisms of change within DBT for EDs or empirically tested the DBT skills deficit model in EDs. Thus, the present study sought to investigate whether early improvements in DBT skills use mediated the relationship between emotion regulation skills deficits at admission and eating and psychiatric symptoms at discharge from a DBT-based partial hospital program (PHP) for adults with EDs.

Method: Seventy-nine adults (24.4 ± 6.7 years old) with primary EDs completed self-report measures at treatment admission, one-month post-admission, and discharge from PHP. Mediation path analysis models using bias-corrected bootstrapped 95% confidence intervals tested the indirect effect of emotion regulation skills deficits at admission (independent variable) via change in DBT skills use (change score from admission to one-month post-admission; mediator variable) on eating, depression, and anxiety symptoms at discharge (dependent variables).

Results: DBT skills use increased by 14.91% from admission to one-month post-admission and increased by 27.95% from admission to discharge. Early improvements in DBT skills use mediated the relationship between emotion regulation skills deficits at admission and ED and depressive symptoms, but not anxiety symptoms, at discharge.

Conclusions: Results are the first to provide support the DBT skills deficit model within EDs. Findings further reinforce the importance of examining mechanisms of treatment change, and add to a growing literature supporting the use of DBT for EDs.

Physical Activity and Nutrition in Adults with and without HIV/AIDS:
Relationships with Successful Cognitive Aging

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Background: Engagement in physical activity (PA) is related to better cognitive functioning in people living with HIV (PLWH) and HIV-uninfected (HIV-) adults; however, less is known about the effects of nutrition on cognitive functioning. We examined associations of PA and nutrition with successful cognitive aging (SCA) among PLWH and HIV- adults.

Methods: 106 PLWH and 92 HIV- adults, aged 36-65 (M=51.2; SD=7.9), 76.8% male, 62.1% non-Hispanic white, were administered the International Physical Activity Questionnaire (minutes/week x intensity) and the By-Meal Screener to assess average fruit and vegetable (FV) consumption (servings/day). A continuous SCA composite was calculated based on performance on a comprehensive neuropsychological battery, self-report of instrumental activities of daily living, and depressive symptoms. Covariates examined included diabetes, hypertension, hyperlipidemia, lifetime smoking, and lifetime methamphetamine use disorder.

Results: In separate multivariable models predicting SCA, lower PA ($p=0.006$) and HIV+ status ($p<0.001$) (model 1), and lower FV ($p=0.060$) and HIV+ status ($p<0.001$) (model 2) were associated with worse SCA. After controlling for covariates HIV- status ($p<0.001$) and greater PA ($p=0.036$) were independently associated with better SCA; however, FV was not significantly related to SCA ($p=0.464$). No interactions were observed.

Conclusion: Greater PA, but not FV, was related to SCA after adjusting for covariates. The By-Meal Screener may not be a sensitive measure of overall nutrition, and FV consumption may be related to developing other medical conditions (e.g., diabetes) which may relate to SCA. Interventional and longitudinal studies that utilize objective measures should further investigate the relationships among PA, nutrition, and SCA.

Stress Correlates in Bipolar I Disorder: An Ecological Momentary Assessment Study

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Background: Bipolar disorder (BD) is characterized by mood shifts potentially triggered by stressful daily life events. Research has been hampered by use of retrospective self-report over weeks, which is susceptible to bias and does not measure daily stress variability. To address this, we measured daily stress over a two-week period using ecological momentary assessment in those with and without BD.

Methods: Twenty-five BD and fifty-six healthy comparison (HC) participants completed tri-daily surveys over two weeks via study-provided smartphone. Participants rated their momentary stress level from 1-7. Ratings were averaged across surveys to create a daily mean; individual mean and standard deviation of daily ratings across two weeks was calculated and compared between groups. Relationship to baseline demographic and clinical measures, and to mean blood-based inflammation levels over two weeks, was assessed.

Results: BD showed higher mean levels of daily stress compared to HC. Intra-individual variability in stress across two weeks was equivalent in BD and HC. Mean stress was highest in women with BD and among BD participants who had suffered from more manic episodes, especially men with such history. Finally, there was a trend for BD with higher stress variability to have higher proinflammatory and lower anti-inflammatory blood levels.

Discussion: Momentary assessment of stress suggests that women with BD suffer from more daily stress; men with a history of many manic episodes also report higher levels of stress. Trends towards relationships of stress variability to inflammatory markers suggest that enhancing stability in coping with stress might reduce biological aging.

Gender Differences in Trauma Symptomatology, Anxiety, and Relations to Alcohol Craving among Individuals with Comorbid Posttraumatic Stress and Alcohol Use Disorders

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Background: PTSD and AUD frequently co-occur and women and men with these comorbid conditions exhibit different illness trajectories. The aim of this pilot study was to identify the magnitude of effect of gender differences on trauma symptoms and the relationships among stress and alcohol use characteristics in recently abstinent individuals with PTSD.

Methods: Thirty-two abstinent (mean=43.7days) women (n=18) and men (n=14) with current DSM-5 AUD and current or lifetime diagnosis of PTSD were enrolled. Participants completed the State-Trait Anxiety Interview (STAI), Penn Alcohol Craving Scale (PACS), and Obsessive Compulsive Drinking Scale (OCDS). Gender differences in trauma symptoms were examined with independent sample t-tests and associations among variables with Pearson correlation coefficients.

Results: Women reported greater severity and higher numbers of PTSD symptoms (Cohen's $d=0.67$ and 0.72 , respectively). Higher CAPS-5 scores among women were characterized by increased severity on intrusion, avoidance, and arousal subscales (Cohen's $d=0.68$, 0.75 , and 0.73 , respectively). PACS was associated with the STAI for women ($r^2=0.34$, $p=0.03$; $r^2=0.41$, $p=0.01$, respectively). Conversely, there was an association of OCDS total score with state and trait anxiety for men ($r^2=0.42$, $p=0.02$; $r^2=0.38$, $p=0.02$, respectively).

Conclusions: These preliminary findings suggest that recently abstinent women with PTSD exhibit more and greater severity of trauma symptoms than men. Further, greater anxiety in women predicted greater alcohol craving; whereas in men, anxiety was associated with obsessive thoughts about alcohol. The magnitude of these gender effects and evidence for sex-specificity between stress and alcohol make it important to consider gender differences when studying comorbid AUD and PTSD.

Construction and Analysis of Gene and Isoform Co-Expression Networks from the Brain Developmental Transcriptome

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Background: Gene co-expression networks are highly informative in terms of transcription-related processes. Genes with correlated expression patterns tend to code for highly interconnected proteins in cellular networks. However, most co-expression networks have only been explored at the gene-level resolution, even though each gene produces on average five splicing variants. We hypothesized that splicing isoform co-expression networks will provide higher resolution to the fundamental processes governing human brain development, and further insights into neurodevelopmental disorders.

Methods: To explore the potential of isoform co-expression networks in the analysis of brain processes in health and disease, we created a pipeline for network construction, quality control and analysis. We used gene and isoform expression data from the developing human brain, provided by the BrainSpan Database and the PsychEncode consortium. We employed Weighted Gene Co-Expression Network Analysis (WGCNA) to verify scale-free topology of the networks, and for subsequent module discovery. After gene and isoform network construction, we identified gene and isoform co-expression modules enriched in various biological functions. We then compared the isoform modules to the gene modules by computing module eigengene correlations. We also explored redistribution of isoforms into their respective modules relative to parent gene module assignment.

Results: We observed that although there are many gene-isoform module pairs that exhibit high eigengene correlations, approximately one-third of the isoform modules clearly stand out as not having a corresponding gene module according to this metric. Gene Ontology term enrichment analysis shows that some of these unique isoform modules are highly enriched for interesting functionality, such as mRNA splicing. We also found high isoform redistribution, indicating divergence of co-expression partner distributions between the two networks.

Conclusions: Given the identification of unpaired, unique isoform-level modules, in addition to the high level of isoform redistribution, these results represent a high potential for splicing isoform co-expression networks to provide new insights into human brain development.

Atypical Sensorimotor and Language Network Connectivity in
Toddlers with Autism Spectrum Disorders

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Lindsay Olson, Sarah Reynolds, Inna Fishman.

Background: Among the first signs of Autism Spectrum Disorders (ASDs) are gross motor and language delays, and atypical auditory processing. Additionally, toddlers with ASDs do not show the rapid growth in vocabulary that typically coincides with the onset of walking, indicating atypical links between motor and socio-communicative development in ASDs. However, the neural underpinnings associated with this atypical developmental pattern remain understudied.

Methods: Resting state fMRI data were acquired from nine toddlers with ASDs and 11 typically developing (TD) toddlers between 15 and 31 months old. Intrinsic functional connectivity (iFC) analyses were performed with 14 regions of interests (ROIs), covering somatomotor, auditory, and language regions.

Results: Toddlers with ASDs showed intra- and interhemispheric underconnectivity within auditory regions, and between somatomotor and auditory regions. Underconnectivity between one auditory and one language ROI was also found. However, there were no group differences in connectivity within the language network or between somatomotor and language regions.

Conclusion: Results suggest that weaker connectivity within auditory circuitry, between motor and auditory regions, and between auditory and language networks is present in toddlers with ASDs as early as second year of life. However, we did not observe connectivity differences within the language network, unlike previously reported in older toddlers with ASDs, or between motor and language regions. This suggests that atypical connectivity of auditory regions might precede differences in language network activation and connectivity that have previously been observed in older toddlers and children with ASDs.

Relationship between Cognitive Impairment and Functional Capacity in Veterans
with a History of Traumatic Brain Injury

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Background: Performance-based tests of functional capacity are rarely used in research on mild to moderate traumatic brain injury (TBI), but they may function as a link between cognitive impairment and functioning. We sought to examine the relationship between cognitive functioning and performance-based functional capacity, as measured by the University of California San Diego Performance-based Skills Assessment-Brief (UPSA-B), in Veterans with TBI histories.

Method: 50 Operation Enduring Freedom/Operation Iraqi Freedom Veterans with mild to moderate TBI histories and impairment in at least one neuropsychological domain completed baseline assessments during a randomized controlled trial of CogSMART cognitive training in the context of supported employment. Functional capacity was assessed by the UPSA-B (total, financial subscale, and communication subscale scores). Greater scores indicated greater functional capacity. A global deficit score was calculated based on neuropsychological performance on assessments of attention/working memory, processing speed, learning, delayed recall, prospective memory, and executive functioning. Executive functioning domain and processing speed domain deficit scores were also calculated.

Results: Pearson correlation coefficients indicated that worse global neuropsychological performance was related to worse communication capacity ($r = -.31, p = .027$). Worse executive functioning was related to worse functional capacity ($r = -.37, p = .008$), particularly in the domain of communication ($r = -.44, p \leq .001$). Processing speed performance was not related to functional capacity.

Conclusions: Executive functioning was associated with communication and overall everyday functioning capacity. Improvement in executive functioning deficits may improve functional capacity, specifically in communication tasks.

Physostigmine Increases Punishment Sensitivity in Mice,
a Translational Biomarker for Depression

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Background: Affecting nearly 5% of the global population, major depression (MD) is the leading cause of disability (WHO, 2018). Modern treatments induce heterogeneous responses with delayed efficacy and undesirable side effects. Most treatment development is based on perceived ‘despair’, as opposed to sensitivity to negative feedback often reported. Physostigmine, an acetylcholinesterase inhibitor, increases immobility in traditional despair tasks, an effect blocked by chronic lithium and acute muscarinic and nicotinic antagonist pretreatment. We hypothesize that physostigmine increases punishment sensitivity in a probabilistic reversal learning (PRL) task, as in humans with MD or bipolar depression (BD).

Methods: Male and female wild type mice (n=19) on a C57BL/6 background strain were trained to perform the PRL and progressive ratio breakpoint task. Three doses of physostigmine (0.01, 0.03, 0.1 mg/kg) or saline were administered in a counterbalanced repeated-measures design.

Results: Consistent with humans with MD or BD, physostigmine dose dependently increased punish sensitivity (non-target responding on trials following a low-frequency punishment) resulting from a target response (Target Lose-Shift, $F_{(3,54)}=6.23$, $p<0.01$). This increased sensitivity coincided with a poorer but non-significant decrement in PRL switches, without changes in breakpoint.

Conclusions: Physostigmine increases punishment sensitivity in the PRL. Consistent with results in humans with MD or BD, this increase is not coincident with impairments in reversal learning or decreased motivation. This physostigmine-induced punishment sensitivity likely represents a relevant translational biomarker for MD and an opportunity for novel treatment development.

These studies were supported by NIH grant R01-MH0104344, and the Veteran's Administration VISN 22 Mental Illness Research, Education, and Clinical Center.

Electronic Cigarette Use among Cancer Patients: Reasons for Use, Beliefs, and Patient-Provider Communication

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Background: Smoking tobacco cigarettes after a cancer diagnosis increases risk for several serious adverse outcomes. Thus, patients can significantly benefit from quitting smoking. Electronic cigarettes are an increasingly popular cessation method. Healthcare providers routinely ask about combustible cigarette use, yet little is known about use and communication surrounding e-cigarettes among cancer patients. This study aims to describe e-cigarette use by cancer patients, as well as patients' beliefs and communication with oncology providers about e-cigarettes.

Methods: Cancer patients (N = 121) who currently used e-cigarettes were surveyed in a cross-sectional study about their patterns of use, reasons for use, beliefs, and perceptions of risk for e-cigarettes, combustible cigarettes, and nicotine replacement therapies (NRT). Patient perspectives on provider communication regarding e-cigarettes were also assessed.

Results: Most participants identified smoking cessation as the reason for initiating (81%) and continuing e-cigarette use (60%). However, 51% of patients reported current dual use of combustible cigarettes and e-cigarettes, and most patients reported never having discussed their use of e-cigarettes with their oncology provider. Patients characterized e-cigarettes as less addictive, less expensive, less stigmatizing, and less likely to impact cancer treatment than combustible cigarettes (p 's < .05), and more satisfying, more useful for quitting smoking, and more effective at reducing cancer-related stress than NRT (p 's < .05).

Conclusions: Cancer patients who use e-cigarettes have positive attitudes towards these devices and use them to aid in smoking cessation. This study highlights the need for improved patient-provider communication on the safety and efficacy of e-cigarettes for smoking cessation.

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The Role of Dopamine D1 Signaling Pathway in COMTval158met-modulated Response to Immune Challenge: A First Study Linking COMTval158met Polymorphism and Inflammation

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Background: The catechol-*O*-methyltransferase (COMT) val158met polymorphism has been associated with a greater risk of posttraumatic stress disorder (PTSD). In a “humanized” COMT mouse line, male Val/Val carriers, compared to Met/Met carriers, exhibited enduring inflammatory and anxiety-like responses to trauma exposure. Similar effects were found following a severe immune challenge, suggesting a role of COMTval158met-modulated inflammation in stress-induced behaviors. However, the mechanisms underlying the COMTval158met and its contributions to immune function and to trauma-induced inflammation remain unclear. Based on a previous study reporting dopamine D1 receptor-moderated systemic inflammation, we hypothesized that D1 signaling pathway regulates the COMTval158met-modulated response to immune challenge.

Methods: Lipopolysaccharide (LPS; 1 mg/kg IP) was injected in male Met/Met or Val/Val carriers to induce immune challenge. Simultaneously with LPS treatment and again for two following days, the dopamine D1 agonist SKF-82958 (1 mg/kg IP) was administered. One week later, enduring anxiety-like behaviors were assessed in the open field and light/dark box tests.

Results: Val/Val, compared to Met/Met, carriers showed the greatest increase of anxiety-like behaviors following LPS treatment. The D1 agonist SKF-82958 prevented the immune-induced behaviors only in Val/Val mice.

Conclusions: These results indicate that dopamine D1-regulated immune pathways play a role in the COMTval158met-modulated response to immune challenge. Taken together with our previous data, these findings indicate that altered dopamine signaling may underlie the alterations in immune and behavioral responses to trauma in COMTval158met carriers. Future work will examine the sex-dependent immune mechanisms related to COMTval158met and their modulation by the D1 signaling pathway.

Dietary Restraint and Weight Loss in Relation to Disordered Eating in Obese Veterans
following a Behavioral Weight Loss Intervention

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Background. Dieting and weight loss are proposed risk factors for eating disorders. However, high rates of obesity among Veterans suggests dieting and weight loss are medically necessary for this population. To inform appropriate treatment models for Veterans with overweight/obesity (OW/OB) who binge eat, the current study examined whether weight loss and various forms of dietary restraint were related to disordered eating in this population following completion of a behavioral weight loss intervention (Veterans Health Administration MOVE!).

Methods. MOVE! program completers were recruited for an adjunctive treatment study for binge eating behaviors ($N=89$; 75% male). Percent weight loss from pre- to post-MOVE! was measured immediately following MOVE! completion. Dietary restraint and disordered eating were measured at baseline for the adjunctive study. Dietary restraint was measured by the Restrained Eating subscale of the Dutch Eating Behavior Questionnaire (DEBQ R) and Restraint subscales of the Eating Disorder Examination (EDE) interview. Disordered eating was measured by the Binge Eating Scale (BES) and External Eating and Emotional Eating subscales of the DEBQ.

Results. Pathological dietary restraint (EDE Restraint-shape/weight; DEQB R-intent) was significantly positively correlated with disordered eating and not correlated with weight loss. Adaptive dietary restraint (DEBQ R total; DEBQ R-behavior; EDE Restraint for Control) was significantly positively correlated with weight loss and not correlated with disordered eating.

Conclusions. Dietary restraint behaviors taught in MOVE! and concomitant weight loss are not risk factors for disordered eating in this population. Treatment targets for Veterans with OW/OB who binge eat can include behavioral weight loss components.

White Matter Connectivity & Social Cognition Across Psychotic Disorders

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Social cognitive deficits are impaired mental operations underlying social interactions and are present across psychotic disorders, including schizophrenia spectrum, bipolar, and depressive disorders. It is unclear what neurobiological factors underlie social cognitive impairment, thus rendering it difficult to prevent these deficits and their downstream functional consequences. Research suggests that impaired white matter connections within social cognitive cerebral networks may be the culprit. This study will extend current diffusion tensor imaging (DTI) neuroimaging research to a transdiagnostic sample of individuals with psychotic disorders. Twenty-five individuals with clinically significant psychotic symptoms and eight demographically-matched controls completed diagnostic, symptom severity, general cognitive, social cognitive, and social functioning assessments in the first visit, and DTI scanning during the second visit. Analyses will collapse across groups and examine white matter integrity within the uncinate fasciculus (UF) and inferior longitudinal fasciculus (ILF) through fractional anisotropy (FA) values to investigate their relation to social cognition and social functioning. Further, a whole brain approach will be employed to examine potential additional white matter tracts involved. We hypothesize that FA within the UF will be positively associated with theory of mind, emotion recognition, and social functioning; FA within the ILF will be positively associated with emotion processing and social functioning. Lastly, we hypothesize that, in comparison to social cognition, general cognitive ability will not account for a significant amount of variance within FA in the UF and ILF.

Association between Marital Factors and Weight Behaviors in Bariatric Surgery Patients

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Background: Weight loss surgery is one of the most effective interventions for obese individuals; however, 10-40% of individuals are not able to maintain weight loss long term (Elder & Wolfe, 2007). Spouses may be an important target to examine adherence to post-operative lifestyle changes, given that specific spousal behaviors could provide help or hindrance with these changes. Extending previous research, the current study examined the association between marital factors and weight behaviors in a bariatric surgery sample.

Methods: Participants for this study were 101 married or cohabitating post-operative weight loss surgery patients. Questionnaires assessed marital factors and health behaviors related to weight.

Results: Results indicated the average number of days participants weighed each week was negatively predicted by emotional support and positively predicted by positive social interaction. Impact of weight on physical functioning was positively predicted by tangible support. Impact of weight on sexual functioning was negatively predicted by positive social support interactions. Impact of weight on work life was negatively predicted by emotional support. Impact of weight on sexual functioning negatively predicted marital satisfaction and positive social support interactions.

Conclusions: Results provide support for the bidirectional association between marital factors and health behaviors in a bariatric surgery sample. This provides important treatment implications such that treatments designed to teach spouses specific support behaviors may have benefits for increasing adherence to post-operative recommended lifestyle changes.

Accounting for Genetic Context: Incorporating Interactions between Polygenic Risk Scores for Alzheimer's and Associated Risk Factors and Their Relation to Mild Cognitive Impairment

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Background: Alzheimer's disease (AD) is under considerable genetic influence and polygenic risk scores (PRSs) represent a useful approach to summarize small effects across the genome. We previously showed that AD-PRSs were associated with increased odds of mild cognitive impairment (MCI). Risk factors for AD such as cardiovascular disease and obesity are also under genetic influence, yet it is unknown how genetic risk for these conditions interacts with genetic risk for AD.

Methods: We included 1118 cognitively normal participants, 89 amnesic MCI (aMCI), and 46 non-amnesic MCI (naMCI) from the Vietnam Era Twin Study of Aging (VETSA). We calculated PRS for AD as well as for coronary artery disease (CAD) and BMI—known AD risk factors. We tested main and interaction effects of the AD-PRS and these risk factor PRSs in both MCI groups.

Results: There was a significant main effect of the AD-PRS in both MCI groups. There was a significant AD-PRS x CAD-PRS interaction in aMCI subjects, and an AD-PRS x BMI-PRS interaction in naMCI subjects. In both cases, the association between the AD-PRS and MCI was attenuated as scores on the risk factor PRS increased.

Conclusions: These results indicate the importance of considering broader genetic context when examining risk for MCI or AD. Genetic risk for other factors may moderate the predictive utility of an AD-PRS, or alternatively, may identify cognitive impairment due to non-AD related causes. Incorporating PRSs for other AD risk factors and their interactions may better characterize variability in the genetic etiology of AD.

A Moderation Analysis of Personality and Environmental Protective Factors
for Problem Drinking: Does Resilience during Teenage Years Predict
Less Problem Drinking during Young Adulthood?

Candace Fanale, Ph.D., Robin Tan, Ph.D., & Joanna Jacobus, Ph.D.

Introduction: Studies analyzing personality and alcohol use typically focus on risk factors rather than protective factors or resilience. Resilience factors (temperament-based and environmental) may inform clinical interventions that promote adaptation to adversity. In this study, we aim to identify specific internal (e.g., personality) and environmental protective factors that moderate the risk of problem drinking among adolescents in a prospective cohort.

Methods: Data was extracted from an ongoing longitudinal study (n=93), with participants ages 12-14 years at baseline. Hierarchical linear regression models will use variables computed from independent time points (baseline, 4-year, and 9-year follow-up) to test the main effects of alcohol risk and the interaction effects of resilience (alcohol risk by environment protective factors, alcohol risk by internal protective factors) on alcohol use behaviors by ages 20-23.

Results: Preliminary results revealed that the alcohol risk by internal protective factors interaction predicted more binge drinking behaviors in the past year by ages 20-23 ($r=0.17-.22$; $p<0.05$). The main effect of environment predicted fewer binge drinking behaviors by ages 20-23 ($r=-0.27$; $p=.01$). Therefore, early alcohol risk predicted binge drinking behaviors even among those who were high in internal protective factors, such as conscientiousness; whereas environmental protective factors predicted fewer binge drinking behaviors.

Conclusion: Findings are preliminary, yet promising and may provide insight to how early risk factors, internal resilience, and environmental protective factors predict binge drinking behaviors by young adulthood. Early identification of predictors of resilience to problematic drinking among adolescents may inform interventions that promote resilience during vulnerable adolescent years.

Association between Inflammation and Alcohol Dependence in PTSD

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Background: There is high comorbidity between Post-traumatic stress disorder (PTSD) and Alcohol Use Disorder (AUD). The inflammatory factor C-reactive protein (CRP) has been identified as a PTSD risk factor, while chronically elevated blood alcohol levels can increase CRP. We tested the hypothesis that inflammation, measured by CRP, interacts with PTSD symptoms predicting alcohol dependence.

Methods: In the Marine Resiliency Study, active duty service Marines and Navy Corpsmen (N=1890) were given the AUD Identification Test (AUDIT) for consumption and dependence, as well as the Clinician Administered PTSD Scale (CAPS) after combat deployment to Afghanistan or Iraq. CRP was measured from plasma by enzyme-linked immunosorbent assay.

Results: PTSD diagnosis predicted alcohol consumption (N=1446; $p < 0.01$), though without main CRP effects or interactions. PTSD diagnosis predicted a ~10% lower chance of avoiding dependence (N=1446, $p < 0.001$). In those endorsing dependence symptoms, PTSD diagnosis interacted with CRP predicting dependence severity (N=353, $p < 0.02$), with CRP associated with dependence symptoms only with PTSD. Of those reporting some dependence, symptom severity in PTSD subjects was 2.51 (range= 1-11) and those without PTSD averaged 2.37 (range=1-10) ($p > 0.5$) suggesting that CRP association with dependence severity in PTSD is not simply due to greater dependence.

Conclusions: These data support a possible synergy between PTSD and CRP, which is associated with alcohol dependence but not consumption. It is possible that PTSD with inflammation may increase vulnerability for alcohol use.

Sex Differences in Serotonin-Mediated Stress Reactivity in Individuals
with and without Histories of Alcohol Dependence

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Background: Alcohol dependence (AD) is marked by changes in limbic-hypothalamic-pituitary-adrenal (LHPA) axis function and serotonergic (5-HT) neurotransmission, and studies have demonstrated sex differences in these systems. We hypothesized that history of AD and female sex would interact to influence stress hormone responses to the selective serotonin reuptake inhibitor, citalopram.

Methods: One hundred participants with (AD+, N = 57) and without (AD-, N = 43) histories of alcohol dependence (53 Men, 47 Women) underwent both citalopram and placebo challenges in a randomized, double-blind, counterbalanced design on two separate days. AD participants were abstinent from alcohol; no participants had an independent psychiatric disorder in the past 12 months. The primary outcomes were plasma adrenocorticotropin hormone (ACTH) and cortisol responses to each pharmacologic challenge.

Results: The model revealed no effect of AD on stress reactivity for either ACTH or cortisol. For cortisol, there was an overall main effect of sex on both treatment days with men demonstrating a significantly higher elevation in levels from baseline regardless of condition ($p < 0.001$), smaller decrease in concentrations ($p < 0.001$) with placebo, and greater increase in levels ($p = 0.034$) with citalopram. For ACTH, a treatment by sex interaction ($p < 0.001$) was found with men demonstrating a trend for a greater response to citalopram ($p = 0.081$) but not placebo.

Conclusions: Regardless of history of AD, we found sex differences in stress hormone responses to both placebo and 5-HT stimulation. These results provide further evidence that serotonergic mechanisms play an important role in mediating sexually dimorphic endocrine responses in humans.

Symbolic Play in Autism Spectrum Disorders:
Evaluating Two Empirically Supported Treatments in a Randomized Controlled Trial

Gould, Hilary, & Kasari, Connie

Background: Play is an important aspect of childhood development. Difficulty with imaginative, or symbolic play, is a core deficit of children with an autism spectrum disorder (ASD; DSM-5, APA, 2013).

Methods: This study represents the first attempt to compare the focal target of play between two interventions. Sixty-five pre-school aged, minimally verbal children (less than 30 spoken words) with ASD and their parents participated in this study. Children were randomly assigned to receive six months of Discrete Trial Training (DTT) or Joint Attention, Symbolic Play, Engagement & Regulation (JASPER) interventions, which are both empirically supported treatments for ASD.

Results: A randomized controlled trial found that symbolic play types increased across both interventions when targeted, but children receiving the JASPER intervention demonstrated greater gains compared to children receiving DTT ($p = .039$, $R^2 = .19$). Additionally, only children in the JASPER condition were able to maintain these gains six months later at follow-up. Improvements in symbolic play types were associated with higher scores on cognitive (e.g., Visual Reception: $p = .004$) and language (Expressive: $p = .004$; Receptive: $p = .015$) outcomes for both treatments. Improvements made with therapists in both treatments did not generalize to parent child interactions at home.

Conclusion: These findings suggest further adaptations must be made to improve generalization from school to home, and across partners. Overall this research suggests that JASPER is more effective at teaching and maintaining symbolic play skills for preschool-aged minimally verbal children with ASD compared to DTT, which is a more widely used approach.

Genetic and Environmental Influences on Verbal Fluency in Middle Age: A New Framework

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Background: Neuropsychological measures of verbal fluency are some of the most widely used tests for detecting age-related cognitive decline and dementia. Although mounting evidence suggests that phonemic and semantic fluency measures are differentially associated with other cognitive and health phenotypes, few studies have examined the shared/unique variance between these aspects of fluency, especially using genetically-informative studies.

Method: 1464 middle-aged twins from the Vietnam Era Twin Study of Aging completed phonemic and semantic fluency tests at up to two time-points (mean age 56 and 62 years).

Results: Results supported a two-factor solution at both waves: a General Fluency latent factor predicted variation in all six tests and a Semantic-Specific factor accounted for additional variation in semantic fluency tests only. Both factors were explained primarily by genetic influences (heritability=.56 to .76). There was considerable stability over six years ($r=.90$ for General Fluency, $r=.81$ for Semantic-Specific), especially for genetic influences ($r_g=.99$ and 1.0, respectively). Further analyses of the first wave data revealed that General Fluency was more strongly related to vocabulary ($r=.57$) and executive functions ($r=.40$), whereas Semantic-Specific was more strongly related to episodic memory ($r=.58$).

Conclusions: These results provide a new framework for viewing semantic fluency as a combination of general and semantic-specific variance, both of which have unique genetic underpinnings and differential relations with other cognitive abilities. In contrast, phonemic fluency is explained entirely by the general factor. It will be important to further examine the role of Semantic-Specific, especially regarding the transition to mild cognitive impairment and Alzheimer's disease risk.

Negative Fateful Life Events in Midlife and Advanced Predicted Brain Aging

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Background: Negative fateful life events (FLE) such as interpersonal conflict, death in the family, financial hardship and serious medical emergencies can act as allostatic stressors that accelerate biological aging. However, the relationship between FLEs and neuroanatomical aging is not well understood.

Methods: We examined 359 men (mean age 62 years) participating in the Vietnam Era Twin Study of Aging (VETSA) to determine whether negative midlife FLEs are associated with advanced brain aging after controlling for physical, psychological and lifestyle factors. At two different timepoints participants were assessed for negative FLEs, health and well-being, general cognitive ability, socioeconomic status (SES), depression, and ethnicity. Participants underwent an MRI examination and T1-weighted images were processed with FreeSurfer. Subsequent neuroanatomical measurements were entered into the BARACUS software to predict brain age.

Results: Having more midlife FLEs, particularly relating to interpersonal relationships, was associated with advanced predicted brain aging (i.e. higher predicted brain age relative to chronological age). This association remained after controlling for the significant covariates of alcohol consumption, cardiovascular risk, adult SES, and ethnicity. Although post hoc analysis showed that non-amnestic, but not amnestic, MCI was also associated with advanced predicted brain aging, this association did not hold up after controlling for these other factors.

Conclusion: In middle age, cardiovascular risk factors, low adult SES, alcohol consumption and ethnicity were significantly associated with advanced predicted brain age. It remains to be determined whether the influence of midlife FLEs and other factors on brain age may change with increasing chronological age.

Acceptance and Commitment Therapy for Veterans with Chronic Pain:
Does PTSD Impact Treatment?

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Background: Studies have shown greater psychosocial impairment in those with comorbid chronic pain and PTSD compared to those with chronic pain alone; however, we are unaware of any study that has examined the impact of PTSD on outcomes of psychosocial pain interventions.

Methods: Veterans with chronic pain and PTSD ($n = 43$) or without PTSD ($n = 83$) participated in an 8-week Acceptance and Commitment Therapy (ACT) intervention for chronic pain. Measures of pain interference, pain intensity, pain acceptance, PTSD symptoms, depressive symptoms, and pain-related anxiety were collected at baseline, posttreatment, and 6-month follow-up. Linear mixed models were used to analyze change from baseline to posttreatment and baseline to follow-up.

Results: Veterans with PTSD were significantly younger, more likely to use psychotropics, and exhibited greater psychosocial impairment at baseline (p 's <0.05). Improvements were found at posttreatment across measures and results did not differ by group (p 's <0.05). Significant improvements were also found at follow-up (p 's <0.05), except for PTSD symptomology, which did not improve in either group. Further, a significant group by treatment interaction was found for depressive symptoms, such that only those without PTSD showed significant improvements in depressive symptomology at follow-up ($b=-0.61$; $p=0.002$).

Conclusions: Overall, Veterans with PTSD exhibit similar improvements as Veterans without PTSD in ACT treatment. However, Veterans with PTSD do not maintain improvements in depressive symptomology, and no improvements in PTSD symptomology were found at follow-up. Future research is encouraged to integrate evidence-based PTSD interventions with traditional chronic pain interventions for Veterans with comorbid chronic pain and PTSD.

Environmental Reward, Goal-Directed Activation, and Depressive Symptoms as Predictors of Transdermal Nicotine Patch Adherence in a Randomized Controlled Trial of Behavioral Activation for Smoking

Elana M. Hoffman, Julia Felton, Laura MacPherson, and Andrea Chronis-Tuscano

Introduction: Rates of cigarette smoking remain high in the U.S. Nicotine Replacement Therapy (NRT) is effective when used properly. Rates of NRT adherence are low, and there is little research on the psychological predictors of compliance. Depressive symptoms predict poor medication adherence, though this has never been studied as it relates to NRT use. Behavioral Activation Treatment for Smoking (BATS) is hypothesized to reduce depressive symptoms through increases in both positive reinforcement from the environment and goal-directed activation. Individuals who receive this treatment may exhibit increased compliance to the patch first through increases in environmental rewards or goal-directed activation, and subsequently through decreases in depressive symptoms.

Methods: Using data from a stage-II RCT examining BATS compared to standard smoking cessation treatment (ST), we utilized SEM to examine a serial mediation model. Study aims: (1) to examine a model in which BATS would affect NRT adherence through increases in environmental reward at mid-treatment and decreases in end-of-treatment depressive symptoms; and (2) to examine a model in which BATS would affect NRT adherence through increases in goal-directed activation mid-treatment and decreases in end-of-treatment depressive symptoms.

Results: Neither of our serial medication models were supported, however we found significant pathways from mid-treatment goal-directed activation and NRT adherence, and end-of-treatment depressive symptoms to NRT adherence in our model examining goal-directed activation.

Discussion: Changes in both goal-directed activation and depressive symptoms may be key when predicting NRT adherence in a sample of adult smokers enrolled in smoking cessation treatment.

Hippocampal Volume Independently Predicts Subjective Memory Complaints in Mild Traumatic Brain Injury

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Background: Veterans with mild traumatic brain injury (mTBI) frequently report memory deficits, which are not always supported by objective neuropsychological testing and are often related to psychiatric symptoms, such as posttraumatic stress disorder (PTSD). Neuroimaging allows for examination of possible neural correlates of subjective memory complaints. Thus, we examined the relationship between hippocampal volumes, objective memory performance, and PTSD symptoms on subjective memory complaints in mTBI Veterans.

Methods: 61 mTBI Veterans with optimal effort completed tests of objective verbal and visual memory (WMS-IV Logical Memory and Visual Reproduction), subjective memory (NSI-14), the PTSD Checklist, and structural magnetic resonance imaging. FMRIB's Software (FSL) was used to obtain hippocampal and intracranial volume (ICV) estimates. A hierarchical regression analysis examined whether bilateral hippocampal volume, visual or verbal memory performance, and/or PTSD symptoms predicted subjective memory complaints controlling for ICV and age.

Results: The regression analysis demonstrated that although objective memory performance was not associated with subjective memory complaints, hippocampal volumes were significantly and independently associated with subjective complaints ($p=.001$), with smaller volumes relating to greater complaint severity. As expected, PTSD strongly predicted subjective memory complaints ($p's<.001$).

Conclusion: In mTBI Veterans, subjective memory complaints are best accounted for by PTSD symptoms and hippocampal volume, but not objective performance. Importantly, smaller hippocampal volumes are independently associated with greater subjective memory severity, suggesting a neural basis of memory complaints in mTBI not accounted for by PTSD or objective memory performance. Future research is needed to elucidate the behavioral manifestations of subjective memory complaints in mTBI.

Examining variability in community therapist delivery of evidence-based mental health intervention strategies for ASD: Do child client characteristics matter?

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Background: Therapist fidelity to evidence based interventions (EBIs) is a key indicator of success of community implementation. Given the documented variability in therapist fidelity, identifying factors influencing therapist delivery of EBIs is critical to inform implementation efforts. In response to limited research specifically on the role of child characteristics in therapist fidelity, this study examines the associations between client socio-demographic and clinical characteristics and therapists' delivery of EBI strategies for children with ASD. Data were drawn from a community effectiveness trial of AIM HI (An Individualized Mental Health Intervention for ASD¹), an intervention designed specifically for delivery in publicly-funded mental health services.

Methods: The sample includes a subset of therapists (n=126) and children with ASD (n=143; 58% Latino) participating in the AIM HI training condition of the effectiveness trial. Session recordings were coded to measure therapist use of AIM HI active teaching strategies.

Results: Mixed model analyses indicated that child ethnicity and gender were not significantly associated with therapist delivery of individual AIM HI strategies. Greater child age ($F=3.502$, $p=.065$) and autism severity ($F=3.634$, $p=.059$) were related to the active teaching summary composite. For individual strategies, greater child age ($F=15.28$, $p<.001$) and lower autism severity ($F=8.95$, $p=.003$) were associated with therapist delivery of more psychoeducation.

Conclusions: Although it is promising that child ethnicity was not associated with therapist delivery of AIM HI strategies, older children and those with lower ASD severity were associated with higher therapist fidelity. These results suggest that AIM HI therapists serving younger children with more severe symptoms may need additional training support with specific AIM HI strategies.

¹ Brookman-Frazee & Drahota, 2010

Emotional and Psychosocial Functioning are Problematic in HIV and Methamphetamine Dependence and Associated with Significant Functional and Health-related Outcomes

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Background: HIV and methamphetamine (METH) use frequently co-occur and have been linked both independently and in combination to numerous adverse everyday functioning and health-related outcomes. This study sought to explore the impact of HIV and METH on important aspects of emotional and psychosocial functioning as measured the NIH Toolbox – Emotions Battery (NIHTB-EB) summary composite scales for Negative Affect (NA), Social Satisfaction (SS), and Psychological Well-Being (PWB), and subsequent associations with adverse everyday functioning and health-related outcomes.

Method: Participants included 144 individuals stratified by HIV (HIV-/HIV+) and METH-dependence (METH-/METH+) into four groups. Each participant was administered the NIHTB-EB as part of a comprehensive evaluation. Summary T-scores for NA, SS, and PWB were derived using published summary score formulas based upon the NIHTB normative sample. Summary scores beyond one standard deviation in the direction of distress were characterized as “problematic”.

Results: Adjusting for potential confounds (e.g., neurocognitive impairment), multivariable regression analyses revealed significant independent, but not interactive, effects of HIV and METH on problematic NA and SS scores ($ps<0.05$), and a significant independent effect of METH on problematic PWB ($p<0.0001$). Within the risk groups, problematic NIHTB-EB scores were significantly associated with adverse functional (e.g., unemployment) and health-related outcomes (e.g., cardiovascular risk; $ps<0.01$).

Discussion: Findings support the validity of the NIHTB-EB for individuals with HIV and/or METH dependence, and highlight the need to comprehensively assess psychosocial-emotional functioning, as certain aspects may be particularly relevant to important outcomes and targets for intervention.

A Randomized Clinical Trial Using Auditory-based Computerized Cognitive Training
in Patients with Chronic Schizophrenia:
Interaction of Anticholinergic Burden with Treatment Effects

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Background: Early auditory information-processing impairments contribute to cognitive deficits in schizophrenia (SZ). Targeted cognitive training (TCT) is an emerging computerized intervention for remediating these deficits. TCT gains in SZ are thought to depend on appropriate brain cholinergic signaling, but SZ patients are vulnerable to elevated anticholinergic burden stemming from psychotropic medications. Anticholinergic medications are known to contribute to cognitive deficits in general, but the extent to which they alter TCT effectiveness is not well characterized. Here we report preliminary findings from an ongoing randomized clinical trial investigating the effectiveness of TCT in SZ inpatients and the interaction of anticholinergic burden on treatment effects.

Methods: SZ patients (n=48) were randomized to treatment as usual (TAU) or treatment as usual augmented with TCT. Anticholinergic Cognitive Burden Scale (ACCB) scores were calculated from medical records. Auditory discriminability, cognitive functioning, and symptom ratings were assessed before and after ~40h of TCT. Groups did not differ at baseline in clinical, demographic or cognitive variables. ACCB scores at baseline and follow up were similar in both groups.

Results: TCT improved auditory discriminability ($d=0.63$), verbal learning and memory ($d=0.82$), and positive symptoms ($d=-0.62$). Baseline ACCB negatively correlated with change in verbal learning ($r=-.61$, $p<0.02$) and auditory discriminability ($r=-.53$, $p<0.05$) among TAU patients but not TCT patients.

Conclusion: Results demonstrate that improving auditory sensory processing using TCT yields clinically meaningful outcomes, even in SZ patients with a high degree of anticholinergic burden. Results also suggest that TCT may overcome anticholinergic burden-associated cognitive impairment in SZ.

Inflammatory Biomarkers in Early Psychosis

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Background: There is evidence that perinatal inflammation may stand at the top of a cascade of neural events that disrupt cell structure and function, leading to later-life sensitivity to immune challenges. The release of pro-inflammatory cytokines by prolonged microglial hyperactivity may lead to neuronal apoptosis, which is potentially related to the loss of brain tissue observed in patients with schizophrenia. Neuroinflammatory processes were assessed in first episode psychosis patients, individuals at clinical high risk for psychosis, and normal comparison subjects. A panel of peripheral markers of neuroinflammation linked to cognitive impairments in HIV positive adolescents was investigated. The goal of this study was to collect pilot inflammatory biomarker data in preparation for a larger translational study that will investigate neuropathological mechanisms and intervention in early psychosis.

Methods: Subjects were included if they were in their first episode psychosis (FEP). Clinical high risk (CHR) for psychosis subjects met CHR criteria per the Structured Interview of Prodromal Syndromes (SIPS). Normal comparison subjects did not meet criteria for any diagnosis. A panel of peripheral biomarkers linked to neuroinflammation and neurocognitive abnormalities was obtained.

Results: The sample included 84 individuals ages 12-35, 61 FEP, 13 CHR, and 10 normal comparison subjects. A variety of markers significantly differed between groups. Bonferroni corrections were used for multiple comparisons. These group differences were primarily accounted for by the CHR and antipsychotic naive FEP groups compared to normal comparison subjects. In addition, greater levels of inflammatory biomarkers were associated with more symptoms in early psychosis subjects.

Conclusions: Overall, CHR subjects and antipsychotic naive FEP patients displayed higher concentrations of peripheral biomarkers linked to neuroinflammation compared to normal comparison subjects. These findings provide evidence that a period of hyper-plasticity or increased neuroinflammation is present during the at-risk phase of psychosis, which then presumably progresses to a stage of hypo-plasticity and reduced neuroinflammation after the onset of psychosis.

Expanding Intimacy Theory: Vulnerable Disclosures and Partner Responding

Chandra E. Khalifian, MA and Robin A. Barry, PhD

Background: Theorists agree that intimacy increases when individuals' vulnerable disclosures are met with partners' supportive responses. The present research expands theory by examining two qualities of vulnerable disclosures that may alter their function within intimacy processes: 1) the extent to which the disclosure includes/implicates the partner; and 2) the extent to which the disclosure describes specific, rather than general, thoughts and emotions. Additionally, this research examines emotion-regulatory factors (i.e., attachment style and mindfulness) that may influence the expanded model.

Methods: Eighty-two cohabiting couples first completed questionnaires of emotion-regulation styles, then participated in two randomly assigned video-recorded vulnerability discussions (either partner-inclusive or exclusive), and finally rated how responsive, reinforcing, and punishing their partner was during the discussions.

Results: Individuals perceived lower responsiveness and reinforcement and higher punishment when disclosing specific, partner-inclusive vulnerabilities. Regarding attachment style, women perceived less responsiveness during partner-inclusive disclosures when men had higher avoidant attachment (but not lower). Both men and women perceived lower reinforcement during specific disclosures when their partners had higher avoidant attachment (but not lower). Regarding mindfulness, individuals perceived lower responsiveness when disclosing specific, partner-inclusive vulnerabilities when their partners had lower mindfulness (but not higher). Finally, individuals perceived lower reinforcement when disclosing specific vulnerabilities when their partners had lower mindfulness (but not higher).

Conclusions: This research expands intimacy theories by illuminating two qualities of vulnerable disclosures that influence intimacy process outcomes – partner-inclusiveness and specificity. Further, attachment style and mindfulness may be important emotion-regulation factors to assess and potentially modify to promote couple cohesiveness.

Probing the Effects of Ketamine on the Habenular-circadian Circuit

Matthew Klein, Hema Kopalle, Joshua Chandra, Roberto Malinow

Background: A person is often at highest risk for committing suicide in the weeks immediately after the diagnosis of depression. A major barrier to treatment of suicidal ideation is that current pharmaceutical treatments are significantly time-delayed. Ketamine acts as an acute antidepressant, significantly reducing suicidal ideation in most individuals within 24 hours, though its effects on specific neural regions are not well understood. Hyperactivity in the Lateral Habenula (LHb), a dopaminergic release regulator, leads to depression-like symptoms. We used a line of congenital learned helplessness (cLH) rats, a validated model of Major Depressive Disorder, to examine the effect of ketamine on a putative habenular-circadian circuit and the interaction with circadian neuropeptides. Expression of these, which is regulated by the Lateral Preoptic area (LPO) and Lateral Hypothalamic Area (LHA), enhances the effects of existing antidepressants.

Methods: We used a variety of methods to explore this regulatory circuit. Using an in-vivo rat model, we have characterized long-range projections from the LPO/LHA to the LHb by probing for mRNA and protein expression of neurotransmitters, circadian neuropeptides, and neuronal activity markers. We also measured the behavioral response to ketamine using a series of established methods.

Results: Our results demonstrate a reduction in depressive symptoms after the introduction of ketamine, and altered habenular activity. We found sparse populations of neuropeptide expressing neurons projecting from the LPO/LHA to the LHb which provides support to our predictions.

Conclusions: Understanding the mechanism by which ketamine exerts regulatory effects on the habenular-circadian circuit could lead to the development and optimization of better treatments for depression.

Local Gyrfication Abnormalities in Middle-Aged Adults with Autism Spectrum Disorders

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Background: Neurodevelopmentally, evidence shows early cerebral overgrowth in the first years of life in autism spectrum disorders (ASDs). However, little is known about adults with ASDs, including possible accelerated decline. A few studies of early to middle adulthood suggest increased cortical thinning in ASDs. We investigated cortical morphology in adults with ASDs ages ≥ 40 years, in a comparison with age-matched typical controls (TC).

Methods: Following quality assurance of T1 weighted MRI sequences (0.8mm isotropic), 20 ASD and 21 TC participants matched on age and IQ, were compared. IGI, CT, and SA were measured using FreeSurfer v.5.3.0. Statistical analyses employed a general linear model including age, non-verbal IQ, and total brain volume as covariates.

Results: For IGI, significant main effects of group (ASD<TC) were observed bilaterally in insular and anterior cingulate (ACC) clusters, along with left postcentral and middle frontal, and right orbitofrontal and supramarginal clusters. IGI also declined with age in combined groups in bilateral precentral and right supramarginal clusters. No significant group, age, or interaction effects were observed for CT or SA.

Conclusions: Reduced IGI may suggest accelerated tissue loss in ASDs, possibly consistent with some studies reporting increased cortical thinning in early adulthood. The finding of IGI differences without CT or SA effects indicates that IGI may be more sensitive to abnormalities of cortical macrostructure in ASDs. Differences in ACC are of interest given multiple post-mortem reports of its altered cellular density in ASDs and the importance of ACC in social and emotional function.

Synergistic Effects of Cellular Regulation of Inflammation and Cardiometabolic Risk Factors on Cognition in the Elderly

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Background: Inflammation, cardiometabolic risk (CMR) factors, and autonomic imbalance have been independently associated with cognitive deficits in aging, but their interactive effect on cognition remains unclear. We quantified the magnitude of their associations with cognitive function and determined the extent to which the links were synergistic.

Methods: Eighty dementia-free participants aged 60-93 years (mean=73.6, SD=8.3, 66% female) were recruited for a behavioral intervention study. Cognitive function was assessed with the Montreal Cognitive Assessment (MoCA) and aggregate CMR was ascertained using principal components analysis (PCA) on nine measures of serum glucose, lipids, and resting BP. Autonomic balance was calculated as delta-mean blood pressure (Δ MBP) between 10 min steady-state exercise and 1 min cool-down. Beta-adrenergic receptor-mediated inflammation control (BARIC) was quantified by stimulating immune cells *in vitro* with lipopolysaccharide, while simultaneously administering a beta-agonist, isoproterenol, for monocyte-produced cytokine (TNF- α) expression. Data were analyzed using stepwise multivariate linear regression.

Results: Of 76 participants who completed the MoCA, cognitive function was impaired in 21 (27.6%; MoCA \leq 23) and was correlated with age ($\beta_{std} = -0.30$, $t = -2.56$, $p = 0.013$), but not BMI or gender. For CMR factors, the first principal component explained 31.5% of total variance, for which higher values reflected a hyperglycemic, hyperlipidemic profile, and significantly predicted lower MoCA scores ($\beta_{PC1} = -1.20$, $t = -2.92$, $p = 0.005$). Impaired BARIC and more rapid MBP recovery were independently associated with lower MoCA scores ($\beta_{BARIC} = -1.14$, $t = -2.94$, $p = 0.005$; $\beta_{\Delta MBP} = 0.86$, $t = 2.32$, $p = 0.025$), adjusted for CMR effects. Furthermore, there was evidence of a synergistic effect of CMR and BARIC on MoCA scores ($\beta_{BARIC*PC1} = -1.01$, $t = -3.62$, $p < 0.001$) in the full model.

Conclusions: Inflammation, CMR factors, and autonomic balance exert both independent and synergistic effects on cognitive function in older adults.

Inhibiting a Dopamine Synthesis Enzyme, Tyrosine Hydroxylase, blocks ‘Summer-like’
Photoperiod-induced Mania-like Behavior in Mice

Molly A. Kwiatkowski, BA, Zackary A. Cope, PhD, Loren A. Lavadia,
Davide Dulcis, PhD, & Jared W. Young, PhD

Background: Seasonal variations in daylight can influence switching between mania and depression in some patients with bipolar disorder (BD)¹. BD patients exhibit more frequent mania episodes during the spring/summer when there are longer light (active) periods^{2,3}. Similarly, adult rodents exposed to long active (LA; 5:19 L:D) photoperiods exhibit mania-relevant behaviors⁴. Elevated catecholamines may contribute to the underlying mechanisms of mania⁵. Therefore, we tested whether the tyrosine hydroxylase inhibitor, alpha- methyl-p-tyrosine (AMPT), would prevent LA photoperiod-induced mania-relevant behavior mice.

Methods: Male C57BL/6 mice (N=79) were placed into normal active (NA; 12:12 L:D) or LA (5:19 L:D) photoperiod for two weeks. Mice received three injections of 30 mg/kg AMPT or saline on day 7/8 or day 14/15 of photoperiod exposure. A 5-minute elevated plus maze session was performed on day 15. Primary outcome = %time in open arms.

Results: LA-exposed saline-treated mice spent more time in open arms vs. NA-exposed mice, though this effect was not significant. Mice injected on day 7/8 exhibited a photoperiod x drug interaction ($F(1,34)=7.4$, $p<0.05$). There was no drug effect in day 7/8 NA-exposed mice; day 7/8 LA-exposed mice treated with AMPT spent significantly less time in open arms vs. LA-exposed mice treated with saline ($t(20)=3.4$, $p<0.01$). No photoperiod x drug interaction was observed in day 14/15 mice.

Conclusion: Our results support the hypothesis that LA photoperiod induces mania-relevant behavior as a result of a hyperdopaminergic state. Future studies will include targeted dopamine manipulations and histopathological studies to identify brain regions/circuitry affected by LA photoperiod exposure.

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Nicotine-induced Neurotransmitter Plasticity in the Substantia Nigra

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Background: Cigarette smoking is generally known for its detrimental effects on health; however, extensive epidemiological studies have indicated inverse correlation between smoking and Parkinson's Disease (PD), a progressive neurodegenerative disorder characterized by loss of dopaminergic neurons in the substantia nigra (SN). Subsequent studies have shown that nicotine protects dopamine neurons against nigrostriatal damage in PD primate and rodent models. Nicotine became the focus of these studies due to its well-known ability to modulate the function and activity of dopaminergic neurons in the midbrain. Because altered circuit activation can induce neurons to acquire a dopaminergic phenotype in the mature brain¹, we hypothesized that chronic nicotine treatment in adult mice induces neuroprotection against nigrostriatal damage in an animal model of PD via a mechanism of neurotransmitter plasticity.

Methods: Nicotine was given to adult (P60) mice in drinking water for two weeks. Brains were subsequently processed for immunohistochemical detection of neurotransmitter markers in the SN. A PD animal model² was used to overexpress human alpha-synuclein in dopaminergic neurons.

Results: In wildtype mice, nicotine treatment significantly increased the expression of tyrosine hydroxylase (TH) in the SNr (pars reticulata). We identified a GABAergic neuronal pool in the SNr available for nicotine-induced TH upregulation and expressing the Nurr1 gene, a transcription factor essential for dopaminergic differentiation.

Conclusions: Our findings indicate that neurotransmitter plasticity occurs in the SN in response to chronic nicotine treatment. Ongoing experiments on a PD mouse model are investigating whether nicotine-induced neurotransmitter plasticity ameliorates any motor deficits in these mice.

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Affective and Neurocognitive Dimensions in a Transdiagnostic Eating Disorder Sample:
Examining Measurement Convergence and Associations with Clinical Symptoms

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Background: Eating disorders (EDs) are serious psychiatric illnesses with shared biobehavioral mechanisms. Consistent with dimensionally-oriented research initiatives (i.e., RDoC), the current data are drawn from an ongoing study examining affective and neurocognitive processes underlying ED psychopathology.

Method: A non-ED-specific sample was recruited, requiring clinically significant ED symptoms and ED-related impairment. Participants (N=50 women) completed clinical interviews, questionnaires, and behavioral/neurocognitive tasks. Bivariate correlations were computed to evaluate convergence across tasks and questionnaires assessing corresponding constructs, as well as associations with affective and ED symptoms.

Results: Behavioral and self-report measures converged for emotional reactivity ($r=.30$, $p=.044$), but not inhibition or reward processing. Anxiety symptoms were associated with task based ($r=.38$, $p=.007$) and self-report ($r=.43$, $p=.003$) emotional reactivity, but only self-report inhibition ($r=-.31$, $p=.031$) and neither measure of reward processing. Depression symptoms were associated with task-based ($r=.35$, $p=.013$) and self-report ($r=.32$, $p=.031$) emotional reactivity, but not with inhibition or reward processing. For ED symptoms, binge eating was associated only with self-report inhibition ($r=-.29$, $p=.046$), restriction was associated only with self-report emotional reactivity ($r=.31$, $p=.037$), and purging demonstrated only a trend in relation to self-report reward processing ($r=.28$, $p=.059$).

Conclusions: Preliminary findings suggest the salience of affect and neurocognition in EDs, but also demonstrate discordance between actual performance and corresponding self-reported capabilities/experiences. This has implications for understanding ED onset, maintenance, and/or treatment. Specifically, actual performance deficits would indicate certain potential neurobiological mechanisms and treatment approaches, whereas perceived difficulties in the absence of actual deficits may suggest the need to investigate and intervene on alternative targets.

Demographic, Clinical and Inflammatory Correlates of Sleep in Schizophrenia

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Background: In persons with schizophrenia (SZ), sleep disturbances are common, have been associated with worse psychopathology and are potentially treatable. In the general population, poor sleep has been shown to be associated with increased inflammation, an important pathophysiological mechanism in SZ. Persons with SZ have increased inflammation, which has been associated with worse pathophysiology and physical health. Few studies systematically examine clinical correlates of inflammation and sleep in this high-risk group.

Methods: We studied 135 subjects with SZ and 128 non-psychiatric comparison (NC) subjects (mean age 48.4 ± 10 years). We used subjective sleep measures to assess total sleep time and identify subgroups of sleep quality. We compared age, sex, duration of illness, antipsychotic dose, positive and negative symptoms, depression, anxiety, BMI, comorbidities; and inflammatory biomarkers (hsCRP, TNF-alpha, IL-6, IL-10) across diagnostic and sleep quality groups.

Results: The SZ subjects reported higher total sleep time and worse sleep quality compared to NCs. Among the NC subjects, age, depression, and physical comorbidities differed significantly between sleep quality subgroups. NCs who slept <6 hours had significantly higher IL-6 levels, compared to those who slept 6-9 hours. Among the SZ subjects, depression, positive symptoms and anxiety differed significantly between the sleep quality subgroups. While inflammatory markers were similar in NC subgroups, hsCRP levels were significantly higher in the SZs with poor vs. good sleep quality.

Conclusions: Self-reported measures of sleep quality and quantity were associated with different clinical variables and inflammatory markers in SZ and NCs. These findings suggest a role for sleep interventions in reducing inflammation and psychopathology in SZ.

Understanding Emergent Life Events (ELEs) in Evidence-Based Practice Delivery
within Children's Mental Health Services

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Background: System-driven implementation of multiple evidence-based practices (EBPs) is an increasingly common policy (Lau & Brookman-Frazee, 2016). There are concerns, however, that EBPs delivered in community mental health settings do not produce the same results as those in research settings (Rotheram-Borus, Swendeman, & Chorpita, 2012). Community providers have raised the concern of the frequent intrusion of client life stressors during the course of treatment and delivery of EBPs (Southam-Gerow, Hourigan, & Allin, 2008). These stressors, or “emergent life events” (ELEs), consist of significant, unexpected life incidents (e.g., expulsion from school, job loss, illness) that negatively impact the child or family (Chorpita, Korathu-Larson, Knowles, & Guan, 2014). While these events can impact therapist’s ability to deliver an EBP with fidelity, the prevalence and correlates of ELEs are not well understood. The purpose of this study was to characterize the occurrence of ELEs in the context of multiple EBP delivery in children’s mental health services in Los Angeles County.

Methods: This study included data from 679 therapy sessions with 272 clients treated by 103 therapists within the context of multiple EBP implementation in agencies contracted for services from the Los Angeles Department of Mental Health. Sessions for five different EBPs were audio-recorded and coded for the number of ELEs that occurred in each session.

Results: At least one ELE was observed to be reported by clients in 20.9% of sessions and for almost half of the clients (41.5%) in at least one session. Multi-level negative binomial regression analyses examined potential predictors of the number of ELEs reported in each session. Results showed that shorter session length was associated with fewer ELEs ($\beta = -1.18$, $p = 0.04$), older client age was associated with more ELEs ($\beta = 0.09$, $p = 0.01$), and sessions of both Child-Parent Psychotherapy (CPP) and MAP-Trauma had significantly more ELEs compared with sessions of Trauma-Focused Cognitive Behavioral Therapy (TF-CBT; $\beta = 0.84$, $p = 0.03$; $\beta = 1.39$, $p = 0.01$).

Conclusions: These results suggest that a significant proportion of children and families receiving EBPs in community mental health settings report ELEs. In addition, session- and child-level predictors are associated with the number of ELEs reported. These findings highlight the importance of considering ELEs in the development and implementation of EBPs for use in community settings.

Anxiety Predicts Survival in People Living with HIV Followed for up to 10 Years

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Background: While anxiety has been established as prevalent among people living with HIV (PLWH), limited research has been conducted to examine its impact on survival. In this study, we examined the relationship between anxiety and long-term survival for up to 10 years. We also explored the role of different mediators in this relationship.

Methods: Anxiety (STAI), Adherence (ACTG), depression (BDI), substance use (brief COPE and alcohol consumption frequency) were obtained via self-reports. In addition, blood draws (VL, CD4), and a urine sample (cortisol) were collected. Data were collected every 6 months for a period of 2 years among a diverse sample of people living with HIV. Survival status was obtained by consulting the Death Master File from the Social Security Administration. Survival analyses and hierarchical regression analyses were used in this study.

Results: Consistent with our hypothesis, baseline anxiety predicted longer survival in PLWH for up to 10 years. However, average anxiety measured from T1 to T4 did not predict survival. Depression, adherence, substance use, and cortisol were not found to mediate the relationship between anxiety and survival.

Conclusions: To our knowledge, this is the first study to highlight that higher anxiety predicts poorer survival in PLWH over an extended period of time. Screening for anxiety should be part of routine care in HIV. Future studies should examine whether interventions targeting anxiety (e.g., CBT) may positively impact long-term HIV outcomes, including survival. Additional research is needed to examine mediators of the relationship between anxiety and survival in PLWH.

Popularity among Peer Role Models: A Moderator of Peer
Victimization and Depressive Symptoms

Tana Luo

Background: Recent research on peer victimization and depressive symptoms during adolescence has turned to interactive models of risk that incorporate factors that exacerbate or mitigate negative outcomes associated with victimization. This short-term, longitudinal study builds on the available findings by focusing on the popularity of adolescents' peer role models as a moderator that may intensify links between peer victimization and depressive symptoms.

Methods: This study was conducted with 469 adolescents (255 boys, 214 girls, *M* age = 12.7 years), who were followed over a one-year period. These youths completed a self-report questionnaire of depressive symptoms, as well as a peer nomination inventory identifying victimized and popular peers. The inventory also asked adolescents to identify peers they want to be like, respect, and/or admire. We calculated mean popularity levels among peers identified as role models.

Results: To address our study aims, we conducted a series of hierarchical regression analyses. Results from these analyses revealed that, for boys, high popularity levels among peer role models were associated with intensified associations between peer victimization and depressive symptoms.

Conclusions: Our results provide evidence that that being victimized by peers is especially detrimental to adolescent boys who aspire to be like their peers who are characterized by high levels of popularity. For these boys, peer victimization may uniquely signal a failure to attain desired school experiences, which may in turn increase risk for depressive symptoms and other negative emotional outcomes.

Development of an Olfactory 5-Choice Task for Mice: Interactions of MK-801 and Nicotine

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Background: Cognitive deficits are a hallmark feature of numerous psychiatric disorders and contribute to global functional outcome. Cross-species tasks are required to determine neurobiological substrates and evaluate putative therapeutics. Currently, rodent cognitive tasks often require extensive training limiting testing during adolescents, a critical period of development. We developed an odor-based 5-choice task for mice requiring only 10 training sessions.

Methods: Male C57BL/6 mice (n=13) were trained to stability. Subjects provide lick responses to target odors (5/6) yielding sucrose delivery, while non-target odor responses (1/6) were punished with time-out. At stability, the effects of an NMDA antagonist (MK-801; 0.17mg/kg) and nicotine (0.03 & 0.30mg/kg) were assessed in a fully-crossed, within-subjects design.

Results: Significant nicotine/MK-801 interactions were observed on hit-rate [$F_{(2,22)}=4.2$, $p<0.05$], early trial termination, [$F_{(2,22)}=5.0$, $p<0.05$], and lick-rate [$F_{(2,22)}=6.8$, $p<0.005$]. When co-administered with saline, nicotine significantly reduced hit-rate and lick-rate, and increased early trial termination ($ps<0.05$), while these effects disappeared when co-administered with MK-801. Neither drug solely impacted attention as measured by hit-rate, false alarm-rate, or D' (all $ps>0.05$).

Conclusion: The present study demonstrates the feasibility of the odor-based task which can be rapidly trained, enabling high-throughput drug screening and testing in adolescents. Nicotine impaired performance on multiple measures which was prevented by co-administration of MK-801. These results suggest a mechanism which may relate to the high smoking rates observed in psychiatric conditions associated with NMDA hypofunction.

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Compensatory Cognitive Training for Psychosis: Effects on negative symptom subdomains

Zanjbeel Mahmood, Jillian M. R. Clark, Elizabeth W. Twamley

Background: A growing body of literature suggests a two-factor structure of negative symptom subdomains in schizophrenia [i.e., expressive deficits (ED) and social amotivation (SA)], with each domain demonstrating differential relationships with functional and psychosocial outcomes. Although compensatory cognitive training (CCT) has exhibited efficacy in improving overall negative symptoms in patients with psychosis, research identifying the effect of CCT on ED and SA negative symptoms in individuals with psychosis is limited.

Methods: This study examined the differences in post-treatment ED and SA subdomains, as measured by the Positive and Negative Syndrome Scale, between forty-three outpatients with DSM-IV primary psychotic disorders randomized to receive either standard pharmacotherapy (SP; $n = 24$) or standard pharmacotherapy + CCT (CCT; $n = 19$) for 12 weeks.

Results: ANCOVA analyses demonstrated a significant difference at posttreatment between the CT and SP groups on the ED ($p = .028$) and SA ($p < .001$) negative symptom factors, such that the CCT group exhibited significantly lower post-treatment scores on ED and SA subdomains, as compared to the SP group, when adjusting for baseline scores.

Conclusion: CCT appears to be a beneficial treatment approach for improving multiple aspects of negative symptoms.

Chronic Pain and PTSD: A Pilot Study of Cognitive-Based Compassion Training (CBCT®)

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Compassion meditation (CM), a meditative practice that focuses on the wish to remove suffering, has been associated with increases in positive emotion (Engstrom & Söderfeldt, 2010) and social connectedness (Mascaro et al., 2013) in non-clinical samples. In clinical samples, CM is also associated with decreased negative affect (Khusid, 2015). Several pilot studies provided preliminary evidence that CM is associated with reductions in pain severity in civilians with persistent musculoskeletal pain (PMP; Chapin et al., 2014; Parry & Malpus, 2017). However, CM has never been evaluated in relation to PTSD.

We conducted a pilot study of CM for veterans with PTSD ($N=28$). Veterans were randomized to CM training or Veteran.calm (VC), an enhanced relaxation intervention; both consisted of ten weekly sessions. Participants completed pre- and post-treatment evaluation of PTSD (CAPS-5), pain severity and interference (PROMIS), and weekly measures of PTSD (PCL-5) and depression (PHQ-9).

In a series of mixed model analyses, participants in the CM group experienced a significantly greater reduction of both PTSD symptoms (PCL-5: $F(1, 21.08)=5.23, p=.03$; CAPS-5: $F(1, 53.33)=9.56, p=.003$, Cohen's $d=1.20$) and depressive symptoms (PHQ-9: $F(1, 22.58)=4.41, p=.05$) than those in the VC group. There were no significant changes in pain severity or pain interference in either group.

This study and our prior work demonstrate the feasibility of CM for veterans with PTSD. CM participants experienced significant reductions in PTSD and depressive symptoms, and CM was superior to relaxation. Future directions include more systematic research on the use of CM for veterans with co-occurring PMP and PTSD.

Predicting Service Utilization in Families of Children with Autism Spectrum Disorder
in Community Mental Health Settings across Time

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Background: Children with Autism Spectrum Disorder (ASD) have complex needs that may necessitate multiple service involvement, including mental health (MH) and developmental disability-focused services. Little is known about service utilization for children with ASD receiving MH services. Using Anderson's Behavioral Model of Health Service Use (Andersen, 1995), we examined determinants (i.e. predisposing, enabling, and need factors) of service use over 18 months for children in an effectiveness trial of a MH intervention (*An Individualized Mental Health Intervention for ASD; AIM HI*) delivered within publically-funded MH services.

Methods: 202 children (ages 4-14 years) with ASD participated in the trial. Child IQ and autism severity were assessed at baseline. Caregiver ratings of child behavior problems and family service use were collected at baseline, 6, 12 and 18 months. Primary outcome was the number of developmental services (e.g., ASD specialty interventions, occupational therapy) utilized. Multiple regression models were conducted, one for each time point. Potential predictors of service use included in each model were: intervention condition, predisposing (child age, caregiver preferred language); enabling (household income); and needs factors (ASD severity, IQ, behavior problems).

Results: Across time, service use was higher for families with a higher income and for younger children. At baseline and 18 months, youth with lower IQ used more services. The intervention groups differed only at 18 months, when service use was higher for youth in the usual care condition than for youth who received *AIM HI*.

Conclusions: These findings indicate that predisposing (age), enabling (household income), and need (lower IQ) factors emerged as independent predictors of developmental service use. These preliminary findings indicate that the *AIM HI* intervention may impact long-term service use. Future research will examine intensity and types of services over time.

The Impact of Attentional Control on Emotional Regulation in Anxiety-Disordered Youth

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Background: Research has linked anxiety and difficulties in early attentional processes (e.g. Roy et al., 2008). Research also suggests that there is a strong relationship between impairments in emotion regulation and the development of anxiety (e.g. Southam-Gerow & Kendall, 2000). Importantly, difficulties in early attentional processes, such as attentional control, having been implicated as important factors in the modulation of the emotional response (e.g. Oschsner & Gross, 2005). The current study will explore the role of attentional control on the relationship between emotion regulation and anxiety severity. We predict that poor attentional control will be significantly related to the presence of poor emotion regulation strategies, and that attentional control will moderate the relationship between emotion regulation and child anxiety.

Methods: Participants will be 92 treatment-seeking youth meeting criteria for an anxiety disorder. The Attention Network Task (ANT) will be used to index attentional control. The ANT indexes three major attentional networks: altering, orienting, and executive control (e.g. Posner, Rueda, & Kanaske 2007), each representing a different aspect of attention. The Emotion Regulation Questionnaire will be used to assess difficulties in emotion regulation. Anxiety severity will be assessed via a multimodal assessment including parent and child report.

Results: Poorer attentional control was correlated to parent-report of anxiety. Further, executive control was found to moderate the relationship between child anxiety and emotion regulation.

Discussion: These results suggest another pathway through which attentional control processes impact the development and maintenance of anxiety. Interventions aimed at improving attentional control may warrant further research.

Repetitive Mild Traumatic Brain Injury in Military Veterans is Associated with Increased Neuropsychological Intra-Individual Variability

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Background: We examined measures of intraindividual variability (IIV) in military Veterans with and without a history of mild TBI. Secondly, we examined how measures of IIV relate to traditional indices of mean cognitive performance, TBI characteristics, and neuropsychiatric symptoms in mild TBI.

Methods: Participants included 122 Veterans (69 mild TBI, 53 military controls [MCs]) who completed a comprehensive neuropsychological test battery. Two IIV indices were calculated using 13 norm-referenced variables: an average standard deviation (ASD) score and a maximum discrepancy (MD) score.

Results: Compared to MCs, Veterans with a history of mild TBI demonstrated greater IIV as indicated by ASD and MD scores ($p=.008-.016$), even after adjusting for mean-level cognitive performance. Among the mild TBI participants, the two IIV indices were positively correlated with each other ($p<.001$) and negatively correlated with mean cognitive performance ($p=.009-.012$). In contrast, ASD and MD scores were *not* associated with a measure of premorbid intellectual functioning or neuropsychiatric symptoms (all $p<.05$). Higher ASD scores were positively related to lifetime number of TBIs, such that greater cognitive variability was observed in Veterans with a history of multiple TBIs (i.e., ≥ 3 TBIs; $p=.026$). A trend in the same direction was found for the MD score ($p=.079$).

Conclusions: Our results demonstrate that Veterans with mild TBI show greater IIV relative to MCs, and that repetitive TBI is associated with increased cognitive performance variability. Findings indicate that, in the context of mild TBI, measures of dispersion may be more sensitive indicators of cognitive dysfunction when compared to traditional mean neuropsychological scores.

Neuroimaging Features Predictive of High and Low Performing
Adolescent Drinkers versus Nondrinkers

Meruelo AD, Castro N, and Tapert SF

Background: Academic performance has important bearings on the opportunity to attend college, graduate school, and professional school.

Methods: We analyzed morphometry metrics of surface area, cortical thickness, and subcortical volume from high-resolution magnetic resonance images collected during early adolescence (age 12-14 years) in relation to high school academic performance (GPA at 11th and 12th grade) and alcohol use. Subjects were divided into high (GPA ≥ 3.54 ; n=87) and low (GPA < 3.54 ; n=83). Drinkers and non-drinkers were divided according to the Customary Drinking and Drug Use Record. We used a machine learning approach to differentiate low GPA alcohol users from low GPA nondrinkers, and high GPA alcohol users from high GPA nondrinkers, using neuroimaging features. Group differences between parameters of predictive regions for drinking v. non-drinking low academic performers were identified by performing independent t-test comparisons.

Results: The machine learning approach differentiated low GPA alcohol users from nondrinkers based on 22 predictive regions. Independent t-tests compared the identified regions and found all to be lesser in thickness, surface area, or volume in drinkers than nondrinkers, except in the left transverse temporal gyrus, which was thicker in drinkers. The machine learning approach also differentiated high GPA alcohol users from high GPA nondrinkers based on two predictive regions. Independent t-tests found both left middle temporal thickness and left lingual surface area to be greater in drinkers than nondrinkers.

Conclusions: Features distinguishing low-performing drinkers from nondrinkers, in addition to high-performing drinkers from nondrinkers, shed some light on differences in baseline brain maturation and development.

The Impact of Psychological Distress on Pain Volatility in Adults
with Chronic Pain and Prescription Opioid Addiction

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Background: Prescription opioid misuse and abuse are major public health concerns. Adults with chronic pain have heightened risk for prescription opioid addiction and relapse. Findings linking pain volatility to relapse elucidate these poor treatment outcomes. Psychological distress has also predicted poor outcomes. The current study examined if baseline measures of trauma exposure and depression would predict pain volatility in chronic pain patients receiving treatment for prescription opioid addiction.

Methods: Secondary data analysis was conducted on 149 adults with chronic pain from an outpatient, multi-site clinical trial of medication and counseling for 12 weeks. Pain volatility was derived from multilevel models of weekly pain scores. Predictors were baseline measures of depression severity and lifetime variety of trauma exposure. Relations between these predictors and pain volatility were examined with Pearson correlations and regression models.

Results: Correlations with pain volatility were significant for depression severity ($r = .31; p < .001$) and trauma exposure ($r = .19; p = .01$). In a multiple regression model both depression severity ($\beta = .28, t(142) = 3.92, p < .001$) and trauma exposure ($\beta = .19, t(142) = 2.53, p < .001$) significantly predicted pain volatility ($R^2 = 12.17\%$).

Conclusion: Baseline psychological distress predicted pain volatility during 12 weeks of medication and counseling for prescription opioid addiction. Because pain volatility has predicted treatment failure, chronic pain patients with more severe depression and/or trauma exposure are at risk for poor treatment outcomes. Future work should examine if treatment of baseline distress can impact rates of relapse to optimize intervention efficacy.

In Bipolar Patients that Respond to Lithium, Targeted Sequencing of Candidate Genes Reveals Associated Variant in the Promoter of TENM4, NTRK2, and GABRA4

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Background: We previously identified a candidate group of genes by sequencing large families with bipolar disorder. This included calcium channels, CAM kinases, and GABA receptors. We also studied the neurotrophin signaling pathways for BDNF and NGF, which have repeatedly been associated with bipolar disorder and lithium response. In regard to BDNF, lithium induces its release which is essential for its function. We have also previously shown that genetic variants in the TrkB gene are associated with lithium response and bipolar disorder. The goal of this study was to identify novel and common sequence variants in these genes that affect the action of lithium in bipolar disorder.

Methods: Retrospective samples were collected in regard to lithium responsiveness. 73 good responders, (LiR), 49 moderate responders (Mod), and 47 poor responders (NR) individuals were used for a sequencing study of these two genes. We targeted exons, non-coding regions with putative regulatory functions, 5' and 3' untranslated regions, and numerous DNase hypersensitive regions. Samples were combined into pools of 23 to 37 individuals. Paired-end sequencing was done using Custom Amplicons (Illumina). Variants were called with CRISP. Then, PLINK was used to calculate a chi-square statistic between individual groups. Annotation of identified variants was done using SIFT and PolyPhen-2.

Results: Overall, 2692 single nucleotide variants were called. No single gene had an overwhelming burden of variants in lithium responders versus non-responders. The top hits included an intronic variant in TENM4, with a FDR-adjusted p-value of 3.8×10^{-7} . There was also a variant in the promoter of NTRK2 with an FDR-adjusted p-value of 1.1×10^{-3} . RegulomeDB predicts this variant is important for transcription factor binding. And finally a variant was found in the 3' UTR of GABRA4 at an FDR-adjusted p-value of 0.037.

Conclusion: Targeted sequencing revealed the association of a number of with lithium responsiveness. Lithium efficacy for the treatment of bipolar disorder is likely to involve these pathways. This study provides likely candidate regions to further investigate the function of lithium in bipolar individuals.

History of Cannabis Use Disorder is Associated with Greater Impairment in Neurophysiological, Clinical and Functional Measures in Schizophrenia Patients

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Background: Cannabis use disorders (CUD) are common in schizophrenia patients. However, the impact of a history of CUD on neurophysiologic, clinical, and psychosocial domains is not well understood. Therefore, we sought to clarify the relationship between a history of CUD and measures of early auditory information processing (EAIP) as well as measures of clinical symptoms and psychosocial functioning in schizophrenia.

Methods: Schizophrenia patients (N=901) were assessed on neurophysiologic measures of EAIP, clinical symptoms, and psychosocial functioning via their participation in the Consortium on the Genetics of Schizophrenia (COGS-2) study. After excluding patients with histories of other substance use disorders, the remaining sample was stratified based on a history of a CUD (n=74), and a comparison group of schizophrenia patients without a history of substance abuse (n=265).

Results: Patients with a history of CUD showed greater impairment in measures of EAIP ($F=6.3$, $p<0.015$), greater severity of both positive and negative ($F_s>11.0$, $p_s<0.001$), and worse daily psychosocial functioning ($F=10.5$, $p=0.001$).

Conclusions: Among COGS subjects diagnosed with schizophrenia, a history of CUD was associated with greater deficits in MMN and P3a amplitude, greater clinical severity and worse functional outcome. These findings suggest that biological factors leading to cannabis abuse, or other factors associated with that abuse (i.e. modulation of the endocannabinoid systems), may have persistent effects on neurophysiological measures of EAIP and on clinical domains. Future prospective studies are needed to elucidate how cannabis use contributes to the variance in measures of neurophysiologic performance and impacts clinical and functional outcome in schizophrenia.

Plasma D-dimer Relates to Physical Health and Motor Skills Across the Age Span in HIV

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Objective: Inflammatory processes have been suggested to underlie early neurologic abnormalities among persons living with HIV (HIV-positive), such as deficits in complex motor function, that are purported to remit with effective antiretroviral treatment (ART). We hypothesized HIV will have negative direct and indirect effects via inflammation on complex motor performance.

Method: The sample consisted of 90 ART-treated virally suppressed HIV-positive and 94 HIV-negative adults, ages 36 to 65 years, with balanced recruiting in each age decade (36-45, 46-66, 56-65). Biomarkers of inflammation (d-dimer, IL-6, MCP-1/CCL2, sCD14, and TNF- α) were measured, and a composite inflammation burden score was calculated. Complex motor performance was evaluated using the Grooved Pegboard Test.

Results: The HIV-positive group had worse complex motor performance ($p = 0.001$; hedge's $g = -0.49$) and a higher average inflammation burden composite score ($p < 0.001$; hedge's $g = 0.78$) than the HIV-negative group. Path analyses indicated that the indirect effect of HIV disease on complex motor performance through inflammation burden was statistically significant, accounting for 15.1% of the effect of HIV on complex motor performance.

Conclusions: Inflammatory processes may contribute to worse complex motor skills throughout the course of HIV disease. Although neurologic findings (e.g., deficits in motor speed/dexterity) commonly associated with HIV infection have been suggested to largely remit with ART, our analysis indicates that inflammation plays an important role in complex motor skills among HIV-positive adults. Further research is needed to understand the clinical relevance of managing inflammation in comprehensive HIV care.

Transcriptional Consequences of 16p11.2 CNV in Patient-derived iPSCs

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Background: The 16p11.2 copy number variant (CNV) is associated with several neurodevelopmental disorders including autism and schizophrenia. There is a documented dosage effect of this CNV on the head size phenotype, with macrocephaly observed in the deletion carriers, and microcephaly observed with the duplication carriers. However, pathways disrupted by this CNV are still largely elusive.

Methods: Fibroblasts were collected from 16p11.2 deletion (DEL) and duplication (DUP) patients and iPSCs were then derived. RNA-seq was performed on these iPSCs. To process the RNA-seq data, we adopted the long-rna-seq-pipeline used by the ENCODE Consortium and extensive quality control steps were taken. Differential gene expression and gene co-expression network were used to analyze the data. We identified genes and pathways that are altered by the 16p11.2 CNV.

Results: Most of the genes within the 16p11.2 were upregulated in DUP while downregulated in DEL, confirming a strong cis-effect. In addition, genes outside of 16p11.2 were also found to be differentially expressed, such as IQSEC3, VIM and ACTA1.

We discovered three co-expressed gene modules that are strongly associated with 16p11.2 copy number status. One module that was upregulated in DUP while downregulated in DEL contains most genes within the 16p11.2. A group of genes involved in cell adhesion and migration were strongly upregulated in DUP. On the other hand, a collection of histone subunits gene as well as other genes functioned in chromatin assembly was found to be upregulate in DEL.

Conclusions: Our iPSC model faithfully capture the biology of 16p11.2 patients. DUP iPSC shows increased cell adhesion and migration while DEL iPSC shows increased histones. This suggests an imbalance between cell differentiation and cell proliferation caused by the 16p11.2 CNV. Our next goal is to generate neurons and brain cerebral organoids from the 16p11.2 patient.

Poor Social Cognition Negatively Influences Methamphetamine Addiction Characteristics

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Background: Social cognition deficits in methamphetamine (MA)-users may contribute to poor addiction treatment outcomes by facilitating erosion of social reward in favor of drug reward, which is relevant for HIV transmission risk. This study examined social cognition in relation to MA addiction characteristics.

Methods: Forty-four individuals with lifetime MA-dependence (HIV+ $n=26$) completed outcome measures characterizing MA addiction: outcome expectancies (OE; expectations about experience of MA use) and abstinence self-efficacy (ASE). Independent variables measuring social cognition included alexithymia, emotion dysregulation, and mentalizing.

Results: Controlling for current affective distress, HIV infection, and MA use recency, regression analyses revealed significant interactions of HIV by alexithymia and emotion dysregulation in relation to OE, and an HIV by mentalizing interaction in relation to the ASE ($ps<.05$). Higher alexithymia and emotion dysregulation were associated with more positive (i.e., riskier) OE scores in the HIV- MA-users, whereas poorer mentalizing scores related to lower ASE in the HIV+ MA-users ($ps<.05$).

Conclusions: Social cognition deficits appear to influence MA addiction characteristics differentially by HIV status. Poor understanding and regulation of internal emotional experiences may drive riskier beliefs about benefits of MA use in HIV- MA-users, while poor ability to take others' perspectives may lower HIV+ MA-users' confidence in their ability to sustain abstinence.

What Drives the Association between Weigh-Conscious Peer Groups and Disordered Eating?
Disentangling Genetic and Environmental Selection from Pure Socialization Effects

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Objective: Previous studies suggest strong associations between exposure to weight-conscious peer groups and increased levels of disordered eating. This association has been attributed to socialization effects (i.e., membership leads to disordered eating); however, selection effects (i.e., selecting into peer groups based on genetic and/or environmental predispositions toward disordered eating) could contribute to or even account for these associations. The current study was the first to use a co-twin control design to disentangle these types of selection factors from socialization effects.

Methods: Participants included 610 female twins (ages 8–14) drawn from the Michigan State University Twin Registry. To comprehensively examine a range of eating pathology, several disordered eating attitudes and behaviors (e.g., body dissatisfaction, binge eating) were examined via self-report questionnaires. Questionnaires also were used to assess peer group emphasis on body weight and shape.

Results: Replicating previous results, significant individual-level associations were found between membership in weight-conscious peer groups and disordered eating. However, co-twin control analyses indicated that these associations were largely due to genetic and/or shared environmental selection factors rather than pure socialization effects. Importantly, results remained unchanged when controlling for pubertal status, suggesting that effects do not vary across developmental stage.

Discussion: Overall, these findings question whether associations between weight-conscious peer groups and disordered eating are due entirely to socialization processes. Future studies are needed to identify the specific genetic and/or shared environmental factors that may drive selection into weight-conscious peer groups.

Broadly Reduced Intrinsic Functional Connectivity in Girls Compared to Boys with Autism Spectrum Disorders

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Background: The high male:female prevalence ratio of autism spectrum disorders (ASDs) has been recognized dating back to Leo Kanner's initial description in 1943. The majority of studies in autism reflect this strong male bias. Research with adequate female samples is necessary to inform our understanding of gender-related neurobiological differences in ASDs.

Methods: Resting-state functional MRI data for 142 children and adolescents (ages 7-18 years) were selected from the Autism Brain Imaging Database Exchange and an in-house sample ($n = 31$). Functional connectivity (FC) was estimated by generating ROI-ROI correlation matrices. ROIs were categorized into three domains: sensorimotor, default mode, and executive. Chi-square tests of independence were used to test for differences in the proportion of significant within- and between-domain ROI-ROI correlations ($r_s > |0.4|$).

Results: Within the TD group, boys (TD-B) showed significantly more positive correlations within the sensorimotor domain than girls (TD-G) ($X^2 = 14.7, p < 0.001$). TD-B and TD-G did not differ in their within- or between-domain connectivity for any other domains. In contrast, girls with ASDs (ASD-G) showed broad underconnectivity compared to boys with ASDs (ASD-B). Specifically, ASD-G showed fewer positive correlations between the sensory networks and executive and default mode networks ($X^2 = 5.11, p = 0.02$); within the DMN ($X^2 = 5.00, p = 0.03$); between the DMN and other domains ($X^2 = 15.78, p = < 0.0001$); within the executive domain ($X^2 = 6.12, p = 0.01$); and between executive and other domains ($X^2 = 10.85, p < 0.0001$).

Conclusions: We found a pattern of pervasive underconnectivity in girls compared to boys with ASDs, whereas in the TD group, gender differences in connectivity were seen only within the sensory domain.

The Role of Food Cravings in Excess Gestational Weight Gain

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Background: Half of pregnancies in the U.S. result in excess gestational weight gain (GWG), which is linked to complications in gestation and delivery, maternal postpartum weight retention, and overweight/obesity in the offspring. Food cravings are implicated in various eating and weight-related pathologies and commonly reported during the perinatal. These findings suggest that cravings play a role in excess GWG. The current study aimed to identify the role of craving in GWG. We hypothesized that women who gain excess weight would endorse more frequent cravings.

Methods: Pregnant women (N=68) were recruited from an OBGYN department (n=23) and from online forums (n=45). The Food Craving Inventory (FCI) assessed “frequency” of cravings, along with the likelihood of “giving in” to these cravings.

Results: At the time of survey completion, 23.8% had gained more than the recommended amount. The most commonly endorsed cravings were for “sweets” and “fast foods.” Ratings of “frequency” of cravings for “high fat” and “fast foods” were positively correlated with excess GWG, but only cravings for “high fat foods” had a significant partial effect in the linear regression model ($p=.002$). Craving “frequency” and “giving in” accounted for a substantial portion of the variance in excess GWG (25% and 19%, respectively).

Conclusion: Findings suggest that the frequency and consumption of craved foods impact risk of excess GWG. Identifying craving as a risk factor provides support for the development of interventions targeting cravings. Findings serve as a starting point for studies of mediating factors in the relationship between cravings and GWG.

Depressive Symptoms Are Associated with Cognitive Decline in HIV/AIDS

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Objective: Depression is common among persons living with HIV/AIDS (PLWHA). The relationship between depression and cognition, however, is unclear. The current study explores associations between depressive symptoms (DS) and global cognitive functioning (GCF) over time.

Methods: Participants included 508 PLWHA enrolled in longitudinal studies at the HIV Neurobehavioral Research Program from 2002-2016. On average, participants had 4.8 visits (range=2-18) over 4.0 years (range=0.5-12.4). DS were assessed via the Beck Depression Inventory (BDI-II) and categorized by cutoffs: minimal (0-13), mild (14-19), and moderate-to-severe (20-63). GCF was examined using a practice effect-corrected scaled score ($M=10$, $SD=3$) comprised of all tests in a cognitive battery. Multilevel modeling was used to examine within- and between-person associations between DS and GCF over time (i.e., years). Covariates included baseline sex and education, and time-varying age, current CD4 count <200 , and nadir CD4 count <200 .

Results: Within individuals: On visits when participants reported mild or moderate-to-severe DS, they exhibited worse GCF ($b=-0.131$, $p=0.024$ and $b=-0.143$, $p=0.032$, respectively) compared to visits with minimal DS. Between individuals: When averaging each participant's BDI-II scores across visits, higher mean DS severity was associated with greater declines in GCF from baseline to last visit. Specifically, those whose mean BDI-II score fell within the moderate-to-severe range exhibited a faster decline compared to those with minimal DS ($b=-0.074$, $p=0.009$).

Conclusions: Among PLWHA, DS are related to worse GCF per visit and faster declines in GCF over time. Future research is needed to determine directionality of effects and explore domain-specific cognitive deficits related to DS.

Metabolic Risk Factors as Differential Predictors of Profiles of Cognitive Impairment
among Older HIV+ and HIV- Aging Adults

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Background: Neurocognitive (NC) functioning among older individuals and among those living with HIV (PLWH) exhibits significant heterogeneity, suggesting subpopulations with differing risk for NC impairment (NCI). Metabolic factors are associated with NC decline; however, their relationship to profiles of NCI and differential effects by HIV serostatus are unknown.

Methods: Participants (144 HIV+, 102 HIV-) aged 50-79 years ($M=57.96$, $SD=6.10$) completed a neuropsychological battery assessing seven domains (verbal, executive functioning, speed of processing, learning, recall, working memory, and motor). Latent class analysis (LCA) was used to identify subgroups with differing NCI profiles and validity was examined against the Montreal Cognitive Assessment (MoCA). Additionally, multinomial regression was used to identify metabolic factors associated with classification.

Results: LCA identified three subgroups: Class1: Multidomain NCI, Class2: NC impaired in learning and recall, and Class3: NC normal. Relative to those in Class3_{NC Normal}, individuals in Class1_{Multidomain NCI} and Class2_{Learning & Recall NCI} had lower MoCA scores (Class1_{Multidomain NCI}: $\chi^2(1)=18.63$, $p<0.001$ and Class2_{Learning & Recall NCI}: $\chi^2(1)=25.27$, $p<0.001$). PLWH were more likely to be classified as Class1_{Multidomain NCI} ($OR=4.11$, $p=.005$), relative to classification in Class3_{NC Normal}. Furthermore, PLWH with hyperlipidemia ($OR=3.68$, $p=.029$), central obesity ($OR=2.80$, $p=.035$), hypertension ($OR=3.79$, $p=.019$), and a greater number of metabolic risk factors ($OR=1.69$, $p=.022$) had greater odds of classification in Class1_{Multidomain NCI}.

Conclusion: Metabolic risk factors confer heightened risk of multidomain NCI in the context of HIV. Early intervention upon metabolic risk may have implications for improving the neurocognitive outcomes of PLWH.

Social Stress Induces Neurotransmitter Plasticity in the Dorsal Raphe Nucleus

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Background: Anhedonia, or lack of pleasure, is a core symptom of major depressive disorder and is common in other mood disorders. Stress is known to induce anhedonia in some individuals (susceptible), but not others (resilient)¹. We hypothesized that neurotransmitter plasticity, an alteration of neurotransmitter expression in response to activity leading to changes in behavior², plays a role in susceptibility to stress.

Methods: We used the intracranial self-stimulation (ICSS) procedure to measure anhedonia in rats. Rats were trained to respond to stimulation of the brain's reward circuitry. The minimum current needed to elicit a response was defined as the reward threshold. Rats underwent 21 days of social defeat stress and their reward thresholds were measured daily. Their brains were subsequently processed for immunohistochemical detection of neurotransmitter markers.

Results: Social defeat elevated reward thresholds, indicating anhedonia. There was an increased number of serotonergic neurons (TPH2+) in the ventral region of the dorsal raphe nucleus (DRN) in stressed animals compared to controls. This was accompanied by an increase in nitric oxide synthase (nNOS+) expression within the serotonergic population. The total number of neurons was unchanged, indicating that preexisting neurons acquired TPH2 and nNOS expression.

Conclusions: Our results suggest that neurotransmitter plasticity occurs in the DRN in response to chronic social stress. Current experiments aim to reveal anatomical and functional mechanisms that explain behavioral susceptibility to stress. We are measuring neuronal activity in the DRN across experimental groups and manipulating DRN inputs to understand how circuit activity drives transmitter plasticity and behavior.

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Circuit-specific DNA Modifications Change as Photoperiod-induced
Neurotransmitter Plasticity Declines with Aging

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Background: Chronic exposure to short-day (5L:19D) or long-day (19L:5D) photoperiods alters the number of dopamine(DA)- and somatostatin(SST)- expressing neurons in the paraventricular nucleus (PaVN) of the hypothalamus via neurotransmitter switching. Previous research has identified reserve pool neurons able to switch identity, a transcriptional regulation and their behavioral effects. We extend previous findings by examining the stages of aging and the epigenetic patterns of histone acetylation and DNA methylation through which changes in environmental light regulate neurotransmitter respecification.

Methods: Rats from 1-18 months of age were exposed for 1 week to either a long day(19L:5D), normal day(12L:12D) or short day(5L:19D). Brains were processed for immunohistochemical analysis of epigenetic markers for de novo methylation and 3rd histone acetylation in DA & SST- expressing PaVN neurons.

Results: PaVN DA/SST plasticity occurs early in life and is maintained throughout adulthood. Dopaminergic plasticity is reduced at 12 months and abolished in both cell types by 18. Methylation increased following (5L:19D) in both cell types in younger animals while an overall increase in methylated SST neurons paralleled neuroplasticity reduction at 12-18 months. Histone acetylation at 3 months was increased in DA neurons and decreased in SST neurons following (5L:19D).

Conclusion: The linkage between age-dependent reduction in neurotransmitter plasticity, as well as associated changes in DNA methylation & acetylation patterns within cells known to switch identity, provides new insights regarding the stages of neuroplasticity in the aging brain. This work is important for understanding approaches for efficacious, non-invasive treatment in disorders characterized by neurotransmitter dysfunction and neurodegeneration.

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Amyloid β and HIV Relevant Stimuli Promote a Pro-inflammatory Phenotype in
Brain Macrophages that May Be Reversed by Cannabinoids

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Background: Chronic neuroinflammation contributes to the pathogenesis of neurodegenerative diseases including HIV-associated neurocognitive disorders (HAND) and Alzheimer's Disease (AD). The balance of microglial/perivascular macrophage phenotypes dictates much of the inflammatory milieu in the central nervous system (CNS) in these diseases. Generally, two phenotypes have been described: M1, the pro-inflammatory phenotype; and M2, the phagocytic/anti-inflammatory phenotype. Increased amyloid-(A) β and neuroinflammation is associated with a higher prevalence of M1 phenotype and neurodegeneration, however, it is unknown how HIV and HIV proteins affect microglial differentiation. Here, we hypothesized that HIV-relevant stimuli and A β promote proinflammatory phenotype in brain macrophages.

Methods: We investigated the macrophage phenotype after exposure to Alzheimer's Disease (AD)- and HIV-relevant stimuli and HIV-infection. We also tested the anti-inflammatory potential of a cannabinoid receptor agonist, WIN55,212-2 (WIN). To model microglia/perivascular macrophages, peripheral blood mononuclear cells (PBMC) were differentiated into monocyte derived macrophages (MDMs) and then either treated with A β , IL-1 β , and/or infected with HIV-1.

Results: AD- and HIV-relevant stimuli reduced expression of triggering receptor expressed on myeloid cells (TREM2), increased expression of the histocompatibility complex HLA-DRA mRNA, and increased HIV replication. Interestingly, pretreatment of MDMs with WIN reversed these effects. WIN also altered the morphology of MDMs, promoting more sickle-shaped cells, indicative of M2 phenotype.

Conclusions: These results suggest that AD- and HIV-relevant stimuli induces a proinflammatory microglial phenotype in the brain. However, this may be blocked with cannabinoid receptor agonists. These findings identify a novel mechanism of HIV-induced neuroinflammation and a novel role for cannabinoid receptor agonists.

Low Frequency Brain Activity is a Neuromodulatory Target that Tracks Recovery after Stroke

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Background: Recent work has highlighted the importance of transient low-frequency oscillatory (LFO, < 4 Hz) activity in the healthy motor cortex (M1) during skilled upper-limb tasks. These brief bouts of oscillatory activity may establish the timing or sequencing of motor actions. However, the functional role these bouts of oscillatory activity may play during recovery after stroke has not been established.

Method: We implanted rats with neural probes capable of measuring single unit and local field potentials in motor and premotor cortex before and after stroke to probe the basic physiological circuits involved in skilled motor reaching; and how these circuits are perturbed after injury. In an additional set of animals, we implanted stimulating electrodes on the surface of the brain to study whether stimulation timed to these oscillations could improve recovery in stroke animals.

Results: We found that reach-related LFOs, as measured in both the LFP and related spiking activity, were greatly diminished after stroke and that spontaneous recovery was closely correlated with their restoration in perilesional cortex. Sensorimotor LFOs were also diminished in a human subject with chronic disability after stroke in contrast to two non-stroke subjects who demonstrated robust LFOs. Strikingly, delivery of electrical stimulation time-locked to the expected onset of LFOs was found to significantly improve skilled reaching in stroke animals.

Conclusion: Together, our results suggest that restoration or modulation of cortical oscillatory dynamics is important for recovery of upper-limb function and that they may serve as a novel target for clinical neuromodulation.

Evaluating Intolerance of Uncertainty as a Predictor of Treatment Response for
Individuals with Anorexia Nervosa: A Pilot Investigation

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Background: Although consistent research suggests that individuals with anorexia nervosa (AN) report elevated intolerance of uncertainty (IU), few studies have evaluated whether there is a significant change in IU over the course of evidence-based treatment, as is the case for mood and anxiety disorders. Additionally, no research has tested the influence of trait IU on treatment response. The current study aimed to test the stability of IU over the course of intensive treatment for AN and to investigate whether baseline IU accounted for significant variability in discharge symptomatology.

Methods: Individuals with AN (N = 63) receiving treatment at the UCSD Eating Disorders Center completed well-validated self-report surveys at intake and discharge from treatment.

Results: A paired-samples t-test indicated that there was no significant change in IU from intake to discharge, $p=.387$. Multiple regression analyses indicated that after accounting for length of stay, diagnosis subtype, and baseline symptom severity, IU was a significant predictor of both discharge BMI, $b=-.21$, $se=.10$, $p=.032$, and cognitive symptoms of eating pathology, $b=.18$, $se=.08$, $p=.024$.

Conclusion: Results suggest that individuals with elevated IU may demonstrate a worse response to evidence-based psychological treatments. Future work should evaluate the utility of directly targeting IU within treatments for AN.

Auditory Discrimination Learning in a Rodent Model of Human Targeted Cognitive Training

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Introduction: After 50 hours of Targeted Cognitive Training (TCT) schizophrenia patients show large gains in neurocognition. However, durable changes may require extended training, functional gains are modest, and individual responses are variable. We describe a novel paradigm for studying mechanisms of learning in TCT, in advance of testing interventions to enhance its clinical impact.

Methods: Male Long Evans rats (n=15) were trained to respond for reward in 3 distinct auditory discrimination tasks (ADT). Auditory stimuli were either a 500 ms pure tone of high (7 kHz) or low frequency (4 kHz) (ADT#1); a 200 ms sound sweep ranging from low to high frequency ("upsweep") or high to low frequency ("downsweep") (ADT#2); or a 500 ms upsweep or downsweep (ADT#3). The primary outcome variable was accuracy in choosing the lit aperture associated with the stimulus.

Results: Learning was reflected in a main effect of session on accuracy ($F_{(16,160)}=3.467$, $p<0.05$). A session x group interaction ($F_{(32,160)}=1.522$, $p<0.05$) revealed that the 500 ms sweeps group (ADT#3) learned faster than the other two groups. By training day 6 of 17, rats in ADT#3 exhibited greater accuracy vs. day 1. Performance superior to day 1 was never achieved in ADT#1, and required 13 days in ADT#2.

Conclusions: Long Evans rats: 1) can discriminate auditory frequency upsweeps vs. downsweeps; 2) learn faster from sweeps than pure tones; and 3) learn faster from long (500 ms) vs. short (200 ms) sweep duration. Studies will now assess the impact of pharmacologic agents on this model of TCT learning.

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Depression and Aging with HIV: Associations with Health-related Quality of Life and Positive Psychological Factors

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Background: Depression is highly prevalent among persons living with HIV (PLWH), yet little is known about factors associated with elevated depressive symptomatology. We investigated relationships between health-related quality of life (HRQoL), positive psychological factors (resilience, grit, and self-rated successful aging [SRSA]), and depressive symptomatology in PLWH.

Methods: One hundred twenty-two PLWH and 94 HIV- individuals, recruited in three age decades (36-45, 46-55, 56-65), completed self-report questionnaires on current depressive symptoms (CES-D), HRQoL, and positive psychological factors. Participants were classified into four groups: HIV status and elevated depressive symptoms (H+/D+; H-/D+) and HIV status and non-elevated depression (H+/D-; H-/D-).

Results: Fifty-eight percent of PLWH had elevated depressive scores, compared to 33% of HIV- individuals ($p < 0.05$). The proportion of individuals reporting elevated depressive symptoms differed among those aged 36-45 (HIV+/D+ group: 61.5%; HIV-/D+ group: 17.9%; $p < 0.001$); there were no group differences in proportion of depressive symptoms in the other age decades ($p > 0.05$). Within each age decade, the H+/D+ group reported the lowest physical and mental HRQoL and lowest scores on the positive psychological factors compared to the other three groups. However, those in the oldest H+/D- age group reported the highest SRSA ($p < 0.001$).

Conclusions: PLWH aged 36-45 years may be especially vulnerable to elevated depression symptomatology compared to age-matched persons without HIV. Additionally, among PLWH depressive symptoms may have a particularly negative impact on HRQoL conversely, a lack of elevated depressive symptoms may relate to greater SRSA. Future work should examine the complexities of depression and HIV across the lifespan.

Physician Communication of Genomic Results in a Diagnostic Odyssey Case Series:
A Preliminary Study

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Background: The availability of whole genome sequencing (WGS) in clinical care is increasing and WGS has been shown to be promising for diagnostic odyssey cases. Physicians' ability to effectively communicate genomic information, however, is unclear. This study assessed physicians' communication of patient genome sequencing information in a diagnostic odyssey case series from multiple perspectives.

Methods: We evaluated physician communication of genome sequencing results in an ongoing study of WGS utility for diagnosis of rare, idiopathic diseases. A modified Medical Communication Competence Scale (MCCS) was used to compare patients' ratings of their physician's communication of general medical information versus communication of genome sequencing information. Physician self-ratings were also compared to patient ratings.

Results: A total of 47 patients, parents, and physicians across 11 diagnostic odyssey cases participated. In 6 of 11 cases (54%), the patient respondent rated the physician's communication of genome sequencing information as worse than general medical information ($p = .110$). In 9 of 11 cases (82%), physician self-ratings of communication of genome sequencing information were lower than the patient respondents' ($p = .062$). Physician self-ratings were positively associated with identification of a diagnosis ($p = .021$), but diagnosis was not associated with patient respondent ratings ($p = .330$).

Conclusions: Findings from this study suggest that even in diagnostic odyssey cases where genome sequencing is of clinical benefit, physicians may not be well-equipped to communicate this type of information. Future studies may benefit from using a multi-perspective approach to assess and understand physician communication of genome sequencing information.

Cognitive SuperAging in Persons Living with HIV:
Demographic, Neuromedical and Everyday Functioning Correlates

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Background: Studies of cognitively elite older adults, termed *SuperAgers*, have yielded novel insights into mechanisms of resilience against age-related cognitive decline. Despite rising rates of older persons living with HIV (PLWH), SuperAging in PLWH remains undefined. We aimed to establish neuropsychological criteria for SuperAging in PLWH and examine clinically-relevant correlates of SuperAging.

Methods: 734 PLWH between 50 and 64 years of age underwent neuropsychological and neuromedical evaluations. SuperAging was defined as demographically-corrected (i.e., sex, race/ethnicity, education) global cognitive performance within normal range for 25-year-olds. Remaining participants were labeled cognitively normal or impaired based on current age. Chi-square and ANOVA tests explored cognitive status group differences on demographics, HIV disease characteristics, medical comorbidities, and everyday functioning. Multinomial logistic regression explored independent predictors of cognitive status.

Results: 124 (17%) individuals who met SuperAging criteria had significantly higher premorbid verbal IQ (WRAT), fewer self-reported depressive symptoms (BDI), and lower rates of diabetes than non-SuperAgers. Cognitive status groups were comparable on demographic and HIV disease characteristics. Age, WRAT, diabetes, and BDI all independently predicted SuperAging status. SuperAgers reported higher rates of functional independence, employment, and health-related quality of life than non-SuperAgers.

Conclusion: Despite combined neurotoxic risk of aging and HIV, youthful cognitive performance is possible for older PLWH. Elite cognitive performance relates to improved functional outcomes and may be better explained by markers of cognitive reserve and physical health (e.g., absence of metabolic syndrome) than HIV disease characteristics. Future research investigating lifestyle (e.g., physical exercise) correlates of SuperAging may help identify modifiable neuroprotective factors against HIV-related neurobiological aging.

Neuronal Network Alterations in Methamphetamine-treated HIV-1/gp120 Transgenic Mice

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Background: Neurodegenerative diseases like HIV-associated neurocognitive disorders (HAND) are attributable to inflammation of the nervous tissue, and thus loss of functional neurons. In addition, abuse of methamphetamine (METH), one of the most common recreational drugs among HIV-infected population, can lead irreversible damage in the brain, causing neuroinflammation and compromising several neurotransmitter systems. Still, the combined effects of HIV-1 and METH on the brain are incompletely understood at the molecular level.

Methods: Due to limited viability of post mortem brain samples, expression of HIV viral protein gp120 in mouse brains were used as a model that mimic some key neuropathological features observed in AIDS brains. Therefore, we treated 3-4 months old HIV-1/gp120 transgenic (gp120tg) and the respective wild type (wt) controls with either a 25 day escalating METH binge or a long-term low-dose regimen.

Results: We performed behavioral studies at 10-12 months of age. HIV-1/gp120tg and METH-exposed animals showed significant impairment in spatial learning and memory. In order to investigate underlying mechanisms different regions of the animals' brains (cortex, hippocampus and striatum) were analyzed using RT² Profiler™ PCR arrays to determine the changes in expression of genes related to the dopaminergic, serotonergic, GABAergic, and glutamatergic neurotransmission systems. Using Ingenuity Pathway Analysis (IPA) we found that the most affected networks were: Cell-to-cell Signaling and Interaction, Nervous System Development and Function, Behavior and Neurological Disease.

Conclusion: METH exposure and HIV-1/gp120 expression in the brain are all associated with significant, specific and lasting alterations of the four major neurotransmission systems. Supported by NIH, MH087332, MH104131, MH105330 and DA026306 (to M.K.)

Genetic and Environmental Architecture of Processing Speed Across Midlife

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Background: Processing speed (PS) declines with age and accounts for a substantial proportion of age-related change in cognition. However, differences exist between PS assessments, and measures may not uniformly change with age. We performed confirmatory factor analysis (CFA) in the context of multivariate twin models to evaluate the genetic and environmental relationships of 6 measures of PS and their change from midlife to late midlife.

Methods: Participants were male-male twins drawn from wave 1 (N=1268; mean age=55.9, SD=2.4) and wave 2 (N=1162; mean age=61.7, SD=2.5) of the Vietnam Era Study of Aging (VETSA). Using multivariate twin analysis, we evaluated a series of models to determine the relationship among PS measures at each time point and across time.

Results: The best-fitting model included a higher-order common PS factor that accounts for the covariance among 3 test-specific factors; each test-specific factor accounted for the covariance between 2 observed measures. The PS factor was significantly heritable ($a^2_{\text{wave1}}=.75$, $a^2_{\text{wave2}}=.64$), and stable across time ($r_{\text{phenotypic}}=.91$; $r_{\text{genetic}}=.97$; $r_{\text{environmental}}=.77$). Test-specific factors were significantly heritable (a^2 range: .45-.65), and stability across time varied ($r_{\text{phenotypic}}: .70-.89$; $r_{\text{genetic}} > .96$; $r_{\text{environmental}}: .45-.73$).

Conclusion: Results indicate that different PS measures assess a common PS factor that is principally determined by temporally stable genetic influences. However, different test-specific factors retain unique genetic and environmental influences. These results indicate that, though PS measures do assess a common construct, there are important genetic, environmental, phenotypic, and rate of change differences between assessments that may impact the evaluation of PS change.

The Neurocognitive Implications of Chewing Tobacco among
People Living with HIV in India

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Sanjay Mehendale, Thomas Marcotte

Objectives: Despite the high prevalence of tobacco use (68.3%) among people living with HIV (PLWH) in India, the neurocognitive implications of HIV and tobacco use remain unknown. This cross-sectional analysis sought to examine if the adverse effects of tobacco will exacerbates HIV-associated premature vascular aging, or if the possible positive immunomodulatory effects of nicotine will engender neuroprotective processes.

Methods: An Indian sample of 339 HIV+/- participants completed a gold standard neuropsychological battery and an HIV-related biomarker panel. Separate three-way interaction Least Squares (LS) models of age, HIV status, and tobacco use were constructed to predict global and domain-based cognitive deficit scores. A backwards stepwise logistic regression model identified biomarkers most predictive of cognitive impairment.

Results: The cohort was primarily male (52.2%) and had a mean age of 33.0 (\pm 7.5) years. Global deficit scores were predicted by a two-way interaction between HIV status and tobacco use ($\beta = -.5348, p = .0347$), such that the adverse effects of HIV were lowered among chewers. Global level interactions were primarily driven by worse motor performance due to HIV+ status, recent tobacco use, and older age ($\beta = .0939, p = .0038$). Among HIV+ chewers, IP-10 (an indicator of T-cell migration) was the primary predictor of motor impairment ($X^2 = 4.53, p = .0343, df = 1$).

Conclusion: Chewing tobacco adversely impacts cognition and this effect strengthens with age. However, nicotine may modulate the neuroinflammatory state of PLWH, resulting in neuroprotection. Future studies should investigate the effects of tobacco in a longitudinal fashion.

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Public Outreach and Community Engagement for Genetically Engineered Mosquitoes:
Lessons from Oxitec and MosquitoMate

Cynthia E. Schairer, Ph.D. Cinnamon Bloss, Ph.D.

Background: Concerns about the spread of invasive species of mosquito in the continental U.S. has sparked interest in creating genetically engineered mosquitoes to curb the threat of malaria, zika, dengue, and chikungunya. However, public anxieties about the power of genetically modified organisms (GMOs), in part, has stymied efforts to effectively regulate and test these technologies.

Methods: Based on media reports and interviews with key informants, we compare the case of Oxitec's efforts to test their genetically engineered mosquito in the U.S. with MosquitoMate's similar but more successful trials of their *Wolbachia* infected mosquitoes.

Results: While MosquitoMate does not describe its mosquitoes as genetically engineered, there are compelling technical similarities between *Wolbachia* infected mosquitoes and Oxitec's sterile male mosquitoes. However, in addition to their rhetorical advantage in eschewing the label of GMO, MosquitoMate has managed to avoid obstacles in the regulatory process and community engagement that have plagued Oxitec.

Conclusions: The comparison highlights the complex relationship between regulation, public outreach, and public perceptions of emerging technologies. Analysis of these case studies clarifies the different forms that public outreach and community engagement can take, as well as the variety of technology champions who may initiate outreach and engagement. When planning public outreach or community engagement, the form must fit the stage in the technology's development and appropriately reflect the position of the agents who initiate engagement. Specifically, we suggest forms of messaging and inquiry suitable for engagement by different actors at different stages of technological development.

Stakeholder Attitudes Toward Returning Personal Data Generated by
HIV Molecular Epidemiology

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Michael Kalichman, and Susan Little.

Background: A recent approach to motivating enrollment and democratizing biomedical research is to provide personalized research findings to participants. This paper explores ethical questions surrounding the return of research results to participants by considering the case of HIV molecular epidemiology (HIV ME), a tool that generates powerful knowledge about HIV transmission networks, as well as sensitive data about those in the network. HIV ME presents a scenario where returning research information to the participant can have stark social consequences, raising questions about the limits of participants' rights to research results.

Methods: We conducted qualitative interviews with 40 stakeholders (HIV positive, HIV at risk, medical professionals, and nonmedical professionals) to find out how these individuals respond to the promise and risks of HIV ME. Thirty-eight interviews included a discussion of returning personally relevant research findings derived from HIV ME. The considerations raised in these passages are compared and described.

Results: Most respondents saw the results of HIV ME analysis as potentially powerful, but there was considerable diversity with respect to how respondents felt this data should be handled, from assuming that everyone should be given information about their transmission network, to asserting that the information is too sensitive to share.

Conclusions: HIV ME is a useful case study for thinking about the potential implications of sharing research results with study participants, bringing into focus tensions between protection of participants and a right to know that may be presumed by participants.

Defining the Cell-specific Epigenetic Landscape Leading to Altered Gene Expression Signatures in HIV-Associated Neurocognitive Disorder

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Background: It is vastly unknown what leads to the development of cognitive symptoms in HIV and why only a subset of individuals is prone for HIV-associated neurocognitive disorder (HAND). One risk factor for HAND is age, and with HIV-infected individuals reaching normal life expectancy under the current antiretroviral regimens, HAND may increasingly become a socioeconomic burden. In addition, recent studies revealed striking similarities in the neuropathology of HAND and Alzheimer's disease (AD). Remarkably, little is known about the molecular mechanisms that lead to the development of HAND and whether molecular mechanisms leading to neuronal dysfunction and death are shared between AD and HAND. Here, we will test the hypothesis, that myeloid cells, the latent reservoir of HIV in the brain, have a distinct gene expression signature and epigenetic landscape, which sets the stage to modulate and impair neuronal function.

Methods and Results: We take advantage of our expertise in isolating nuclei from post mortem brain tissue and in sorting for cell type of origin. The transcriptomes of myeloid and neuronal nuclei are obtained by RNA-seq. To assign regulatory functions to non-coding genomic regions and to identify their interaction networks specifically in neurons or myeloid cells in HAND, we will define enhancers and open chromatin regions using genome-wide ChIP-seq and ATAC-seq.

Conclusions: In concert, the proposed studies are expected to greatly advance our understanding of molecular signatures of myeloid cells and neurons in HAND.

Factors, Other than Amnesia, that Predict Performance on Tests of News Event Memory

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Background: Damage to the medial temporal lobe is associated with retrograde amnesia, that is, difficulty remembering information acquired prior to the onset of amnesia. Tests of notable public events (news events) are useful tools for measuring retrograde memory and assessing the severity of amnesia. Yet, memory for news events is likely to be influenced by factors other than amnesia. For example, how often one follows news events or the number of different sources one uses to learn about news events will likely affect performance. These types of factors are problematic when interpreting retrograde amnesia in patients because one does not know to what extent impaired retrograde memory for news events reflects neuropathological changes or factors unrelated to neuroanatomy.

Methods: We tested recall and recognition memory for 60 news events that occurred in the recent past (between 2017-2009) in 150 healthy participants aged 25 to 82. In addition to traditional demographic measures (sex, age, education), we obtained measures of the amount of exposure to news events (frequency of exposure to news events and the number of sources of news event information).

Results: Recall and recognition accuracy for news event questions were significantly predicted by education, the frequency of exposure to news events, and the number of sources of news event information.

Conclusions: Performance on tests of news events are impacted by a number of demographic variables. It is important to account for these variables when using tests of news event memory to determine the severity of retrograde amnesia in neurologic or psychiatric patients.

Multimodal Neuroimaging Fusion Reveals Converging Neural Circuitry
across Trauma-Related Disorders

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Background: Trauma-related neuropsychiatric disorders are associated with a high degree of symptom heterogeneity and diagnostic comorbidity, suggesting that they share a set of underlying neural mechanisms. Trauma-related disorders are characterized by aberrations in separate circuits subserving memory ability and affective anticipation. Yet, how the neural circuitry representing the integration of these mechanisms contributes to trauma-disorders remains unknown. Multimodal neuroimaging fusion analysis may be a useful approach to address this question.

Methods: In a sample of 47 combat Veterans, we measured affective anticipation using functional magnetic resonance imaging (fMRI), verbal memory with fluorodeoxyglucose positron emission tomography (FDG-PET), and grey matter volume with structural magnetic resonance imaging (sMRI). Using a voxel-based multimodal canonical correlation analysis (mCCA), these neural mechanisms were fused with trauma-related disorder measures of mild traumatic brain injury (mTBI), posttraumatic stress disorder symptoms, and depression severity to identify where trauma-related disorders and neural measures mutually relate to each other in the brain.

Results: The first canonical factor revealed convergence across all trauma-related disorders in clusters encompassing the middle frontal gyrus and supplemental motor area, regions implicated in top-down cognitive control and affect regulation. Furthermore, we observed disorder divergence in several regions. Specifically, we found affective anticipation-related activity in the insula/inferior frontal gyrus and the hippocampus positively predicted mTBI and PTSD. In contrast, insula/inferior frontal gyrus glucose metabolism associated with verbal memory predicted depression but not mTBI or PTSD.

Conclusions: These results highlight the potential of leveraging multimodal fusion analysis of neuroimaging for integrating multiple neurobiological mechanisms associated with trauma-related disorders.

Risk and Resilience Factors Associated with Posttraumatic Stress Disorder,
Alcohol Use Disorder, and Their Comorbidity in U.S. Veterans: Results
from the National Health and Resilience in Veterans Study

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Background: Posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) frequently co-occur in veterans and result in greater psychiatric and psychosocial impairment than either disorder alone. Examining how risk and resilience factors differ between veterans with PTSD/AUD and those with either disorder alone may elucidate the mechanisms underlying the comorbidity and inform prevention and treatment strategies.

Methods: This study utilized data from a nationally representative sample of U.S. Veterans ($N = 3,157$) aged 21 and older who completed an online survey.

Results: Weighted prevalence analyses revealed that 16.4% screened positive for probable PTSD, 14.8% for AUD, and 2.8% for comorbid PTSD/AUD. Multivariate logistic regression analyses revealed that veterans with PTSD/AUD were more likely than those with PTSD or AUD alone to report utilizing certain negative strategies to cope with trauma, including behavioral disengagement (PTSD/AUD = 18.4%, PTSD = 13.9%, AUD = 3.8%) and substance use (PTSD/AUD = 43.7%, PTSD = 15.5%, AUD = 18.8%), and less likely to endorse adaptive coping approaches, such as active coping (PTSD/AUD = 6.9%, PTSD = 19.0%, AUD = 18.2%). Veterans with PTSD/AUD also scored significantly lower than the AUD group on two composite factors of protective psychosocial qualities ($p < .001$) and social connectedness ($p < .001$).

Conclusions: These findings suggest that veterans with PTSD/AUD have a profile characterized by heightened risk factors and lower resilience characteristics, which could contribute to the worse psychiatric and functional correlates associated with comorbidity. Developing interventions to target risk factors and augment resilience may enhance clinical outcomes in a particularly vulnerable population.

The Oxytocin Receptor in Response to Inflammation in Macrophages

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Background: Social environment influences the progression of atherosclerosis, a chronic inflammatory process. Oxytocin (OT) has been associated with pro-social behavior; however, plasma OT levels are not elevated in a pro-social environment in animal models of disease. Infusion of exogenous OT in these disease models attenuates inflammation and arterial plaque, which raises the possibility that OT's anti-inflammatory effects may be regulated at the level of the OT receptor (OTR) rather than by changes in plasma OT titers as a function of social environment. In the current study, we examined the role of inflammation on the expression of OTR. We hypothesized that OTR expression is increased during inflammation through a nuclear factor κ B (NF- κ B) mediated pathway, thus responding as an acute phase protein.

Methods: Inflammation was induced by treating macrophages (human primary, THP-1, and murine) with lipopolysaccharide (LPS) and monitored by expression of Interleukin (IL)-6. Expression of OTR and vasopressin receptors was assessed by qPCR and OTR expression was confirmed by immunoblotting.

Results: Inflammation up-regulated OTR transcription 10-250-fold relative to control in THP-1 and human primary macrophages, and increased OTR protein expression. In contrast, vasopressin receptor-2 mRNA expression was reduced following LPS treatment. Blocking NF- κ B activation prevented the increase in OTR transcription. OT treatment of control cells and LPS-treated cells increased ERK1/2 phosphorylation demonstrating activation of the OTR/G α q/11 signaling pathway. OT activation of OTR reduced secretion of IL-6 in LPS-activated macrophages.

Conclusions: Collectively, these findings suggest that OTR is an acute phase protein, and that its increased expression is regulated by NF- κ B and functions to attenuate cellular inflammatory responses in macrophages.

Incidence of Synthetic Oxytocin Administration and Time to Improvement of Depression and Anxiety Symptoms in the UCSD Intensive Outpatient Treatment Program for Postpartum Depression

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Background: The incidence of postpartum depression (PPD) in women is 15-20%. Oxytocin (OT) – a neuroendocrine hormone that mediates social interactions – is essential in lactation. Pitocin, a synthetic form of OT, is commonly used to induce labor, which has been shown decrease endogenous OT production. This reduction has been implicated in abnormal bonding between mother and infant, and in the development of PPD in mothers. Conversely, higher levels of OT in the postpartum period have been associated with lower depressive and anxiety symptoms.

Methods: An intensive outpatient (IOP) treatment program for mothers with PPD was developed at UCSD. Since its inception in March 2017, 25 women have completed the program. Upon admission and discharge, all women undergo the Edinburgh Postnatal Depression Scale (EPDS), Beck Anxiety Inventory (BAI), and Postpartum Bonding Questionnaire (PBQ). A retrospective chart review was utilized to determine incidence of Pitocin administration at time of parturition and analyzed regarding time to improvement of depressive and anxiety symptoms.

Results: Mothers with PPD had symptomatic improvement during the course of IOP treatment. We characterized PPD symptomatology in the new mothers as measured by EPDS, BAI, and PBQ in comparison to Pitocin administration at parturition.

Conclusion: To our knowledge, this IOP is one of only a dozen in the US that offer intensive treatment for PPD. Incidence of synthetic OT administration and the severity of depressive and anxiety symptoms is currently unknown. With the results of this analysis, our future goal is to develop recommendations to improve outcomes for both mothers and infants.

Neurocognitive Development, Pubertal Status, and Social Expectancies Predict Adolescent Drinking Behaviors

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Background: Research has demonstrated a link between cognitive deficits and heavy alcohol use in adolescents and that poorer neurocognitive performance in early adolescence may increase risk for earlier alcohol use onset. Pubertal onset, social behaviors (e.g., dating) and alcohol expectancies are also associated with earlier alcohol initiation and increased risk of later heavy drinking. The current study sought to examine whether neurocognitive functioning, alcohol expectancies, and dating behaviors prior to alcohol initiation predicted age of alcohol and binge drinking onset. The study also aimed to determine if neurocognitive functioning was moderated by pubertal status in predicting drinking outcomes.

Methods: The sample consisted of 295 12- to 14-year-olds at baseline with no prior alcohol or substance use experience who were part of an ongoing 15-year longitudinal project examining substance use and neurocognition.

Results: Results indicated that visuospatial ability significantly predicted age of alcohol initiation, with better performance on visuospatial tasks predicting later alcohol initiation. Processing speed significantly predicted age of first binge, with faster processing speed relating to earlier onset of binge drinking. Baseline social expectancies and dating experience, but not pubertal status, were negatively associated with age of alcohol initiation. Notably, interactions between processing speed and pubertal onset, as well as cognitive inhibition and pubertal onset were marginally significant in predicting age of first drink.

Conclusions: Results from this study suggest that aspects of neurocognition and social development may predict drinking and binge drinking onset in adolescence. These results have important implications for prevention/early intervention efforts of alcohol use disorders.

Marijuana Use in an Aging Population: Global Brain Structure and Cognitive Function

Rachel E. Thayer, M.A.

Background: Scientific literature delineating potential negative impacts or neuroprotective benefits of marijuana consumption has not kept pace with societal changes in acceptance of its recreational use. Further exploration of marijuana use among older adults may help clarify global risks or neuroprotective benefits of using marijuana.

Method: This study collected structural MRI and cognitive assessments within a sample of recreational marijuana users age 60 years and older and healthy control non-users.

Results: Marijuana users ($n=28$) and controls ($n=28$) were not different in terms of global brain structural measures, but groups showed diffuse areas of difference throughout the brain. Users ($n=28$) showed slightly poorer working memory than controls ($n=10$). Lifetime users ($n=15$) performed poorly compared to both short-term users ($n=13$) and controls ($n=10$) in executive function, and poorly compared to controls in general cognition. Estimated total THC consumption in the last 90 days showed negative association with total gray matter volume and diffuse clusters in whole-brain models, and years of regular marijuana use showed consistent negative associations with cognitive performance in executive function, processing speed, and total cognition.

Conclusions: Study results suggest that lifetime marijuana use at a recreational level does not have a strong and consistent effect on brain structure, but it does appear to have a negative association with aspects of cognitive functioning. From a harm reduction perspective, it is valuable to note that any harms associated with long-term marijuana use may be reduced by consuming strains with lower THC concentrations with less frequency.

Dissociation of Performance-Based and Self-Reported Gains Following
Cognitive Training in Schizophrenia Patients

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Background: Cognitive training is effective for improving verbal learning and memory performance among people with schizophrenia. An individual's *perception* of their own cognition, however, is dissociable from objective cognitive performance. Perceived cognition remains an important target for cognitive training, given its association with treatment attitudes and generalization to real world outcomes. Patients who fail to detect benefits may be less motivated to engage in cognitive training. This study aimed to determine whether perceived cognition improves following a 2-month course of cognitive training.

Methods: Patients with schizophrenia or schizoaffective disorder (N=48) were randomized to receive treatment as usual (TAU) or TAU augmented with ~40h of auditory-targeted cognitive training (TCT). All participants completed performance-based measures of cognition, perceived cognition, and symptoms at baseline and follow-up.

Results: TCT participants showed significant improvements in verbal memory and hallucinations, ($d_s = .82$ and $.62$, $p_s < 0.05$). Perceived cognition, however, did not significantly change, even among TCT participants who showed improvements in cognitive performance (all $p_s > 0.05$). Perceived cognition was significantly associated with severity of depressive symptoms and hallucinations ($r = 0.48$ and $r = 0.28$, $p < 0.001$), but not global or individual domains of cognition (all $r_s < 0.1$).

Discussion: Results confirm that cognitive performance and perceived cognition represent dissociable constructs. Perceived cognition does not improve alongside cognitive performance. Identifying mechanisms of change for perceived cognition is key to sustaining treatment engagement and promoting the generalization of cognitive training effects. Concurrent depression interventions could support cognition interventions and enhance perceived cognition. Augmenting cognitive interventions with feedback and motivational strategies may also enhance patients' detection of benefit.

Profiles of PTSD and Moral Injury in Combat Veterans

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Background: Although previous research indicates that posttraumatic stress disorder (PTSD) and moral injury (MI) exhibit similarities, no research has used person-centered analyses to demonstrate whether there are groups of individuals with high PTSD and low MI and vice-versa. This study explored whether subtypes of military veterans could be identified based on profiles of measures of PTSD (using the four DSM-5 based clusters) and MI (Transgressions-Others, Transgressions-Self, and Betrayal).

Method: 208 American veterans and active duty military who deployed to combat missions in Iraq or Afghanistan (91% men; 81% Caucasian) completed self-report measures via an online survey. Latent variable mixture modeling (LVMM) generated participants into groups based on similar response patterns, and multivariate analysis of covariance (MANOVAs) examined differences between groups in attachment and emotional responses.

Method: LVMM generated four groups: Low PTSD/Low MI, Moderate PTSD/Low MI, Moderate MI plus NACM (Negative Alterations in Cognition and Mood) & Hypervigilance, and High PTSD/Moderate MI, and. MANOVAs indicated that the four groups differed in attachment avoidance and anxiety, depression, anxiety, anger, shame, guilt, contempt, and hostility inward (range of η_p^2 .12-.45). Both groups with moderate MI demonstrated higher levels of guilt, shame, anger, hostility inward, and disgust compared to the two groups with low MI.

Conclusions: MI did not occur without symptoms of PTSD in this sample, but future research should examine the overlap of NACM and hypervigilance with MI that occurred in Class 4. It is likely that MI may be addressed with PTSD treatments.

Hell-weed or Heal-All? A Cost-Effectiveness Model for Adjunctive Smoked Cannabis in the Treatment of Painful Neuropathy

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Introduction: A recent meta-analysis demonstrated the benefit of medicinal cannabis for neuropathic pain. This is an exploratory cost-effectiveness analysis of adjunctive cannabis for painful neuropathy.

Methods: A Markov model comparing conventional therapies for painful diabetic neuropathy was modified to include arms for augmenting first-line, second-line (if first-line failed), or third-line (if first- and second-line failed) therapies with cannabis. Microsimulation of 1,000,000 patients compared the cost (\$US) and effectiveness (quality-adjusted-life-years [QALYs]) of standard therapy with and without adjunctive cannabis. Efficacy inputs for cannabis were adapted from trials of cannabis in HIV neuropathy, which approximated clinical practice and demonstrated comparable efficacy to cannabis for painful diabetic neuropathy. Adverse event rate modifiers for cannabis were derived from a year-long prospective study and applied to probability inputs for conventional therapies. Cannabis cost was derived from wholesale market pricing. Parameter uncertainty was addressed with one-way and probabilistic sensitivity analysis.

Results: Adding cannabis to first-line therapy was incrementally less effective and costlier than adding cannabis to second- and third-line therapies. Third-line cannabis-as-adjunct was subject to extended dominance, as the second-line strategy was more effective with a more favorable incremental cost-effectiveness ratio (ICER) of \$73,728.81/QALY gained. Second-line cannabis-as-adjunct was sensitive to price, with an ICER of \$136,243/QALY when cost modeled consumer retail pricing. At a willingness-to-pay threshold of \$100,000/QALY gained, adjunctive cannabis strategies were cost-effective in 67% of simulations.

Conclusion: Cannabis is cost-effective when augmenting second-line treatments for painful neuropathy. Further research is warranted to explore the benefit and workability of concentration-standardized cannabis in this disabling condition.

Cultural and Psychological Factors Impact Treatment Adherence
and HbA1c in Patients with Type 2 Diabetes

Sonika Ung, Ph.D.

Background: Type 2 diabetes (T2D) is a global epidemic that disproportionately affects disadvantaged minorities. Cultural and psychological factors predicted the control of T2D among indigenous patients in Chile (Ung, Betancourt, & Flynn, 2014; Ung, 2015). The present study explored the impact of cultural beliefs, psychological factors, and health behavior on HbA1c among culturally diverse patients in the U.S. It was hypothesized that cultural beliefs would impact HbA1c directly and/or indirectly through diet self-efficacy and diabetes self-care behavior.

Methods: Participants included 175 individuals with T2D. The cultural beliefs scale was developed using the bottom-up cultural research approach (Betancourt & Flynn, 2009). Factor analyses revealed a two-factor solution: explicit social influence ($\alpha=.80$) and susceptibility to social pressure ($\alpha=.83$) to consume unhealthy food. In addition, diet self-efficacy ($\alpha=.92$), how many days patients engaged in poor diabetes self-care behavior, and most recent HbA1c levels were measured.

Results: Using structural equation modeling, the hypothesized structure of relations among cultural beliefs, psychological factors, diabetes self-care behavior, and HbA1c demonstrated excellent fit [CFI=.973, RMSEA=.048, SRMR=0.059, $\chi^2(50, n=156) = 68.33, p=.043, x^2/df=1.37$]. Cultural beliefs impacted HbA1c indirectly through diet self-efficacy and diabetes self-care behavior [$\beta_{\text{indirect}} = -.04, p=.044$ (95% CI=-.076, -.001)]. Specifically, cultural beliefs about social influence and pressure to consume unhealthy food predicted diet self-efficacy. In turn, diet self-efficacy predicted diabetes self-care behaviors, which predicted better HbA1c.

Conclusion: Findings underscore the importance of examining the indirect effect of culture on treatment adherence, rather than solely testing one-to-one relationships when considering interventions among culturally diverse populations with T2D.

The Medial Temporal Lobe, Conscious Memory, and
Experience-dependent Eye Movements

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Background: The medial temporal lobe (MTL) has traditionally been thought to be essential for conscious (declarative) memory but not for unconscious (nondeclarative) memory. Recent studies of experience-dependent eye movements have raised the possibility that unconscious memory can sometimes also depend on the MTL.

Method: We examined the preferential effect, whereby in tests of recognition memory more viewing is directed toward an about-to-be-selected item when the choice is correct than when the choice is incorrect. Eye movements were recorded while participants made three-alternative, forced-choice recognition memory judgments for old and new scenes. 30 young, healthy participants (Experiment 1) and 5 memory-impaired patients together with 8 controls (Experiment 2) participated.

Results: In Experiment 1, the magnitude of the preferential viewing effect correlated with recognition accuracy as well as with the difference in confidence ratings and in response times for correct and incorrect choices. In Experiment 2, memory-impaired patients with medial temporal lobe lesions exhibited a weaker preferential viewing effect than controls. The patients also exhibited poorer recognition accuracy than controls and reduced differences in confidence ratings and response times for correct and incorrect choices.

Conclusions: Eye movements had the same status as standard measures of declarative memory. The preferential viewing effect is a phenomenon of conscious memory, supporting the link between medial temporal lobe function and declarative memory.

Plasma Soluble CD14 is Associated with Apathy in Adults
with a History of Methamphetamine dependence

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Background: Inflammation is a key mechanism of methamphetamine (MA)-induced neurotoxicity. Emerging evidence suggests that inflammation is also linked to apathy, a prevalent neuropsychiatric symptom in MA dependence that is associated with worse everyday functioning. However, no study has examined whether inflammation is associated with increased apathy in the context of MA dependence. We examined the effect of MA dependence on apathy and associations between apathy and a panel of biomarkers indicative of inflammation (IL-6, sTNFR-II), chemotaxis (MCP-1, IP-10) and monocyte activation/microbial translocation (sCD14).

Methods: Excluding severe psychiatric or neurological disease, 75 adults with lifetime histories of MA dependence (MA+, n=24) and a non-drug-using comparison group (MA-, n=52) completed comprehensive neurobehavioral and neuromedical assessments, including measures of five plasma biomarkers by immunoassay. Apathy was measured using a composite of apathy-related subscales from the Frontal Systems Behavioral Scale, Profile of Mood States, and Beck Depression Inventory-II.

Results: Apathy was elevated in the MA+ group relative to MA- group ($p < .0001$), independent of potential confounds (e.g., education, Major Depressive Disorder). In the MA+ group, apathy was strongly associated with plasma sCD14 ($\rho = 0.59$, $p = .002$), while it was not associated with other biomarkers ($p > .05$).

Conclusions: Results suggest that processes involved in monocyte activation, as reflected by sCD14, may contribute to apathy in MA dependence. sCD14 is typically triggered by bacterial lipopolysaccharide, and can be indicative of microbial translocation from the gut. Future work will determine if such translocation reflects MA-related microbiome changes, which in turn may affect gut-brain signaling, impacting affective behavior, such as apathy, relevant to MA dependence.

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Online Dating, Sexual Hookups, and Alcohol Use by Young Women

Emily R. Wilhite, M.A. & Kim Fromme, Ph.D.

The advent of online dating has changed how individuals approach dating over the last few decades. Because online dating is relatively new, there is sparse research on how this modality of dating has impacted alcohol-related sexual hookups. This study tested whether method of meeting a sexual hookup partner (i.e., online dating vs. bar/party, friend, work/school) influenced level of intoxication at the time of the hookup. We also tested whether a sense of familiarity moderated the effect of how the individuals met on the participant's level of intoxication. Participants (N=110) were drawn from a six-week daily diary study of single, post-college, heavy drinking women ages 22-30. Results indicated that meeting a partner online was associated with lower levels of intoxication prior to a sexual hookup relative to meeting partners through other means. Partner familiarity moderated the association between method of meeting a sexual hookup partner and level of intoxication, such that being less familiar was associated with higher intoxication during a hookup for partners met at bar/party and lower intoxication for partners met online. Consequently, these results suggest that online dating may be protective against heavy drinking during sexual hookups, highlighting the importance of contextual factors for drinking and risky sex.

Internet-delivered Dialectical Behavior Therapy Skills Training for Suicidal and Heavy Episodic Drinkers: A Randomized Controlled Trial

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Background: Despite the treatment need for suicidal individuals who engage in problematic drinking, most of them do not enroll in psychotherapy. Computerized interventions have emerged to bridge the gap between treatment need and availability, and dialectical behavior therapy skills training (DBT-ST) is particularly amendable to computerization given its structure and inherent modularity. Therefore, we aimed to evaluate an Internet-delivered DBT-ST against a waitlist among a sample of suicidal individuals who consume alcohol to regulate their emotions.

Method: Participants (N = 59) who endorsed current suicide ideation, two episodes of heavy episodic drinking in past month, and high emotion dysregulation were randomized to immediate access to iDBT-ST or an eight-week waiting period. Overall usability, acceptability, and feasibility was assessed using a variety of methods including overall satisfaction, homework completion, effectiveness, and dropout. Primary outcomes of interest are Alcohol Use Disorder Identification Test, Timeline Followback, Beck Scale for Suicide Ideation, and Difficulties in Emotion Regulation Scale. Multilevel modeling was used to evaluate differential rates of change on key outcomes.

Results: Approximately 50% of the participants finished all eight sessions, and found the intervention to be useful. Results revealed significant main effects of time for all outcomes. Individuals randomized to receive treatment immediately had significantly faster reductions in suicide ideation ($p < .05$) and in drinking quantity and frequency ($p < .05$).

Discussion: Despite the high dropout rate, the high satisfaction and significant reductions in key outcomes suggest an online DBT skills training program could be a potentially useful treatment tool.

Verbal Memory Performance Under Real and Simulated Hearing Loss Conditions

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Background: Previously, we reported that adults with hearing loss performed worse than adults without hearing loss on an auditory-verbal memory test presented at a normal speaking volume, but performance on a *visual* version of the test was equivalent between groups (Wong et al. 2016). This study examined the effects of different presentation conditions on verbal memory performance, and examined the relationship between hearing loss severity and verbal memory.

Methods: Forty-one adults with moderate-to-severe hearing loss (HL) and 41 adults with normal hearing (NH) participated. They completed the Hopkins Verbal Learning Testing-Revised under optimal and non-optimal auditory conditions.

Results: The NH group under the non-optimal condition (hearing loss simulation) performed significantly worse than the HL group under the optimal condition (amplified volume, $p < .001$) with large effect sizes ($d = 0.84$ to 1.52), and was equivalent to HL group performance at normal volume ($d = .01$ to $.28$, $ps > .19$). Within the HL group, hearing loss severity was inversely correlated with non-optimal auditory-verbal memory ($r = -.47$ to $-.59$), but not with optimal auditory-verbal memory.

Conclusions: Hearing loss interferes with performance on tests with a high auditory demand. Under conditions of simulated hearing loss, adults with normal hearing perform like adults with hearing loss. Thus, prior findings reporting cognitive deficits associated with hearing loss are likely contaminated, at least in part, by measurement artifact. Future research should expand clinical measures that assess cognitive functioning independent of auditory modality to facilitate valid cognitive assessment of adults with hearing loss.

Widespread Transcriptome Dysregulation across Autism, Schizophrenia, and Bipolar Disorder

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Background: Neurodevelopmental disorders, such as autism spectrum disorder (ASD), bipolar disorder (BD), and schizophrenia (SCZ), are highly polygenic. Multiple risk variants, act in distinct combinations to contribute to the etiology of these disorders. As a result, high quality datasets with large sample sizes are essential to gain sufficient power in the analyses, as evidenced by the successful gene discovery studies in the field. In contrast, most gene expression studies so far have been performed on relatively small numbers of samples, limiting their power to uncover global transcriptome alternations underlying these disorders.

Methods: Human brain RNAseq data was generated by the PsychEncode Consortium from individuals with ASD (n=82), SCZ (n=593), BD (n=253), and controls (n=1232). Analysis was restricted to frontal and temporal cortex brain samples from postnatal timepoints. To process the RNA-seq data, we adopted the “long-rna-seq-pipeline” used by the ENCODE Consortium, and extensive quality control steps were taken. Differential transcript expression and isoform co-expression network analyses were carried out to gain insights into the cross-disorder transcriptome.

Results: Differential transcript expression analysis identified shared as well as unique transcriptome changes among the three disorders. Upregulated transcripts were enriched for cytokine, immune, and inflammatory pathways, especially in SCZ. In contrast, downregulated transcripts were mostly enriched for synaptic processes in ASD and SCZ. Using isoform co-expression networks, we detected highly-specific cellular and molecular processes altered in three diseases. For example, a cluster of astrocyte modules was upregulated in SCZ and ASD, whereas oligodendrocyte module was downregulated in SCZ and ASD. In addition, a module corresponding to mitochondrial processes was downregulated in both ASD and SCZ.

Conclusions: These results represent the largest genome-wide characterization of brain transcriptome alterations across multiple psychiatric diseases, providing an unparalleled resource for mechanistic insight into these diseases, and suggesting pathways amenable to therapeutic intervention.

The 40-Hz Auditory Steady-State Response: A Sensitive and Predictive Biomarker of Perceptual Learning During Cognitive Training

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Background: Disturbances of auditory perception are characteristic features of schizophrenia (SZ) and contribute to cognitive and functional disability. Targeted Cognitive Training (TCT) of the auditory system has shown great promise for remediating cognitive impairments in SZ, but training-associated gains vary across individuals and are difficult to predict in the early stages of treatment. The Auditory Steady State Response (ASSR) to gamma-frequency stimulation is increasingly used as a functional biomarker of central auditory system plasticity in translational neuroscience. Here we aimed to determine whether gamma evoked power and phase synchronization measures are sensitive to and predict the amount of perceptual learning that occurs during initial exposure to TCT.

Methods: Participants were 29 SZ patients in a residential transitional care facility randomized to either auditory TCT (n=18) or non-auditory computer games (n=11). ASSR was assessed twice: immediately before and after one hour of auditory TCT or non-auditory CG. The auditory cognitive exercises in TCT require participants to make increasingly difficult frequency discrimination time-order judgments. The ASSR paradigm utilized 1-msec, 85-dB clicks presented in 500-ms trains at a frequency of 40-Hz.

Results: Significant increases in gamma evoked power were detected in the TCT ($t(17) = 2.19$, $p=0.04$), but not CG group ($t(10)=.41$, $p=0.69$). A trend towards increased gamma phase locking was also detected in the TCT group in the 100ms-200ms post-stimulus-onset window ($p=0.06$). Baseline gamma evoked power ($r=0.52$) and phase locking ($r=0.45$) were both positively correlated with perceptual learning within auditory training session ($p<0.05$) in the TCT group.

Conclusion: ASSR predicted gains in auditory perceptual learning and exhibited malleability after initial exposure to early stages of auditory TCT in individuals with SZ. These data support the use of ASSR as a biomarker for individual assignment, prediction, and monitoring of patient response to auditory cognitive training in SZ. Ongoing studies will investigate whether ASSR-predicted gains are stable and predict long-term functional gains from TCT in SZ patients.

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