2024

ANA-NINDS CAREER DEVELOPMENT SYMPOSIUM

September 13-14, 2024
Hilton Orlando | Orlando, FL

NIH National Institute of Neurological Disorders and Stroke

DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

ANA AMERICAN NEUROLOGICAL ASSOCIATION®
INNOVATORS IN DISCOVERY, EDUCATION, AND CARE

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ANA-NINDS Career Development Symposium

September 13-14, 2024
Hilton Orlando
Orlando, FL

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Lauren Sansing, MD, MS, FANA
Yale University School of Medicine
Course Co-Director

Tish Weigand, PhD
NINDS Office of Training and Workforce Development
Course Co-Director

COURSE GOALS

The ANA-NINDS Career Development Symposium is designed to provide you with the essential tools to enhance your ability to write successful grant proposals, to obtain grant funding from NIH and other institutions and build an impactful academic career. This course is held in conjunction with the ANA2024 Annual Meeting.

This symposium, now in its nineteenth year, is designed for K08, K12 and K23 recipients and will be chaired by senior neurologists and neuroscientists who have proven success in career building and navigation, scientific grant writing, networking, and balancing clinical and research efforts. In addition, senior staff from the NINDS will provide advice concerning the mechanisms involved in grant submission and evaluation.

COURSE EVALUATION

Participants are asked to complete the evaluation by Friday, November 1, 2024. We sincerely appreciate your constructive feedback and comments and ask that you please take a few moments to complete the evaluation.

2024 ANA-NINDS Career Development Symposium Agenda

All times are listed in Eastern Daylight Time
(EDT) Key West A - C

Friday, September 13, 2024

2:00 PM - 2:30 PM **Registration (Key West A-C Foyer)**

2:30 PM - 2:45 PM **Welcome and Goals for the Meeting**
Speaker: *Lauren Sansing, MD, MS, FANA, Yale University School of Medicine*

2:45 PM - 3:15 PM **View of NINDS Leadership 2024**
Speaker: *Walter Koroshetz, MD, FANA National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH)*

3:15 PM - 4:00 PM **Setting Yourself up for Success**
Speakers: *Tish Weigand, PhD, National Institutes of Health*

4:00 PM - 4:45 PM **Meet Your Peers and Colleagues Networking Sessions**
Table Assignments by Research Focus (20 min) and Clinical vs Lab (20 min). Please find your table assignments on the back of your name badge.

4:45 PM - 5:00 PM **ANA Presidential Address:**
Speaker: *M. Elizabeth Ross, MD, PhD, FANA, Weill Cornell Medicine*

5:00 PM - 6:00 PM **K Independence Panel – How I Did It**
Moderator: *Alexandra Nelson, MD, PhD, University of California San Francisco*
Panelists:
Anli Liu, MD, MA, New York University Langone Health
Eric Landsness, MD, PhD, Washington University in St. Louis
Mercedes Paredes, MD, PhD, University of California San Francisco
William Stacy, MD, PhD, University of Michigan

6:00 PM - 6:30 PM **Leadership: Lessons from Academia and Life**
Speaker: *Nina Schor, MD, PhD, FANA, National Institutes of Health*

6:30 PM - 7:15 PM **Opening Buffet Dinner**

7:15 PM – 8:45 PM **Chairs View Panel**
Moderator: *Lauren Sansing, MD, MS, FANA, Yale University School of Medicine*
Panelists:
Amy Brooks-Kayal, MD, FANA, FAAN, FAES, University of California, School of Medicine
David Standaert, MD, PhD, FANA, University of Alabama at Birmingham
David Greer, MD, MA, FANA, Boston University
Louise McCullough, MD, PhD, FANA, University of Texas Health Science Center at Houston
Thabele Bay Leslie-Mazwi, MD, University of Washington
Thomas Carmichael, MD, PhD, FANA, University of California, Los Angeles

Saturday, September 14, 2024

7:00 AM - 8:00 AM	**Poster Set-Up and Breakfast (Poster Set-Up in Key West D)**
8:00 AM - 9:00 AM	**Developing a Well-Rounded Research Program and Building your Portfolio** **Moderator:** *Annapurna Poduri, MD, MPH, Boston Children's Hospital* **Panelists:** *Ellen Mowry, MD, MCR, FANA, Johns Hopkins University* *Henry Paulson, MD, PhD, FANA, University of Michigan* *Jin-Moo Lee, MD, PhD, FANA, Washington University in St. Louis* *Sarah Berman, MD, PhD, University of Pittsburgh*
9:00 AM - 9:15 AM	**Coffee Break and Head to Breakout Sessions** *Conference Rooms: Lake Sheen A, Lake Sheen B, Lake George A, and Lake George B. Please find your breakout assignment on the back of your name badge.*
9:15 AM - 11:15 AM	**Breakout Session 1 (Conference Rooms Lake Sheen A, Lake Sheen B, Lake George A, and Lake George B)** *1st – 2nd Year Awardees – Abstract for First Major Paper Discussion* *3rd – 5th Year Awardees – Aims Page for R01 Discussion*
11:30 AM - 12:30 PM	**Industry, Philanthropy, and other Financial Relationships** **Moderator:** *David Greer, MD, MA, FANA, Boston University* **Panelists:** *Beau Ances, MD, PhD, MSc, FANA, Washington University in St. Louis* *Frances Jensen, MD, FACP, FANA, FAAN, FAES, University of Pennsylvania* *Oren Becher, MD, Icahn School of Medicine at Mount Sinai*
12:30 PM - 1:15 PM	**Lunch**
1:15 PM - 2:15 PM	**Building Collaborations: Developing and Sustaining Productive Relationships Moderator***: Barbara Vickrey, MD, MPH, Icahn School of Medicine at Mount Sinai* **Panelists:** *Romergryko Geocadin, MD, FANA, Johns Hopkins University* *Roy Hamilton, MD, MS, FANA, University of Pennsylvania* *Lesli Skolarus, MD, FANA, Northwestern University* *William Renthal, MD, PhD, John R. Graham Headache Center at Brigham and Women's Hospital*
2:15 PM - 2:30 PM	**Coffee Break and Head to Breakout Sessions** Please find your breakout assignments on the back of your name badge.
2:30 PM - 4:00 PM	**Breakout Session 2** (Conference Rooms Lake Sheen A, Lake Sheen B, Lake George A, and Lake George B) *"What are the Biggest Challenges you are Facing and How Can we Help Each Other?"*
4:15 PM - 5:45 PM	**Moderated Poster Tours (Key West D)** *Please find your poster group assignment on the back of your name badge.*

Faculty List				
FIRST NAME	**LAST NAME**	**CREDENTIALS**	**INSTITUTION**	**ROLE**
Alexandra	**Nelson**	MD, PhD	University of California, San Francisco	Moderator, Mentor
Amy	**Brooks-Kayal**	MD, FANA, FAAN, FAES	University of California, School of Medicine	Panelist, Mentor
Anli	**Liu**	MD, MA	New York University Langone Health	Panelist, Mentor
Annapurna	**Poduri**	MD, MPH	Boston Children's Hospital	Moderator, Panelist
Barbara	**Vickery**	MD, MPH	The Icahn School of Medicine at Mount Sinai	Moderator, Mentor
Beau	**Ances**	MD, PhD, FANA	Washington University in St. Louis	Panelist, Mentor
Dave	**Standaert**	MD, PhD, FANA	The University of Alabama at Birmingham	Panelist, Mentor
David	**Greer**	MD, MA, FANA	Boston University	Moderator, Panelist, Mentor
Ellen	**Mowry**	MD, MCR, FANA	Johns Hopkins University	Panelist, Mentor
Eric	**Landsness**	MD, PhD	Washington University in St. Louis	Panelist
Frances	**Jensen**	MD, FACP, FANA	University of Pennsylvania	Panelist, Mentor
Henry	**Paulson**	MD PhD, FANA	University of Michigan	Panelist, Mentor
Jin-Moo	**Lee**	MD, PhD, FANA	Washington University in St. Louis	Panelist, Mentor
Lauren	**Sansing**	MD, MS, FANA	Yale University School of Medicine	Chair, Moderator, Mentor
Lesli	**Skolarus**	MD, MS, FANA	Northwestern University	Panelist, Mentor
Letitia	**Weigand**	PhD	National Institutes of Health	Speaker
Louise	**McCullough**	MD, PhD, FANA	University of Texas Health Science at Houston	Panelist, Mentor
M. Elizabeth	**Ross**	MD, PhD, FANA	Weill Cornell Medicine	Speaker
Mercedes	**Paredes**	MD, PhD	University of California, San Francisco	Panelist, Mentor
Nina	**Schor**	MD, PhD, FANA	National Institutes of Health	Speaker, Mentor
Oren	**Becher**	MD	Icahn School of Medicine at Mount Sinai	Panelist
Romergryko	**Geocadin**	MD, FANA	Johns Hopkins University	Panelist, Mentor
Roy	**Hamilton**	MD, MS, FANA	University of Pennsylvania	Panelist, Mentor
Sarah	**Berman**	MD, PhD	University of Pittsburgh	Panelist, Mentor
Thabele Bay	**Leslie-Mazwi**	MD	University of Washington	Panelist, Mentor
Thomas	**Carmichael**	MD, PhD, FANA	University of California, Los Angeles	Panelist, Mentor
S. Thomas	**Carmichael**	MD, PhD, FANA	University of California, Los Angeles	Panelist, Mentor
Walter	**Koroshetz**	MD, FANA	National Institute of Neurological Disorders and Stroke	Speaker
William	**Stacey**	MD, PhD	University of Michigan	Panelist, Mentor
William	**Renthal**	MD, PhD	Brigham and Women's Hospital	Panelist, Mentor

Program Chairs

Lauren Sansing, MD, MS, FANA

Yale University School of Medicine

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Dr. Sansing completed her residency in Neurology in 2006 followed by a Vascular Neurology fellowship from 2006-2008, both at the Hospital of the University of Pennsylvania. Her clinical interests include acute ischemic stroke and intracerebral hemorrhage as well as other complex neurovascular diseases.

Following clinical training, she completed a Master of Science in Translational Research at Penn studying immune mechanisms of injury after intracerebral hemorrhage. She then joined the faculty at the University of Connecticut and Hartford Hospital in 2010, where she was active in the Departments of Neurology, Neuroscience, Neurosurgery, and Immunology. She leads a NIH-funded laboratory identifying immunological treatment targets for intracerebral hemorrhage and stroke. Her laboratory moved to Yale in the summer of 2014, where she continues her work in stroke immunology through basic and translational studies. She has received numerous national and international awards for her research and is the Vice Chair of Faculty and Academic Affairs for the Department of Neurology and the Director for Master in Health Science program for Yale School of Medicine.

Alexandra Nelson, MD, PhD

University of California, San Francisco

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Alexandra Nelson MD, PhD is the Richard and Shirley Cahill Endowed Chair in Parkinson's Disease Research at UC San Francisco. Dr Nelson received her MD/PhD training at UC San Diego, completed her residency and fellowship training at UCSF, and joined the faculty in 2014. In the lab, her research group investigates the cellular and circuit basis of movement disorders, using electrophysiology, optogenetics, and other optical methods in mouse models of disease. In the clinic, she focuses on the care of patients and families with Huntington's Disease, atypical parkinsonian disorders, and Spinocerebellar Ataxias.

Amy Brooks-Kayal, MD, FANA, FAAN, FAES

University of California, Davis, School of Medicine
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Amy Brooks-Kayal, MD is Professor and Chair of the Department of Neurology and the Andrew John Gabor, M.D., Ph.D., Presidential Chair in Neurology at University of California Davis School of Medicine. Clinically, she is a pediatric epileptologist. Her research focuses on the effects of epileptogenic brain injury on neuronal signaling pathways and neurotransmitter systems with particular emphasis on understanding the molecular regulation of GABA(A) receptor expression, and on development of novel therapeutics for the prevention, treatment and cure of epilepsy. Dr. Brooks-Kayal has held numerous leadership roles including as president of the American Epilepsy Society (AES), member of NINDS Advisory Council and Chair of CNNT review panel. She is currently a co-director of the Child Neurology Career Development K12 program, a member of NST-1 study section, a Neurology director of the American Board of Psychiatry and Neurology and Associate Editor of Epilepsy for the Annals of Neurology. She was the recipient of the 2019 recipient of the AES Founders Award, the 2021 International League Against Epilepsy (ILAE) Ambassador for Epilepsy award and the 2023 recipient of the Child Neurology Society Bernard Sachs Award for her leading research in neuroscience relevant to the care of children with neurological disorders.

Anli Liu, MD, MA

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Dr. Anli Liu is an Associate Professor of Neurology at NYU Langone, Principal Investigator of the NYU Memory and Neuromodulation Laboratory, and an Investigator at the NYU Neuroscience Institute. Dr. Liu earned her BA from Stanford University, MA from UC Berkeley, and MD from UCSF. She completed her neurology residency at NYP-Weill Cornell, followed by fellowships in clinical neurophysiology and cognitive neurology at Harvard at Beth Israel Deaconess Medical Center. In the clinic, she cares for adult patients with epilepsy and memory disorders. Her lab works to: (1) develop naturalistic tasks to measure human episodic memory behavior; and (2) clarify the neurophysiological mechanisms of memory by using single unit, micro-, and macro-LFP invasive recordings in epilepsy surgical patients.

Annapurna Poduri, MD, MPH

Boston Children's Hospital

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Professor Ann Poduri is Director of the Epilepsy Genetics and Neurogenetics Programs, Associate Chief for Academic Development in the Department of Neurology, and the Diamond Blackfan Chair of Neuroscience Research at Boston Children's Hospital. Through her multi-disciplinary program that spans from the clinic to the laboratory, she has launched studies of that continue to reveal many genetic causes for epilepsy and other neurodevelopmental disorders, including novel discovery in the area of somatic mutation in pediatric brain disease. At BCH, she is a member of the steering committees of the Children's Rare Disease Cohorts Initiative and the Sandra L. Fenwick Pediatric Health Equity Institute. Beyond BCH, Ann serves as an elected member of the Board of the American Epilepsy Society and has served as an invited member of the Genomics Commission of the International League Against Epilepsy, Chair of the American Epilepsy Society/National Institute of Neurological Disorders and Stroke Benchmarks Stewards Committee, member of the NINDS NST1 study section, and on scientific advisory boards for companies and foundations devoted to developing precision medicine for patients with epilepsy. Her collaborative research and mentorship contributions have been recognized through numerous honors, including the American Neurological Association's Derek Denny-Brown Young Neurological Scholar Award, the American Academy of Neurology's Dreifuss-Penry Epilepsy Award, and the Harvard Club of Boston's Most Influential Women designation.

Beau Ances, MD, PhD, MSc, FANA

Washington University in St. Louis
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Beau Ances, MSc, MD, PhD, FANA is the inaugural Daniel J Brennan MD Professor of Neurology at Washington University in Saint Louis. He graduated from the University of Pennsylvania (1989); completed a masters in Health Planning and Finance at London School of Economics (1994); completed his Ph.D. and M.D. (2001) at the University of Pennsylvania; and completed Neurology residency (2005) at the Hospital of the University of Pennsylvania. He pursued a post- doctoral fellowship in Neuroimmunology at the University of California San Diego (2005-2008). His research focused on developing novel neuroimaging methods to assess changes in brain function due to HIV. He was recruited to Washington University in St. Louis (2008). Over the past 15 years, the Ances Bioimaging Laboratory (ABL) has focused on developing novel biomarkers for neurodegenerative diseases including HIV associated neurocognitive disorders (HAND), Alzheimer's disease (AD), autoimmune encephalitis, and Down syndrome. He has served on numerous NIH and private foundation study sections and more recently led a National Institute of Health (NIH) initiative to develop biotypes of central nervous system complications in people living with HIV. Dr. Ances is an author on over 270 publications (h-index 71) and his work has been cited by numerous media outlets (including the Associated Press, US News and World Report, Time, Discover, Washington Post) and been featured in a PBS documentary (Alzheimer's Disease: Every Minute Counts). He has mentored several undergraduate students, graduate students, post- doctoral candidates, and fellows. Members of his laboratory have received independent funding from NIH and private foundations.

Barbara Vickrey, MD, MPH

Icahn School of Medicine at Mount Sinai
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Barbara G. Vickrey, M.D., M.P.H., is the Henry P. and Georgette Goldschmidt Professor and System Chair of Neurology at the Icahn School of Medicine at Mount Sinai. She specializes in research to translate clinical evidence into improvements in routine medical practice to improve patient health. Among her accomplishments are demonstrating that collaboration among health care systems, community organizations, and caregivers can improve quality of care and outcomes for dementia patients. She has also designed and implemented studies generating evidence that coordinated, team-care models for veterans with Parkinson's disease improves quality of care. Dr. Vickrey is a member of the National Academy of Medicine and a former President of the American Neurological Association. She has mentored over 30 graduate and medical students, fellows, and junior faculty in clinical and health services research, many of whom are now successful faculty members and leaders in academic medicine. Dr. Vickrey earned her M.D. at Duke University School of Medicine and her M.P.H. at the UCLA School of Public Health. She completed postgraduate clinical training in medicine and neurology at the University of Washington in Seattle, and then research fellowships in the Robert Wood Johnson Clinical Scholars Program at UCLA and the RAND/UCLA Center for Health Policy Study.

Faculty

Dave Standaert, MD, PhD, FANA

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Dr. Standaert graduated from Harvard College and received M.D. and Ph.D. degrees from Washington University in St. Louis. Following Neurology residency at the University of Pennsylvania, he was appointed a Howard Hughes Fellow and completed a three-year research and clinical fellowship in Movement Disorders at Massachusetts General Hospital. He was a member of the faculty at Harvard Medical School from 1995 to 2006 and then relocated to the University of Alabama at Birmingham (UAB). Currently he is the John N. Whitaker Professor and Chair of the UAB Department of Neurology and a senior member of the faculty of the Division of Movement Disorders. He directs the NIH-funded Alabama Morris K. Udall Center of Excellence in Parkinson's Disease Research. He is Chairman of the Scientific Advisory Board of the American Parkinson Disease Association, a Deputy Editor of the journal Movement Disorders, a Fellow of both the American Academy of Neurology and the American Neurological Association, and First Vice President of the Association of University Professors of Neurology. He has previously served as a Director and Vice President of the American Neurological Association, and currently is the Vice Chair of the AON/ACTN Oversight Committee. He has also served on the NINDS Board of Scientific Counselors. His lab has a long-standing interest in the basic mechanisms underlying Parkinson disease as well as the complications of therapy.

Eric Landsness, MD, PhD

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Dr. Eric Landsness Is a physician-scientist with 20 years of expertise in stroke and neuroplasticity research. He obtained his MD PhD training at the University of Wisconsin focusing on understanding the underlying mechanisms of sleep and brain plasticity and their impact on disease. After completing clinical training in neurology and sleep medicine he joined the faculty at Washington University where his lab studies the bidirectional role of sleep and stroke. He has been involved in the ANA since residency and is passionate about introducing junior and early career neurologists to the ANA.

David Greer, MD, MA, FANA

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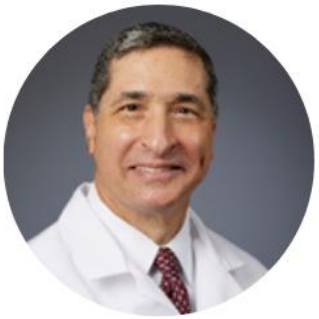

Dr. David Greer is Professor and Chair of the Department of Neurology at Boston University School of Medicine and the Richard B. Slifka Chief of Neurology at Boston Medical Center. He has been a neurointensivist since 2001, having trained at Massachusetts General Hospital, where he began his career. He was then Vice Chair at Yale from 2010-17, before joining Boston University and Boston Medical Center in 2017. Dr. Greer has been editor- in- chief of Seminars in Neurology since 203 and was the inaugural editor-in-chief for Neurocritical Care on Call. He has authored more than 350 peer-reviewed manuscripts, reviews, chapters, guidelines and books. He helped create the NCS Brain Death Toolkit and has previously served the Neurocritical Care Society on both the Board of Directors and the Executive Committee, and is current Treasurer for the NCS.

His research interests include predicting recovery from coma after cardiac arrest, brain death, and multiple stroke-related topics, including acute stroke treatment, temperature modulation and stroke prevention. He is the co-PI for the INTREPID study, evaluating fever prevention for acute vascular brain injury, and is an R01-funded investigator evaluating multi-modality imaging and EEG for assessing neuroprognosis after cardiac arrest. He was the lead author for the World Brain Death Project, and the lead author for the 2023 AAN Practice Parameters in Brain Death. Dr. Greer's greatest passion is in education in mentorship. In 2022, he received the prestigious A.B. Baker Lifetime Achievement Award for Neurological Education from the American Academy of Neurology. He has mentored innumerable students, residents, fellows and faculty, and considers himself a "lifelong mentor" for anyone and everyone he takes under his wing.

Ellen Mowry, MD, MCR, FANA

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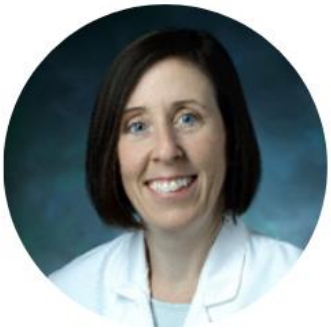

Dr. Ellen Mowry is Richard T. and Frances W. Johnson Professor of Neurology and Professor of Epidemiology at Johns Hopkins University. She completed her undergraduate degree in biology at Georgetown University, medical school at the University of Rochester, internship and neurology residency at the University of Pennsylvania, and a fellowship in multiple sclerosis and Master's degree in clinical research at the University of California, San Francisco. Her research focuses on environmental factors that influence the risk and prognosis of multiple sclerosis (MS) as well as on improving outcome measures for use in the clinic and in clinical trials. She also is/has been Principal Investigator (PI) or Co-PI of several investigator-initiated randomized trials, including Vitamin D to Ameliorate Multiple Sclerosis (VIDAMS), intranasal insulin for cognitive impairment in MS, Altering the Timing or Amount of Calories in MS (ATAC-MS), and the Traditional vs. Early Aggressive Therapy for MS (TREAT-MS) trials. Dr. Mowry also co-directs the Johns Hopkins MS Precision Medicine Center of Excellence and is Chief Medical Officer of Johns Hopkins in Health.

Frances E. Jensen, MD, FACP, FANA, FAAN, FAES

The University of Pennsylvania

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Dr. Jensen is Professor of Neurology and Chairman of Neurology at the Perelman School of Medicine, University of Pennsylvania, and Co-Director of Penn Translational Neuroscience Center. She was formerly Professor of Neurology, Harvard Medical School, Director of Translational Neuroscience and senior neurologist at Boston Children's Hospital and Brigham and Women's Hospital. After receiving her AB from Smith College and her MD from Cornell Medical College, she obtained her neurology residency training at the Harvard Longwood Neurology Residency Program. Her research focuses on mechanisms of epilepsy and stroke, and the mechanistic interaction of epilepsy with other disorders such as autism and dementia, with specific emphasis on elucidating new therapies for clinical trials development. Dr. Jensen received the 2007 Director's Pioneer Award from the NIH to explore the interaction between epileptogenesis and cognitive dysfunction and was elected as a member of the National Academy of Medicine in 2015. She has authored over 150 manuscripts on subjects related to her research and has been continuously funded by NIH since 1987 and received a NIH-NINDS Javits Award in 2020. Dr. Jensen has trained numerous clinical and basic research fellows who now hold independent faculty positions nationally and internationally. Dr. Jensen is currently President of the American Neurological Association (2020-2022) and was President of the American Epilepsy Society in 2012. She has served on multiple leadership boards including Society for Neuroscience and NIH. Dr. Jensen is a Trustee of the Franklin Institute in Philadelphia and is involved in community outreach for brain research and education. In addition, Dr. Jensen is an advocate for awareness of the adolescent brain development, its unique strengths, and vulnerabilities, as well as their impact on medical, social, and educational issues unique to teenagers and young adults, and author of the book "The Teenage Brain", released by Harper Collins in 2015/16, translated and published in over 25 languages worldwide.

Henry Paulson, MD, PhD, FANA

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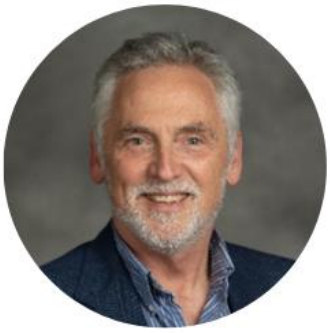

Henry L. Paulson, MD, PhD, is the Lucile Groff Professor of Neurology and director of the Michigan Alzheimer's Disease Center at the University of Michigan. Dr. Paulson received his MD and PhD in Cell Biology from Yale University in 1990, and then completed neurology residency and neurogenetics/movement disorders fellowships at the University of Pennsylvania. Her served on the Neurology faculty at the University of Iowa for ten years before moving to the University of Michigan in 2007. Dr. Paulson's research and clinical interests concern the causes and treatment of age-related neurodegenerative diseases, with an emphasis on polyglutamine diseases, Alzheimer's disease and frontotemporal dementia. Nationally, Dr. Paulson has served on the advisory boards of numerous disease-related national organizations and is currently a member of the National Advisory Council for Neurological Disorders and Stroke Council at the National Institutes of Health. Among his awards, Dr. Paulson was recipient of an Ellison Medical Foundation New Scholar in Aging Award, the Paul Beeson Physician Faculty Scholar in Aging Award, and the NINDS Landis Award for Outstanding Mentorship. He is an elected Fellow in the American Association for the Advancement of Science and a member of the National Academy of Medicine.

Jin-Moo Lee, MD, PhD, FANA

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Jin-Moo Lee, MD, PhD, is the Andrew B. & Gretchen P. Jones Professor, Chair of the Department of Neurology at Washington University School of Medicine, and Neurologist-in-Chief at Barnes-Jewish Hospital. Dr. Lee is a physician-scientist and vascular neurologist, who has dedicated his career towards understanding mechanisms underlying brain injury after stroke and repair of damaged circuits resulting in recovery. He has published more than 250 research articles, chapters, reviews and editorials. A major focus of Dr. Lee's academic career has been research mentoring—he has mentored more than a dozen K-awardees—and has received several awards for mentorship, including the Sven Eliasson Award for Teaching Excellence and the Washington University Distinguish Faculty Mentorship Award. Dr. Lee graduated from Yale College with a degree in Molecular Biophysics and Biochemistry, then attended Weill Cornell Medical College, earning an MD and PhD in neuroscience. After completing residency training at the University of Pennsylvania, he completed a neurovascular fellowship at Washington University, where he subsequently joined the faculty in the Department of Neurology.

Lesli E. Skolarus, MD, MS, FANA

Northwestern University
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Dr. Skolarus is a Professor of Neurology in the Vascular Neurology Division. Dr. Skolarus also serves as Vice Chair of Faculty Development and as Director of community engagement consultations in the Center for Community Health at NUCATS Institute. Her research focuses on promoting health equity and improving neurologic outcomes using community-based participatory research, health services research, and implementation science approaches. Prior to coming to Northwestern, Dr. Skolarus was Professor of Neurology, Professor of Health Behavior and Health Education, and Co-Director of the Vascular Neurology division at the University of Michigan.
Dr. Skolarus also serves as the Secretary of the American Neurological Association on the American Neurological Association's Board of Directors; and is a member of the National Institute of Neurological Disorders and Stroke Health Disparities Steering Committee where she co-leads the Social Determinants of Health Framework subcommittee.

Tish Weigand, PhD

National Institutes of Health
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Tish Weigand, Ph.D. is the Acting Director of the Office of Training and Workforce Development at NINDS. Dr. Weigand's career in science has hit the trifecta of academia, government, and industry. She began at the lab bench conducting research at the intersection of neuroscience, physiology and immunology, after which she entered government service at NINDS as a program analyst and manager in the Training Office. There she oversaw institutional training programs and many other initiatives for a number of years before moving on to work in the pharmaceutical industry as a Medical Science Liaison for UCB, serving as a regional expert on the science underlying the company's epilepsy portfolio. She recently made her return to NINDS to create and lead programs that support research training and career development for graduate students, postdocs, and early career physician scientists. Dr. Weigand holds a PhD from John Hopkins University and completed a postdoctoral training in neuroscience at George Washington University. She is passionate about preparing and equipping the next generation of scientists and professionals for success. Throughout her career she has served as a speaker and mentor throughout the biomedical and neuroscience communities. Dr. Weigand spends much of her free time sharing outdoor adventures with her husband and their three kids.

Louise McCullough, MD, PhD, FANA

McGovern Medical School at
UTHealth
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Dr. Dr. Louise McCullough is the Roy M. and Phyllis Gough Huffington Distinguished Chair and Professor of Neurology at McGovern Medical School at UTHealth. She is a physician-scientist and a practicing vascular neurologist with clinical expertise in sex/gender disparities, the microbiome, stroke and aging, and acute stroke treatments. A renowned investigator, she is well recognized for her work in cerebral vascular disease and is known for her research identifying sex differences in cell death pathways during stroke, which have now been shown to be a major factor in the response to an ischemic insult. Working closely with the Society for Women's Health Research (SWHR) and the Office of Research on Women's Health (ORWH), she was instrumental in the National Institute of Health's requirement to include female animals in basic and translational studies.

Among Dr. McCullough's many honors and awards are the prestigious National Institute of Neurological Disorders and Stroke (NINDS) Javits Neuroscience Investigator Award, the NINDS Landis Award for Outstanding Mentorship, the Inaugural American Heart Association (AHA) Outstanding Stroke Research Mentor Award, the AHA Merit Award, and the AHA Thomas Willis Lecture Award. She completed her PhD in Neuroscience and her MD from the University of Connecticut. She continued her training at Johns Hopkins, completing a neurology residency in 2000. Her residency was followed by a fellowship in cerebrovascular disease and stroke (2000-2002). After completing her training, she joined the faculty at Johns Hopkins Hospital and began her translational research career. Dr. McCullough returned to Connecticut in 2004 and rose to the rank of Professor in the Departments of Neurology and Neuroscience at The University of Connecticut Health Center and at the John Dempsey Hospital in Farmington, Connecticut. She became the Director of Stroke Research and Education at Hartford Hospital, and helped develop one of the largest stroke centers in New England. In 2015, she relocated to the University of Texas Health Science Center in Houston 2015 as the Chair of Neurology. The Neurology Department at UT Health has very active educational, clinical, and research programs, and is ranked highly in NIH funding.

M. Elizabeth Ross, MD, PhD, FANA

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Dr. Ross is the Nathan Cummings Professor of Neurology and Neuroscience and Director of the Center for Neurogenetics in the Brain and Mind Research Institute at Weill Cornell Medicine. She received her MD and PhD from Cornell University Medical College her Neurology residency at Massachusetts General Hospital and molecular genetic fellowships at MGH and Rockefeller University. She built her laboratory at University of Minnesota before returning to Weill Cornell Medicine as a tenured Professor. She is a physician scientist who leads the Laboratory of Neurogenetics and Development. Common threads in her work have been discovery of gene mutations causing neurological disorders as a window on the drivers of brain development and function. In addition to human genetics, her studies use cell biological tools, genetically engineered mice and patient derived stem cells to investigate the molecular mechanisms leading to disease. In 2015, she founded the Center for Neurogenetics at WCM. The Center has both basic science and clinical arms, and operates a patient DNA and cell biobank that supports translational research across the neurological community.

Dr. Ross has devoted much of her career to medical and neuroscience education. While at the University of Minnesota, she directed the NIH funded MD-PhD training program. At Weill Cornell Medicine she is Chair of the Neuroscience Graduate Program and is the founding Chair of the forming Master of Science in Genetic Counseling. Her current national service includes as an editorial board member of Annals of Neurology and Neurology Genetics, Chair of the NIH-CHHD-C study section, and President Elect of the American Neurological Association.

Mercedes Paredes, MD, PhD, FANA

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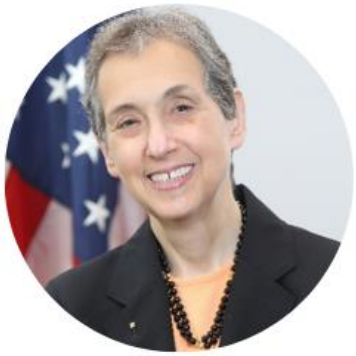
Mercedes Paredes is associate professor in the Department of Neurology and Neuroscience, Developmental and Stem Cell Biology, and Biomedical Sciences graduate programs at UCSF. She received her undergraduate degree from Harvard University and then joined the UCSF MSTP (Medical Scientist Training Program). She subsequently did residency in neurology at UCSF postdoctoral training with the Broad Center for Regenerative Medicine and Stem Cell Research. Her lab focuses on identifying features of neuronal progenitor proliferation and migration that are unique to the gyrated brain, such as in humans, with an emphasis on the perinatal period. She is a practicing neurologist who serves epilepsy patients with neurodevelopmental conditions, is an associate director for the UCSF MSTP, and holds a passion for mentoring UIM (or underrepresented in medicine) in careers in medicine, STEM, and neurology.

Nina Schor, MD, PhD, FANA

National Institute of Neurological Disorders and Stroke nina.schor@nih.gov



Nina F. Schor, MD, PhD is currently NIH Deputy Director for Intramural Research, a post she has held since August 2022. Before coming to NIH, Dr. Schor spent 20 years on faculty at the University of Pittsburgh, ultimately becoming the Carol Ann Craumer Professor of Pediatric Research, Chief of the Division of Child Neurology in the Department of Pediatrics, and Associate Dean for Medical Student Research at the medical school. In 2006, Dr. Schor became the William H. Eilinger Chair of the Department of Pediatrics, and Pediatrician-in- Chief of the Golisano Children's Hospital at the University of Rochester, posts she held until January 2018, when she became Deputy Director of the NINDS. For 27 years in academia, her research on neural crest development and neoplasia was continuously funded by NIH. At NINDS, she led the Division of Intramural Research and the Ultra-Rare GENe-targeted Therapies (URGenT) Network and strategic planning and career development programs. She also continues to serve as a Neurology Director for the American Board of Psychiatry and Neurology.

Romergryko G. Geocadin, MD, FANA

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Dr. Romergryko (Romer) G. Geocadin is a professor of neurology, of neurosurgery and of anesthesiology and critical care medicine at Johns Hopkins University School of Medicine. He holds a joint appointment in medicine. He completed his undergraduate education at the University of the Philippines, medical education at UERM School of Medicine in the Philippines, neurology residency at New York University and neurocritical care fellowship at Johns Hopkins. He is presently specializing in neurocritical care medicine at the Johns Hopkins Medical Institutions. His research focusing on translational studies and clinical trials in brain injury after cardiac arrest resuscitation is funded by the NIH. He has led or contributed to the development of many practice guidelines, scientific statements and reports from the American Academy of Neurology, American Heart Association, The Joint Commission and the Institutes of Medicine. He was Past President of the Neurocritical Care Society and the Vice President of the American Neurological Association for 2022 to 2024.

Oren Becher, MD

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Dr. Oren Becher, MD is a Professor of Pediatrics and Professor of Oncological Sciences at the Icahn School of Medicine at Mount Sinai. As a physician scientist, he leads a research group in addition to teaching students and seeing patients.

Dr. Becher's research, funded by the National Institutes of Health (NIH) and Department of Defense (DOD), uses genetically engineered mouse models to identify more effective therapies for children with DIPG or diffuse intrinsic pontine glioma. DIPG is an incurable childhood brain cancer that arises in the brainstem. Dr. Becher developed the first genetically engineered mouse models for DIPG. His research team is currently evaluating novel therapies in such models and are also developing novel models for other types of childhood brain cancers. Dr. Becher's research has been published in top scientific journals, and he serves on the advisory board of several leading pediatric cancer foundations. Dr. Becher has also initiated clinical trials for children with solid tumors evaluating novel therapies.

In addition to directing a research group, Dr. Becher provides patient care as a pediatric hematologist-oncologist and supervises pre- and post-doctoral trainees. He serves as a grant reviewer for several organizations including NIH. Dr. Becher has won numerous awards including being named a Damon Runyon Clinical Investigator, a St. Baldrick's scholar, a Forbeck scholar, and a Hyundai Hope on Wheels scholar. Dr. Becher earned his BA magna cum laude from the University of Pennsylvania, and MD from Johns Hopkins School of Medicine. He completed his pediatric residency at Children's National Medical Center in Washington DC and fellowship in Pediatric Hematology-Oncology and Pediatric Neuro-Oncology at Memorial Sloan-Kettering Cancer Center in NYC. Dr. Becher was on the faculty at Duke and Northwestern prior to coming to Mount Sinai.

Roy Hamilton, MD, MS, FAAN, FANA

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Dr. Roy Hamilton is a Professor of Neurology at the University of Pennsylvania, where his research focuses on employing noninvasive neuromodulation to characterize and remediate human cognition in neurological disorders. He is currently President of the Society for Cognitive and Behavioral Neurology. Dr. Hamilton has also been recognized for his advocacy for diversity in neurology and academic medicine. He is the Assistant Dean for Cultural Affairs and Diversity at Penn's Perelman School of Medicine, Vice Chair for Diversity and Inclusion for Penn Neurology, and an Associate Editor for Equity, Diversity, and Inclusion for the journal *Neurology* and its associated journals.

Sarah Berman, MD, PhD

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Sarah Berman, MD, PhD, is tenured Associate Professor of Neurology and Clinical & Translational Science, and Vice Chair of Academic Affairs for the Department of Neurology, at the University of Pittsburgh. She is also Director of the Clinical Core for the University of Pittsburgh Alzheimer's Disease Research Center (ADRC) and a Principal Investigator in the Pittsburgh Institute of Neurodegenerative Diseases (PIND). She received her undergraduate degree in Human Biology from Stanford University, MD and PhD (Neuroscience) degrees from the University of Pittsburgh School of Medicine, and residency and fellowship training at Johns Hopkins University. Her scientific research focuses on the role of mitochondrial dysfunction in neurodegenerative diseases such as Lewy Body diseases, initially studying early changes in mitochondrial dynamics and function in cell and animal models of neurodegeneration. More recently, she has developed clinical research utilizing human brain mitochondrial and bioenergetic imaging to elucidate mechanisms of pathogenesis in Lewy Body Dementia (LBD), Parkinson's disease (PD), and Alzheimer's disease (AD). She is also involved in overseeing several clinical research studies, including as Site Principal Investigator of the Dominantly Inherited Alzheimer Network studies and the Dementia with Lewy Bodies Consortium. Clinically, she specializes in care for people with LBD, PD, AD, and other movement disorders and dementias.

Thabele Bay Leslie-Mazwi, MD

University of Washington
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Bay Leslie-Mazwi serves as Chair of the Department of Neurology at the University of Washington. He is dual trained in Neurologic Critical Care and Interventional Neurology/Endovascular Neurosurgery. He co-directs the UW Medicine Neuroscience Institute, a strategic clinical entity that compromises Neurological Surgery and Neurology. Beyond his clinical and institutional duties he has appointments on various national committees, serves in an editorial role of several major cerebrovascular and specialty journals and has multiple societal roles in the key societies in the field. He is involved in clinical trial oversight for a variety of large, randomized, multicenter cerebrovascular trials. He is deeply passionate about improving care delivery.

S. Thomas Carmichael, MD, PhD, FANA

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S. Thomas Carmichael is a neurologist and neuroscientist in the Departments of Neurology and of Neurobiology at the David Geffen School of Medicine at UCLA. Dr. Carmichael is Professor and Chair of the Department of Neurology, co-Director of the UCLA Broad Stem Cell Center and co-Director of the Regenerative Medicine Theme in the David Geffen School of Medicine. He has active laboratory and clinical interests in stroke and neurorehabilitation and how the brain repairs from injury. He received his M.D. and Ph.D. degrees from Washington University School of Medicine in 1993 and 1994 and completed a Neurology residency at Washington University School of Medicine, serving as Chief Resident. Dr. Carmichael was a Howard Hughes Medical Institute postdoctoral fellow at UCLA from 1998-2001. He has been on the UCLA faculty since 2001. Dr. Carmichael's laboratory studies the molecular and cellular mechanisms of neural repair after stroke and other forms of brain injury. This research focuses on the processes of axonal sprouting and neural stem cell and progenitor responses after stroke, and on neural stem cell transplantation. Dr. Carmichael is an attending physician on the General Neurology and outpatient clinical services at UCLA.

Dr. Carmichael has published important papers on stroke recovery that have defined mechanisms of plasticity and repair. These include the fact that the stroke produces partially damage circuits that limit recovery, but can be restored to normal functioning with newly applied experimental drugs. His work has identified a novel brain "growth program" that is activated by stroke and leads to the formation of new connections. These studies have also identified how this growth program changes with age, and how specific molecules in the aged brain block the formation of new connections and of recovery. This and other work has led to new directions in stroke therapeutics, including therapies with stem cell and tissue engineering applications. Dr. Carmichael is in the midst of stroke stem cell development applications with the FDA and with biotechnology companies.

Walter Koroshetz, MD, FANA

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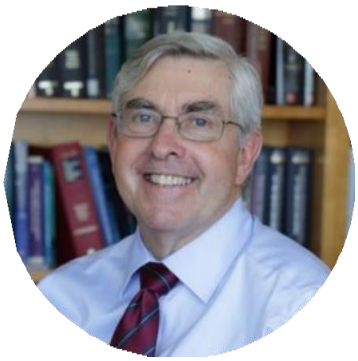

Walter Koroshetz is the Director of the National Institute of Neurological Disorders and Stroke (NINDS). He works to advance the mission of the Institute, to improve fundamental knowledge about the brain and the nervous system, and to use that knowledge to reduce the burden of neurological disorders. He joined NINDS as the Deputy Director in 2007. Before coming to NIH Dr. Koroshetz was a Harvard Professor of Neurology, Vice Chair of Neurology at the Massachusetts General Hospital, director of Stroke and Neurointensive Care, and a member of the MGH Movement Disorders clinic. His research activities spanned basic neurobiology to clinical trials. He directed Neurology training at MGH for 16 years. A graduate of Georgetown University and University of Chicago Medical School, Dr. Koroshetz specialized in Internal Medicine and Neurology.

William Stacey MD, PhD

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Dr. Stacey received both his medical degree and his PhD in Biomedical Engineering from Case Western Reserve University in Cleveland. He completed a Neurology residency at University Hospitals of Cleveland, then went to the University of Pennsylvania, to complete a clinical fellowship in Epilepsy. While there, he completed a post-doctorate in basic epilepsy research and also received a Master's of Translational Medicine. Dr. Stacey's clinical and research interests are integrally connected: he cares for adult patients with epilepsy and has an active research lab researching methods to understand and control seizures with implantable devices. The lab uses a combination of electrophysiology, machine learning, signal processing, and computational modeling. Data for these projects are acquired from a large, growing database of human patients and from rodent models of epilepsy. The lab is specifically researching the relationship of high frequency oscillations with seizure mechanisms, and developing methods to target and stimulate the brain to stop seizures. Concurrently, the lab is developing biophysical and dynamical models of epileptic activity to understand the mechanisms underlying seizures and epileptic oscillations.

William Renthal, MD, PhD

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Dr. Renthal is the Director of Research at the John R. Graham Headache Center at Brigham and Women's Hospital and an Associate Professor of Neurology at Harvard Medical School. He completed his MD, PhD and neurology residency at the University of Texas Southwestern Medical Center, headache medicine fellowship at Brigham and Women's Hospital, and postdoctoral research training at Harvard Medical School. Dr. Renthal treats patients with refractory headache and facial pain and directs a research laboratory that studies the genomic and epigenomic mechanisms that contribute to chronic headache and pain. He also directs the Harvard PRECISION Pain Center, a collaborative network of pain clinicians and scientists who procure phenotyped human pain-related tissues and characterize their cell types and states using single-cell multi-omic technologies. For this work he has received the Career Award in Medical Sciences from the Burroughs Wellcome Fund, the Harold Wolff-John Graham Pain Research Award from the American Academy of Neurology, the Rita Allen Scholar Award in Pain, and the Director's Pioneer and Trailblazer Awards from the National Institutes of Health.

Common Mistakes in NIH Grant Applications

The five review criteria for most NIH grant applications are Significance, Approach, Innovation, Investigator(s), and Environment. Innovation is not necessary, but the results should have compelling significance.

Problems with Significance:

Not significant nor exciting nor new research Lack of compelling rationale
Incremental and low impact research

Problems with Specific Aims:

Too ambitious, too much work proposed Unfocused aims, unclear goals
Limited aims and uncertain future directions

Problems with Experimental Approach:

Inappropriate level of experimental detail Feasibility of each aim not
shown Little or no expertise with approach
Lack of appropriate controls

Not directly testing hypothesis
Correlative or descriptive data
Experiments not directed towards mechanisms
No discussion of alternative models or
hypotheses No discussion of potential pitfalls

No discussion of interpretation of data
Inadequate description of statistical approach/analyses

Problems with Investigator(s):

No demonstration of expertise or publications in approaches
Low productivity, few recent papers
Collaborators needed but none recruited, or no letters from collaborators Inadequate funding

Problems with Environment:

Inadequate institutional support

NIH Websites

FUNDING COMPONENTS OF THE NIH

The NIH Homepage:
https://www.nih.gov

Homepages of the NIH Institutes, Centers & Offices: http://www.nih.gov/icd/

NIH GUIDE FOR GRANTS AND CONTRACTS
Program Announcements (PAs) and Request for Applications (RFAs):
http://www.nih.gov/grants/guide/index.html

NIH Grants Policy Statement:
http://grants.nih.gov/grants/policy/

APPLICATION PROCESS
NIH Grant Application Instructions, Guidelines and Forms: https://grants.nih.gov

SF424 (R&R) Application and Electronic Submission Information (including information on new biosketch formats):
http://grants.nih.gov/grants/funding/424/index.htm

NIH Modular Research Grant Applications:
https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/develop-your-budget/modular.htm

Standard Due Dates for Competing Applications:
https://grants.nih.gov/grants/how-to-apply-application- guide/due-dates-and-submission-policies/due-dates.htm

Center for Scientific Review:
http://www.csr.nih.gov/

NCI's Quick Guide to the Preparation of NIH Grant Applications:
https://deainfo.nci.nih.gov/extra/extdocs/gntapp.pdf

NIAID Samples of grant applications & more:
https://www.niaid.nih.gov/grants-contracts/sample- applications

NCCIH Tips for New NIH Research Grant Applicants:
https://www.nccih.nih.gov/grants/tips-for-new-nih- research-grant-applicants

REVIEW PROCESS

Review Criteria for Evaluation of Research Applications:
https://www.niaid.nih.gov/research/review-criteria

Descriptions of Initial Review Groups at the Center for Scientific Review:
http://www.csr.nih.gov/review/irgdesc.htm

NIH Center for Scientific Review Study Section Rosters:
http://www.csr.nih.gov/committees/rosterindex.asp

DATA ON ACTIVE GRANTS

Research Portfolio Online Reporting Tool (RePORT):
http://report.nih.gov/

NIH eRA Commons:
https://commons.era.nih.gov/commons/

SPECIAL PROGRAMS AT THE NIH

The K Awards:
https://www.niaid.nih.gov/grants-contracts/career- development-awards

Ruth L. Kirschstein National Research Service Awards Institutional Research Training Grants Individual Fellowships:
https://grants.nih.gov/grants/guide/pa- files/PA-23-048.html

R03/Small Grant Program:
https://grants.nih.gov/grants/funding/r03.htm

AREA or R15 for Non-Research-Intensive Colleges and Universities:
http://www.nih.gov/grants/funding/area.html

SBIR/STTR
Homepage:
https://sbir.nih.gov/

K Awardee Attendee List

FIRST NAME	LAST NAME	CREDENTIALS	INSTITUTION	CITY	STATE
Edilberto	Amorim	MD	University of California, San Francisco	San Francisco	CA
Maria	Barnes-Davis	MD, PHD	Cincinnati Children's Hospital Medical Center	Cincinnati	OH
Sarah	Berth	MD, PhD	Baylor College of Medicine	Houston	TX
Jason	Chua	MD, PhD	Johns Hopkins	Baltimore	MD
David	Coughlin	MD, MTR	University of California San Diego	San Diego	CA
Terry	Dean	MD PhD	Children's National Hospital	Washington	DC
Anna	Duncan	MD, MHS	Massachusetts General Hospital	Boston	MA
Darius	Ebrahimi-Fakhari	MD, PhD	Boston Children's Hospital	Boston	MA
Joline	Fan	MD	University of California, San Francisco	San Francisco	CA
Thomas	Foutz	MD, PhD	Washington University in St. Louis	St. Louis	MO
Jason	Gill	MD, PhD	Baylor College of Medicine	Houston	TX
James	Gugger	MD, PharmD	University of Pennsylvania Perelman School of Medicine	Philadelphia	PA
Elan	Guterman	MD, MAS	University of California, San Francisco	San Francisco	CA
Chloe	Hill	MD, MS	University of Michigan	Ann Arbor	MI
Jennifer	Hranilovich	MD	University of Colorado School of Medicine	Aurora	CO
David	Isaacs	MD, MPH	Vanderbilt University Medical Center	Nashville	TN
Michelle	Johansen	MD, PhD, FAHA	The Johns Hopkins University School of Medicine	Baltimore	MD
Eric	Kaiser	MD, PhD	University of Pennsylvania	Philadelphia	PA
Jennifer	Kim	MD PhD	Yale SOM	New Haven	CT
Courtney	Lane-Donovan	MD, PhD	UCSF	San Francisco	CA
Allison	Martin	MD	Albert Einstein College of Medicine	Bronx	NY
Lindsay	McAlpine	MD	Yale University	New Haven	CT

K Awardee Attendee List

FIRST NAME	LAST NAME	CREDENTIALS	INSTITUTION	CITY	STATE
Melanie	McNally	MD	Massachusetts General Hospital	Boston	MA
Niccolo	Mencacci	MD, PhD	Northwestern University	Chicago	IL
Imama	Naqvi	MD, MS	Columbia University	New York	NY
Charlene	Ong	MD, MPHS	Boston University Chobanian	Boston	MA
Archana	Patel	MD MPH Msc	Boston Children's Hospital, Harvard Medical School	Boston	MA
Sam	Payabvash	MD	Yale	New Haven	CT
Jeffrey	Russ	MD, PhD	Duke University	Durham	NC
Rani	Sarkis	MD,MSc.	Brigham and Women's Hospital	Boston	MA
Samuel	Snider	MD	Brigham and Women's Hospital	Boston	MA
David	Soleimani-Meigooni	MD	University of California, San Francisco	San Francisco	CA
Christopher	Stephen	MB ChB, FRCP, SM	Massachusetts General Hospital and Harvard Medical School	Boston	MA
Yunshuo	Tang	MD, PhD	Washington University in Saint Louis	Saint Louis	MO
Thomas	Tropea	DO, MPH, MTR	University of Pennsylvania Perelman School of Medicine	Philadelphia	PA
William	Zeiger	MD, PhD	University of California - Los Angeles	Los Angeles	CA
Julie	Ziobro	MD, PhD	University of Michigan	Ann Arbor	MI
Nick	Brenton	MD	University of Virginia	Charlottesville	VA
Paloma	Gonzalez Perez	MD, PhD	Massachusetts General Hospital	BOSTON	MA
Gunisha	Kaur	MD, MA	Weill Cornell Medicine	New York	NY
Michael	Lopez	MD, PhD	The University of Alabama at Birmingham	Birmingham	AL
Julie	Miller	MD, PhD	Massachusetts General Hospital	Boston	MA
Ranmal	Samarasinghe	MD, PhD	UCLA	Los Angeles	CA
Regina	Triplett	MD, MS	Washington University in St. Louis	Saint Louis	MO
Melissa	Walker	MD, PhD	Massachusetts General Hospital	Boston	MA

2024 ANA-NINDS K-Awardee Abstracts

Autoimmune Neurology and MS

Synaptic Loss in Relapsing and Progressive Multiple Sclerosis: An In Vivo Exploratory Study using SV2A-PET
Presenting Author: ***David Soleimani-Meigooni, MD, University of California, San Francisco***
Co-Authors: Joseph Giorgio, PhD, UC, Berkeley, Ahmed Abdelhak, MD, University of California, San Francisco, Christian Cordano, MD, PhD, University of California, San Francisco, Xi Chen, PhD, University of California, Berkeley, Tyler N. Toueg, University of California, Berkeley, Robby Weimer, PhD, Genentech, Inc, Bastian Zinnhardt, PhD, F. Hoffmann-La Roche Ltd, Suzanne L. Baker, PhD, Lawrence Berkeley National Laboratory, Mustafa Janabi, PhD, Lawrence Berkeley National Laboratory, Ari Green, MD, University of California, San Francisco, William J. Jagust, MD, University of California, Berkeley, Gil D. Rabinovici, MD, University of California, San Francisco
Background: Multiple sclerosis (MS) is a neurodegenerative disease associated with early and widespread synaptic loss in cortical gray matter that dynamically changes and may be prominent in progressive disease phases. [18F]SynVesT-1, which targets synaptic vesicle glycoprotein 2A (SV2A), could be used as an in vivo biomarker of synaptic changes in MS. **Methods**: Ten relapsing MS (RMS) or progressive MS (PMS) participants, with brain MRI, neurological exam, and Expanded Disability Status Scale (EDSS) assessment, underwent [18F]SynVesT-1 PET. We collected 90-minute dynamic PET data after injection of 5 mCi of [18F]SynVesT-1. Participant whole-brain Distribution Volume Ratio (DVR) images were generated using a cerebellar grey matter reference region, with and without two-compartment partial volume correction (PVC). Quantification was performed at a priori selected regions of interest, including bilateral hippocampus, posterior cingulate, frontal lobes, parietal lobes, and temporal lobes. [18F]SynVesT-1 DVR images from seven young healthy controls (YHC) and eight cognitively unimpaired older healthy controls with negative [11C]PiB amyloid-PET (OHC-) were available for comparison. **Results:** MS participants were 52.9Â±10.6 years and 40% female, YHC were 26.1Â±3.8 years and 29% female, and OHC- were 78.6Â±10.6 years and 50% female. For MS participants, six had RMS (mean EDSS 2.3Â±1.0) and four had PMS (mean EDSS 5.1Â±2.2). Visually, RMS had lower cortical tracer uptake than YHC and similar binding to OHC-. PMS had the lowest cortical tracer retention. Quantitatively, at the hippocampus, there was a significant effect of group (ANOVA F(3,21)=4.17, p=0.018), and post hoc Bonferroni test revealed that PMS had significantly lower tracer uptake (p=0.036; median 0.84, interquartile range [IQR] 0.70-0.94) and RMS trended towards lower tracer uptake (p=0.066; median 0.84, IQR 0.82-0.90) compared to OHC- (median 0.96, IQR 0.94-1.08). There was a trend towards significant group differences at the parietal lobes (F(3,21)=2.53, p=0.085) and non-significant numerical differences at other regions that suggested lower synaptic density in PMS compared to RMS and controls. Without PVC, there was a significant effect of group at frontal lobes (F(3,21)=3.70, p=0.028) and parietal lobes (F(3,21)=4.11, p=0.019). In these regions, post hoc Bonferroni test revealed that PMS had significantly lower tracer uptake than YHC (frontal: p=0.042, PMS median 1.06, IQR 1.02-1.17 vs. YHC median 1.22, IQR 1.17-1.29; parietal: p=0.017, PMS median 1.07, IQR 0.99-1.16 vs. YHC median 1.22, IQR 1.18-1.30). **Conclusions:** We demonstrate the first in vivo application of SV2A-PET to estimate synaptic density changes in MS. MS patients could have widespread reduction in synaptic density, greatest in PMS.

Obesity as a Driver of Inflammation and Brain Volume Loss in Pediatric Multiple Sclerosis
Presenting Author: ***Nick Brenton, MD, PhD, University of Virginia***
Co-Authors: Karen C Johnston, M.D. M.Sc. - University of Virginia, Myla D. Goldman, M.D. - Virginia Commonwealth University, Brenda L. Banwell, M.D. - Children's Hospital of Philadelphia
Background: Children with MS experience failure of age-expected brain growth followed by progressive atrophy during adolescence. Childhood obesity is an established risk determinant for pediatric MS, however, the impact of persisting obesity on MS disease course is unknown. In non- MS youth, obesity (a national health epidemic) associates with progressive brain volume loss. In adults with MS, greater levels of obesity are associated with significantly reduced normalized brain volumes. The impact of obesity in children with MS has not been studied and the implications of this are particularly important in a pediatric patient - where the negative impact of obesity on the CNS may exert an even greater detrimental effect on a brain that is still undergoing development. We hypothesize that: a) MS is more severe in obese pediatric subjects compared to normal weight subjects, as measured by whole brain volume and inflammatory demyelinating lesion volume and b) obesity enhances immune dysregulation and inflammation, which accelerates MS severity and progression. **Methods:** This is a multicenter prospective trial of 58 pediatric MS patients that compares to a cohort of age-, sex-, and BMI-matched non-MS controls in 1:1 allocation. The aims of this study are to determine if obesity modifies biomarkers of 1) inflammation (measured radiologically by T2-hyperintense inflammatory lesion volumes & serologically by adipocyte-derived cytokines) and 2) neurodegeneration (measured radiologically by whole brain volumetrics & serologically by neurofilament light chain). For imaging endpoints, MS subjects undergo MRI to quantify total brain and lesion volume. Volumetric Z-scores are determined

using normative data from a large, healthy adolescent cohort and will be compared between our obese vs non-obese MS subjects, after adjusting for important clinical and demographic characteristics. For serologic endpoints, fasting adipocytokine profiles and neurofilament light chain will be compared between MS subjects and matched healthy controls. **Results:** Multisite IRB approval and subcontract execution was completed in March 2021. Validation and calibration of multisite magnetic resonance imaging protocols was completed in April 2021. The first subject was enrolled in May 2021. We have recruited 55 of 58 planned pediatric MS subjects and 43 of 58 age-, sex-, and BMI-matched controls. Mean age of the current cohort is 16.7 Â± 2.3 years and mean BMI is 29.3 Â± 7.3. Two-thirds of the cohort is female. Fifty-eight percent of subjects identify as White, 38% as Black, and 4% as Other. One-fifth identify as Hispanic or Latino/a ethnicity. This study is set to complete enrollment and begin data analysis at the end of summer. **Conclusions:** Our study will define the role of obesity in pediatric MS and will set the stage for future intervention studies aimed at modifiable risk factors in MS. This study represents the first and only prospective study evaluating the role of obesity on pediatric MS disease severity at presentation. Next steps include: 1) understanding the mechanisms of obesity-induced inflammation in MS, 2) longitudinal observation of T2-lesion and brain volume trajectories in obese vs non-obese pediatric MS patients, and ultimately 3) implementation of an obesity intervention to assess the impact of weight loss on progressive brain atropgillhy over time.

Cerebrovascular Disease

Proteomics and the Risk of Incident Embolic and Thrombotic Stroke in the Atherosclerosis Risk in Communities Study
Presenting Author: ***Michelle Johansen, MD, PhD, FAHA, Johns Hopkins University School of Medicine***
Co-Authors: Jinyu Chen, MS, UNC School of Medicine, James Russell Pike, MBA, NYU Langone School of Medicine, Wendy Wang, PhD, University of Minnesota, Lin Yee Chen, MD, MS, University of Minnesota
Background: Ischemic stroke is a devastating disease, with patient treatment and expected outcomes varying depending on the specific stroke type. While vascular risk factors are an important determining factor in stroke etiology, there is frequently overlap, so the presence of one versus the other is not sufficient to define stroke etiology. It is possible that there are intrinsic factors to the person, such as plasma protein levels, that make a particular stroke subtype more likely to occur, even in the setting of similar vascular risk. Research relating proteomics markers to ischemic stroke subtype risk is limited, and prior research has mainly measured proteins after stroke has already occurred, which is not an accurate measure of risk. We propose to use the Atherosclerosis Risk in Communities (ARIC) study, with ~5,000 proteins measured at two time points to determine the proteomic signatures associated with risk of a specific stroke subtype. We hypothesize differences in the proteomic signatures of incident embolic (ES) and thrombotic ischemic stroke (TS) that reflect differences in stroke pathogenesis and differ by age. **Methods:** We leveraged proteins (n=4956) from stroke-free participants in the ARIC Study at their 2nd visit (1990-1992) which were obtained using SomaScan aptamer technology. Briefly, SomaScan uses Slow Offrate Modified Aptamer (SOMAmer) reagents to quantify the relative abundance of thousands of proteins in as little as 55uL of blood, with multiple steps to ensure quality control. These participants were followed into mid-life (visit 2 until visit 5, mean age 60 years) and then late-life (visit 5 until 2020, mean age 78 years). After testing for model fit, adjusted Cox regression models determined the association between log base-2 transformed protein levels and EIS, and TIS by visit 5 (2011-2013), or by the current end of surveillance (2020). Differences between the risk of each subtype was determined by bootstrapping differences in risk estimates for EIS and TIS (1000 iterations). We applied a Bonferroni correction to our results, which was at p<0.05/4956 (number of proteins) =1.008x10-5 for EIS, and TIS individually. The significance level for the difference p-value was set at p<0.05 divided by the number of significant hits discovered in each cohort. **Results:** Among 10929 participants eligible (56% female, 23% Black), the average overall length of follow-up was 24.6 years (IQR 16-27.7) and average time to stroke event was (17.6 years (IQR 11.6-23.1) for EIB events, and 13.4 years (IQR 7.1-20.6) for TIB events). 20 proteins were associated with either EIS (168 events) or TIS (459 events) in mid-life, and 4 in late-life (73 EIS and 124 TIS events) at the Bonferroni threshold p<1E-5. Of the 20 protein associations in midlife, N-terminal pro-B-type natriuretic peptide (NT-proBNP) was significantly associated with EIS, and more strongly associated with EIS than TIS (p-difference=9.14E-7). Of the remaining 19 proteins, eight were strongly associated with TIS and only nominally (p<0.05) associated with EIS (e.g. Thrombospondin-2, TIS HR 1.30 (95%CI 1.19-1.41), EIS HR 1.19 (95%CI 1.03-1.38)) while 11 additional proteins were associated with only TIS (e.g. Interleukin-12, and Interleukin-23). In late-life, NT-proBNP, Serine protease inhibitor Kazal-type 4, Oligodendrocyte-myelin-glycoprotein, and Neurocan core protein were significantly strongly associated with EIS, but not TIS while Plasma protease C1 inhibitor showed the opposite pattern (p-difference=0.04). **Conclusions:** Among participants in a longitudinal cohort study, we identified different plasma proteins that were associated with risk of EIS versus TIS that reflect distinct pathogenesis and underlying stroke mechanisms, with differences by age. We found evidence of increased cardiac dysfunction proteins in EIS (e.g. NT-proBNP) that did march across age, and proteins associated with inflammation and atherogenesis in TIS (e.g. interleukins) that were distinct by age. We plan to expand, and replicate this work in other cohorts, and perform pathway analyses to determine potential causal mechanisms.

Deep-learning Model for Prediction of Hematoma Growth after Intracerebral Hemorrhage from Admission Head CT
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Objective: Hematoma expansion (HE) is associated with early clinical deterioration, poorer long-term outcomes, and increased mortality in patients with intracerebral hemorrhage (ICH). Identifying patients at risk of HE could enable the targeting of anti-expansion or hemostatic therapies in future clinical trials. We aimed to develop, train, and validate a deep learning model that predicts HE based on admission non-contrast head CT scans. **Methods:** We used a publicly available dataset of 9,776 head CT scans (SinoCT) to pre-train a deep learning model for differentiating between normal and abnormal head CTs. For the training of HE prediction, we utilized a dataset of 890 patients from the Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH-2) trial. We combined the pre-trained model with de novo trained models to predict binary HE ranging from >1 to >12 mL. The model was validated on a cohort of 683 patients from Yale. The accuracy of the prediction was determined using the receiver operating characteristics (ROC) area under the curve (AUC). **Results**: In both training and validation cohorts, the admission head CT scans were obtained within 12 hours of onset. In independent validation cohort, the model achieved an average overall AUC of 0.81 in prediction of >1 to >12 mL HE. The AUC for prediction of >2 mL to >12 mL HE ranged from 0.8 to 0.82 in, with sensitivity of 0.71 to 0.93 and specificity of 0.63 to 0.79. Whereas, for prediction of >1 mL HE, the model achieved an AUC of 0.7 with 0.89 sensitivity and 0.38 specificity. **Conclusion:** While prior studies have focused on single binary definition of HE, we devised a series of predictive models to identify patients at risk of 1 to 12 mL HE based on admission non-contrast head CT. Our automated models could predict >2 to >12 mL HE with at least 0.8 AUC in independent validation.

Epilepsy

Global Network Disruption Across Sleep-wake States in Focal Epilepsy
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Background: Sleep and epilepsy have long been known to exert bidirectional influences. While sleep states endogenously facilitate and suppress epileptic activity, epilepsy has been linked to disruptions in sleep architecture. However, less is known about the effects of epilepsy on the large-scale functional network during sleep and how network disturbances relate to the seizure onset zone. Identifying global network disturbance across sleep-wake states may add to the conceptual understanding of epilepsy as a network disorder and provide a mechanism for network-based comorbidities that also relate to sleep, including cognition and mood. **Objective:** To assess the patterns of state-specific network dysfunction of focal epilepsy on multiple spatial scales. **Methods:**
Simultaneous magnetoencephalography (MEG) and electroencephalography (EEG) were collected in 72 individuals with non-lesional focal epilepsy (localization: n=45 temporal lobe; 27 extratemporal lobe) and 17 age-matched healthy controls. Sixty-second artifact-free epochs of wake and stage 2 NREM (N2) sleep were identified by scalp EEG. Atlas-based source reconstructions were performed using adaptive beamforming methods. Network measures were constructed on three spatial scales: 1) local synchrony as measured by spectral power, 2) long-range synchrony as measured by the functional connectivity metric: imaginary coherence, and 3) spatial entropy based on functional activity projections onto structural connectome (SC) harmonics. Specifically, we decomposed the SC into elementary harmonics or eigenmodes, derived from the normalized Laplacian of a group-averaged consensus SC. Source-reconstructed MEG time series were then projected onto the SC eigenmodes to produce eigenmode loadings. Spatial entropy was computed based on the mean distribution of eigenmode loadings for each time point. **Results:** Using the normative connectivity maps derived from the age-matched healthy cohort, we identified widespread network disruption during wakefulness and N2. In N2, local synchrony in focal epilepsy was decreased in the alpha frequency range over the temporal-parietal regions. Long-range synchrony in focal epilepsy was significantly reduced across the delta, theta, alpha, and gamma frequency bands across the entire brain network. Strikingly, the network disruption in both local and long-range synchrony was spatially correlated between extratemporal and temporal lobe seizure onset localization in both wakefulness (local synchrony, r=0.669-0.831; long-range synchrony, 0.577-0.732 across all frequencies) and N2 (local, r=0.623-0.777; long-range, r=0.500-0.745), suggesting that the global network disturbances are independent of seizure onset regions in both sleep-wake states. In addition, global network disturbances of local and long-range synchrony were correlated across all frequency bands (local, r=0.257-0.867; long-range,

r=-0.152-0.338), except in the theta frequency band (local, r=-0.181; long-range, r=0.119). Finally, when considering state and frequency as factors, spatial entropy was decreased in epilepsy as compared to healthy cohorts (F=24.6, p<0.0001). **Conclusion:** Our findings reveal global network disturbances across multiple spatial scales that pervade both sleep and wake states in non-lesional focal epilepsy. Intriguingly, these global network disruptions are largely independent of seizure onset zone, which may relate to a global network process or dysfunction of central source, such as the thalamus. Ultimately, these findings of disrupted network physiology in both sleep and wakefulness support epilepsy as a network disorder and may provide an underlying mechanism for network-based comorbidities.

Insights from Centromedian Thalamic Stimulation Evoked Responses to Improve Brain Stimulation Therapies
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Background: Drug-resistant epilepsy affects approximately 1 million people in the United States. While deep brain stimulation (DBS) presents a promising treatment option for refractory seizures, optimizing its effectiveness has proven challenging due to factors such as inter-patient variability, electrode placement, and the wide range of available stimulation parameters. The centromedian nucleus (CMN) has emerged as a potential therapeutic target for refractory epilepsy, but the optimal implantation target and stimulation settings remain unclear. Therefore, the primary objective of this study is to investigate the effects of CMN-DBS on surface and intra-thalamic EEG through external time-synced, intra-thalamic stimulation to gain valuable insights into optimal programming strategies. **Methods**: In the anesthetized state during the operating room implantation procedure, high-frequency stimulation (40-50 Hz) was administered pairwise to each of 8 contact pairs. This stimulation was delivered in 5 trains of 5 stimulation periods, using amplitude intensities ranging from 2-6 mA and a pulse width of 250 microseconds. Simultaneous recordings were obtained from the scalp and intrathalamic regions and subsequently analyzed. Interpolation over the stimulation artifacts was used, and the frequency band activity during stimulation was compared to the non-stimulated baseline.
Results: Seven patients (ages 11 to 29) with medically refractory epilepsy, including four individuals with Lennox-Gastaut syndrome, underwent comprehensive surgical evaluation at our institution. Following a multidisciplinary conference, DBS implantation was recommended. Pooled analysis of all stimulation settings revealed a significant increase of beta-frequency activity during stimulation by 37% (p=0.01) and theta-frequency activity by 26% (p<0.01) with high-frequency stimulation. Additionally, individual patients exhibited a spatial dependence in the effects of beta and theta frequency power, suggesting potential therapeutic significance. **Conclusions:** Our findings indicate that evoked EEG responses to high-frequency stimulation can be reliably detected through CMN-DBS stimulation in the anesthetized state. This approach holds promise as a valuable biomarker for improving implantation and optimizing stimulation settings in DBS treatment. **Acknowledgments**: This work was supported by the American Epilepsy Society and the National Institutes of Health

Structural Neuroimaging Phenotypes of Post-Traumatic Epilepsy
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Background: Both traumatic brain injury (TBI) and epilepsy are disorders of abnormal, distributed structural brain networks. Widespread abnormalities in the white matter scaffolding of brain networks represent a shared pathophysiologic mechanism between TBI and epilepsy and warrants investigation as a biomarker for epilepsy prediction after TBI. The objective of this study is to assess alterations in structural networks inferred from structural neuroimaging during the subacute and chronic periods after TBI and use these measurements as features to distinguish patients who will develop post-traumatic epilepsy (PTE) from those who will not. **Methods**: This study will utilize anatomic and diffusion weighted imaging data from participants with TBI as well as orthopedic and uninjured friend controls enrolled in the Transforming Research and Clinical Knowledge in Traumatic Brain Injury Epileptogenesis Project. Participants in this study undergo telephone screening for seizures annually for up to five years post-injury. Using orthopedic and uninjured friend control data, we will establish the control distribution for measures of structural network topology (i.e., degree, strength clustering coefficient, global efficiency, betweenness centrality) and structural network integrity. Next, we will examine differences in network measures between patients with and without PTE. As each cohort undergoes two MRIs approximately six months apart, we will utilize linear mixed effects models

to compare the evolution of structural network measures over the six-month post-injury period. Due to the small number of participants who screened positive for late post-traumatic seizures (i.e., PTE), we included an additional cohort with a pre-existing seizure disorder complicated by TBI. Inclusion of this cohort will permit us to assess for differences in structural networks between TBI participants with a pre-existing seizure disorder and PTE. **Results:** At the time of writing, we identified 887 who completed at least one MRI. Of these participants, 18 screened positive for PTE, 52 had a pre-injury seizure disorder, and 817 had trauma-only. Results of network analyses are forthcoming.

Evaluating the Feasibility of Prehospital Point-of-care EEG: The Prehospital Implementation of Rapid EEG (PHIRE) Study
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Background: Conventional electroencephalography (EEG) is an established technology used to monitor brain electrical activity that takes time to apply and requires a specialized technologist. Point-of-care EEG is applied more rapidly and does not require a specialized provider, creating new opportunities to use Point-of-Care EEG during prehospital Emergency Medical Services (EMS) care. We evaluated the feasibility of obtaining high-quality Point-of-Care EEG recordings during real-world ambulance transport for 911 calls. **Methods:** This mixed-methods study was conducted at Alameda Fire Department between May 28, 2022 and October 28, 2023. Data included provider surveys, field notes, chart review, and structured review of Point-of-Care EEG recordings. There was mandatory training for all paramedic and emergency medical technician clinicians who were instructed to identify eligible individuals during their routine clinical duties, treat the patient according to the standard EMS agency treatment protocol, apply the Point-of-Care EEG headband after treating any emergent medical issues, and obtain an EEG recording while driving to the destination hospital. Eligible individuals included patients aged six years or older who were being evaluated for seizure, stroke, or altered mental status. EMS clinicians completed a survey and participated in a brief phone call following every enrollment. Two epileptologists reviewed point-of-care EEG recordings for interpretability and artifact. **Results:** There were 34 prehospital encounters in which Point-of-Care EEG was applied. Patients had a mean age of 69.2 years (SD 21 years), and 14 (41.2%) were female. EEG recordings had a mean duration of 13 minutes and 22 seconds. It took EMS clinicians an average of 2.5 minutes to apply the EEG device. There were 13 (46.4%) recordings where clinicians achieved a high-quality connection for all ten electrodes, 32 (94%) recordings of adequate quality to interpret, 23 (67.6%) recordings with two or more channels free of artifact in each hemisphere for 5 minutes or more, and 20 (66.7%) recordings with seven or more channels free of artifact. The two (6%) recordings that could not be interpreted included one recording that was 2 seconds long and one recording with substantial artifact. All clinicians agreed or strongly agreed that the device was easy to use. **Conclusion:** Among real-world prehospital encounters for patients with seizures, stroke, and altered mental status, Point-of-Care EEG was rapidly applied and yielded EEG recordings that could be used for clinical interpretation, demonstrating the feasibility of incorporating point-of-care EEG technology into future prehospital care.

Developing a Clinic-Based Priority Communication Tool to Improve Outcomes for Patients with Drug-Resistant Epilepsy
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Background: While pursuit of seizure freedom dominates epilepsy care, there are other important determinants of quality of life, such as mental health or cognitive function, that may be overshadowed in a clinic visit. Optimizing patient-provider communication about individual health priorities may lead to opportunities to improve patient-centered outcomes. Priority communication tools have been employed in the primary care setting to elicit patient priorities and facilitate patient-provider goal setting, but no such tools yet exist for patients with drug-resistant epilepsy. Thus, we are partnering with patients with drug-resistant epilepsy to develop a priority communication tool, the Epilepsy Visit Planners, to be used prior to epilepsy clinic visits. **Methods:** To start, we performed a systematic literature search to identify health goals of patients with drug-resistant epilepsy. We then conducted 22 semi-structured interviews of patients with drug-resistant epilepsy. In early interviews (n=12), we confirmed the list of clinic visit goals and added novel clinic visit goals identified by participants. In later stages (n=10), we adapted the language to be patient-centric and prioritized the goals based on frequency using patient participatory design approaches. We made further adaptations after reviewing with health communication experts. **Results:** The initial list of 25 items included seizures, comorbidities, side effects, work/disability, transportation, social/family considerations, safety restrictions, cost of care, and access to care. With feedback from participants regarding both content

and language, we developed a list of six medical goals that could be reliably understood and ranked. These included: 1) “Decreasing the number or severity of my seizures”, 2) “Improving my memory, thinking, or speech”, 3) “Improving my mental health (mood, stress, anxiety, depression, anger)”, 4) Increasing my energy and/or reducing my fatigue, 5) “Improving my physical symptoms (such as tremor or poor balance or weight change)”, 6) “Improving my sleep (such as falling asleep or staying asleep)”. We also included categories of non-medical goals: daily activities, driving or transportation, safety, emotional support, family planning, and money. **Discussion:** Partnering with patients with drug-resistant epilepsy, we identified key goals for clinic-based patient prioritization communications. We will next adapt an existing primary care prototype to include the above-developed content specific for epilepsy. Our Epilepsy Visit Planners will then undergo usability testing in the target population, guided by principles of user-centered design. Once completed, we will test our Epilepsy Visit Planners in a clinical trial, with primary patient/provider communication outcomes and secondary clinical outcomes.

Late Onset Unexplained Epilepsy is Associated with Verbal Memory Impairment and Lower Amydala Volumes
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Background: Late-onset unexplained epilepsy (LOUE) has been associated with a higher risk of dementia, although the reasons for this elevated risk are unclear. Thus, there is a need to understand the pathophysiology behind LOUE and whether neurodegenerative and cerebrovascular pathologies contribute to its etiology. The goal of the study was to characterize the cognitive profile, and MRI findings of patients with LOUE in contrast to a healthy older sample to better understand potential underlying disease mechanisms. **Methods**: In this prospective cross-sectional cohort study we recruited participants with at least 1 new-onset unexplained seizure in the last 5 years with onset >55 years, and absence of MRI cortical lesions. A neuropsychological battery was administered to generate the Preclinical Alzheimer Cognitive Composite (PACC) and composite scores for delayed verbal recall, processing speed, and executive function. A 24-hour EEG was obtained and evaluated for the presence of epileptiform abnormalities. Additionally, MRI volumetric analysis of hippocampal (HV), amygdala (AV), and white matter hyperintensity volumes (WMV) was performed. The control group consisted of 353 participants from the Harvard Aging Brain Study (HABS) who were older than 55 and had no history of neurologic disease. **Results**: Sixty-five participants were recruited, mean (Â±SD) age 70.8 Â± 7.0 years, 48% female. EEG captured epileptiform abnormalities in 46% with left temporal predominance (57%). Cognitive performance in the mild cognitive impairment range (z-score-1.5) for LOUE participants included: 15.5% for PACC, 25.0% for delayed verbal recall, 15.3% for processing speed, and 6.6% for executive function. When controlling for age, sex, and race, LOUE group had lower AV(%) (β =-0.006, 95%CI[-0.010 to -0.003], p=0.0009) and log transformed WMV(mm3) (β =-0.19, 95%CI[-0.38 to -0.01], p=0.035) compared to HABS. There were no differences in HV(%) (β =-0.004, 95%CI[-0.011 to +0.003], p=0.24) between groups. **Discussion:** In this single-center study, we found that LOUE is predominantly a temporal disease with left sided predominance, and cognitive impairments mostly in the verbal memory domain. Neuroimaging shows lower amygdala and white matter hyperintensity volumes compared to controls. Future studies extending these findings to Alzheimer’s disease biomarkers and longitudinal follow-up will further inform predictors of cognitive decline.

Fusion Brain Organoid Studies to Uncover Circuit Dysfunction in Genetic Epilepsy
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Neural circuit dysfunction is a hallmark of neurological disease, including in the genetic epilepsies. This not only involves neuronal loss and anatomical changes, but also the electrophysiological dysfunction of brain circuits. However, neuronal circuit dysfunction
has been largely ignored as an endpoint of disease in cellular disease models representing a major gap in our capacity to use technological innovations like high-throughput genetic and drug screens to discover novel therapeutics. One promising new platform to model circuit dysfunction in epilepsy is human brain organoids (or simply organoids), 3D brain-like structures that are created from either human embryonic or induced pluripotent stem cells (hESCs or hiPSCs). In recently completed studies we generated “fusion” organoids in which cortex-like organoids predominantly containing excitatory neurons and ganglionic eminence (GE)-like organoids primarily with inhibitory neurons integrate. These fusions resulted in organoids with complex network activity including neural oscillations with similar frequencies as observed in human cortex in vivo (1). Here we expanded on this approach and generated hippocampus-GE in addition to cortex-GE fusion organoids (2). Like cortex,

hippocampal fusions generated neural oscillations at multiple frequencies, but additionally generated fast ripple activity and stereotyped patterns of theta-gamma phase
amplitude coupling (PAC). These patterns of circuit activity are associated with hippocampal learning and memory. We next generated organoids from the iPSCs of a patient with developmental epileptic encephalopathy-13 (DEE-13) due to a pathogenic gain
of function mutation in the SCN8A sodium channel. Using extracellular recordings of local field potentials we found substantial hyperexcitability as well as a loss of sustained oscillatory activity in the cortex-GE fusions compared to isogenic controls. In contrast, in DEE-13 hippocampus-GE fusion organoids we did not observe overt hyperexcitability. Instead, we found more subtle changes including reduced frequency of SWRs and disordered patterns of theta-gamma PAC. The changes in hippocampal activity were
associated with a selective loss in interneuron expression, not seen in cortex-GE fusions. These data suggest that (1) hippocampus and cortex fusion organoids generate complex and distinct circuit activities and (2) that human brain organoids may provide unique
insights into brain-region specific circuit changes that result from the identical pathogenic gene mutation.

Epilepsy and Neurodevelopmental Risk Stratification in Very Preterm Infants with Intraventricular Hemorrhage
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Epilepsy is a prevalent pediatric neurologic condition that remains treatment-resistant for 30% of patients. It is increasingly recognized as a disorder of brain networks, with network changes shown to underlie seizures, neurodevelopmental impairments, and treatment effects. Limited targeted therapies for epilepsy have been most successful in high-risk populations when administered before seizures start, suggesting that they may prevent pathologic brain network changes. Assessing the development of brain networks using functional connectivity (fc) is therefore a promising technique for early prediction of epilepsy and neurodevelopmental outcomes. Thus, to evaluate network changes as susceptibility markers, fc must be studied prospectively in populations at risk for epilepsy. Very preterm infants (VPT; <32 weeks gestation) with high-grade intraventricular hemorrhage (IVH) have increased rates of epilepsy and may provide important insights into risk stratification if studied early. This ongoing study aims to identify prospective biomarkers of epilepsy susceptibility in VPT infants with IVH, by collecting high-density (HD)-EEG data at the bedside in the Neonatal Intensive Care Unit (NICU) in parallel with a longitudinal R01 study collecting functional (f)MRI data and developmental assessments of VPT infants with and without high-grade IVH. Early life epilepsy outcomes are also being collected through a parent questionnaire and medical record review. HD-EEG is being used to detect clinical EEG abnormalities among VPT infants with high-grade IVH (Aim 1), reductions in HD-EEG and fMRI measures of brain network connectivity, particularly in injured brain regions (Aims 1 & 2), relationships between HD-EEG and fMRI connectivity measures (Aim 2), and relationships between the strength of HD-EEG connectivity metrics, developmental outcomes, and a diagnosis of epilepsy in early life (Aim 3). This study will provide foundational data to identify prospective epilepsy markers for infants and children at highest risk. To date (fMRI recruitment beginning in Summer 2022, HD-EEG recruitment beginning in December 2022), 108 very preterm infants have been recruited for neuroimaging (26 with high-grade IVH and 82 controls). Of those infants, 17 have been enrolled and tolerated high-density EEG at term-equivalent age (37-45 weeks) with 7 with high-grade IVH and 10 controls. To date, 30% (n=5) of EEG participants demonstrated clinical EEG abnormalities at term equivalent age. From the whole high-risk cohort, 6% (n=7) of participants have had at least one lifetime seizure thus far. More are anticipated as the participants approach 2 years of age in the future. Data collection and quantitative processing/analyses are all ongoing.

Global Neurology

The Impact of Malaria on the Central Nervous System - Does coma really matter?
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Background: Malaria affecting the central nervous system can present with coma (cerebral malaria – CM) or without (CNS malaria). CM affects 500,000 children annually, with neurodevelopmental sequelae in approximately 30%. Limited evidence suggests similar sequelae rates in the more common CNS malaria, but it remains poorly understood whether CM is a severe subtype of CNS malaria or different pathophysiology. We tested whether the CM and CNS malaria are distinguished by clinical and EEG metrics in a cohort of Zambian children. **Methods**: Children 6 months – 11 years without epilepsy and with confirmed malaria and meeting criteria for CM (Glasgow coma score (GCS)≤10 or Blantyre coma score (BCS)≤2), or CNS malaria (prolonged seizures or impaired consciousness without coma) were included. Baseline data, including Ten Questions Questionnaire (TQQ) pre-illness development screen, and acute illness clinical metrics were collected. One-month follow-up was performed obtaining caregiver perceptions of recovery and scores on Behavior Rating Inventory of Executive Function (BRIEF) and Malawi Developmental Assessment Tool (MDAT) in children <6 years. EEG was recorded at admission and one-month; analyzed visually and via quantitative EEG (qEEG) analyses, including frequency band power and sample entropy. CM and CNS malaria were compared using Fisher exact test for categorical outcomes and two-sampled t-tests for numeric outcomes. **Results:** 144 children were included (CM = 45, CNS malaria = 99). Children with CM were older (mean 51 months (range 11.1 - 121.6) vs 38.8 (6.3-125.7) $p<0.05$). There was no difference in sex, HIV status, TQQ or duration of illness prior to presentation. During hospitalization, CM had more clinical seizures (58.5% vs 35.8%, $p<0.05$); Tmax, length of stay, and mortality did not differ. CM admission EEGs showed expected increased slowing and absent normal sleep features, state change, and reactivity more frequently than CNS malaria, but notably also increased epileptiform activity ($p<0.05$). At one-month, there were no significant differences in visual EEG, caregiver perceptions, MDAT, or BRIEF scores. qEEG metrics did differ between groups. At admission, mean delta power was higher in CM (0.9018 vs. 0.8469, $p<0.001$), while all other metrics were lower- theta (0.0649 vs 0.1022, $p<0.001$), alpha (0.0071 vs 0.0124, $p<0.001$), beta (0.0081 vs 0.0126, $p<0.05$), gamma (0.0181 vs 0.0258, $p<0.001$), and sample entropy (0.2819 vs 0.3628, $p<0.001$). By 1-month, mean delta power was no longer significantly different, but all other metrics were. Interestingly, theta activity was now higher in CM (0.191 vs 0.1813, $p<0.05$), as was alpha (0.0349 vs 0.029, $p<0.001$), while beta, gamma, and sample entropy remained lower (beta 0.0192 vs 0.0215, $p<0.05$, gamma 0.014 vs 0.0252, $p<0.001$, sample entropy 0.388 vs 0.4034, $p<0.05$). **Conclusions:** Measures of the burden of malaria on the pediatric brain focus predominantly on CM, however evidence suggests CNS malaria- which affects a larger proportion of younger children- has similar, substantial risks of neurological sequalae. Our study supports that the two groups are more clinically similar than different, however, differences in qEEG at admission and one-month indicate increased cortical dysfunction in CM, with increased slower frequencies and decreased variability (entropy). The clinical and visual EEG differences are consistent with coma in the CM group, as expected. However, the CM group notably also had increased epileptiform activity and seizures during hospitalization, potentially indicating that patients presenting with convulsions (CNS malaria) benefited from early treatment of seizures, as those presenting with coma (CM) were less likely to receive anti-seizure medications on presentation. We found CNS malaria affected younger children, which may represent increased vulnerability to febrile seizures in this population. The impact on outcomes remains to be seen, including if qEEG findings are predictive of longer-term risk for epilepsy and other neurodevelopmental disorders. CM and its mechanism of brain injury through cerebral vasculature parasitic sequestration, inflammation and cerebral edema is often treated as a unique entity in research and public health reports; however, our findings found the two groups are similar in acute and subacute outcomes with the notable difference one of increased cortical dysfunction, suggesting CM is a severe subtype of CNS malaria versus a different pathophysiology. Our study indicates research for diagnosis and management of CM needs to incorporate consideration of the larger group of children with any CNS involvement during malarial infection.

Chronic Somatic Pain in Refugee Torture Survivors in the United States

Presenting Author: ***Gunisha Kaur, MD, MA, Weill Cornell Medicine***

An estimated 87% of torture survivors (27 million people) worldwide suffer chronic somatic pain related to trauma mechanism, such as brachial plexopathy from suspension by upper extremities or lumbosacral plexus injury from leg hyperextension. However, a vast majority of this pain is likely undiagnosed by providers who use only the standard evaluation protocol of torture survivors, the United Nations Istanbul Protocol. Without evidence based diagnostic tools and treatment guidelines for use by general providers, the complex clinical presentation of torture survivors results in somatic pain being confounded by concurrent psychiatric illness such as posttraumatic stress disorder, major depression, or somatization. Rehabilitation from complex trauma is possible, but it requires considering somatic pain a substantial component of pathology. We conducted a blind comparison to gold standard study with 100 refugee torture survivors to compare the diagnosis of somatic pain using the standard United Nations Istanbul Protocol (UNIP) versus the UNIP with the novel application of a validated pain screen. We then assessed the biopsychosocial influences on pain in qualitative interviews with

30 refugee torture survivors, and evaluated the acceptability of somatic pain treatment. We also assessed the feasibility of recruiting and retaining refugees in a digital program for pain, stress, and cardiovascular disease diagnosis and treatment.

Headache and Pain

Baseline Clinical Characteristics from a Prospective Multiple Cohort Study of Headache in Transgender/Gender Diverse Youth and Their Cisgender Male Comparators: Preliminary Findings
Presenting Author: ***Jennifer Hranilovich, MD, University of Colorado School of Medicine***
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This is a prospective observational study to compare changes in migraine burden and brain growth and development between a group of cisgender (congruent sex assigned at birth and gender identity) male youth and a group of transgender/gender diverse (TGD) youth with male sex assigned at birth and nonbinary or female gender identity; these baseline data reflect characteristics of the two groups before start of estrogen in the context of a longitudinal study.
Background: Estrogen has been linked to the development of greater prevalence, severity and frequency of headache in cisgender females compared to cisgender males. We hypothesized that TGD youth who receive gender affirming hormone therapy with estradiol during puberty will have a greater increase in headache frequency than cisgender male youth over their first year of exposure. Here, we compare these two groups at baseline. Given higher rates of anxiety and depression reported in transgender youth and the bidirectional link between these conditions and headache, we hypothesized that there would be higher prevalence of headache at baseline in the TGD group. **Methods:** Prospective multiple cohort study. Rolling enrollment of youth with or without a diagnosis of headache at a tertiary care gender management clinic and the surrounding community in the mountain west, US over December 2021-January 2024 (clinicaltrials.gov/NCT05607303). Cisgender youth were recruited through word of mouth, on-campus flyers, advertising on campus research websites and through campus email-based research newsletters. Recruitment of patients ages 11-20 and in the case of TGD youth, having no history of gender affirming hormone therapy with estrogen but intending to start within 6 months. Baseline data collected include diagnostic headache interview, modified 30-day PedMIDAS score (pediatric headache disability measure), pubertal (Tanner) staging, PROMIS (Patient-Reported Outcomes Measurement Information System) Pediatric Short Forms v2.0 – Depressive Symptoms 8a and Anxiety 8a. Baseline data collected but not yet analyzed include serum hormone levels and both structural and resting-state functional connectivity brain MRI. Participants will be followed for one year to assess for 1) change in number of headache days per month as measured by a one year daily electronic headache diary 2) change in amygdala volume 3) change in resting state functional connectivity. Means (standard deviations) or medians [25th, 75th] are given for continuous variables depending on their distribution; normality assessed using the Shapiro-Wilks test. Categorical variables show counts (percent). Between-group comparisons are made using Fisher's exact test for categorical data and either Student's 2-independent t-tests or Wilcoxon rank sum tests for continuous data depending on their distribution. Significance was set at $p<0.05$. Results: Data collection is ongoing. The sample enrolled thus far includes 32 TGD youth mean age = 15.7 years±1.7 at baseline visit and 37 cisgender males mean age = 15.2 years±1.6. Higher anxiety was observed in the TGD youth (52.88±(10.84) – mean PROMIS scores in the mild range), almost one standard deviation higher than in the cisgender males (46.37±(7.41) – mean value within normal limits), p=0.004. Similar results were observed for depressive symptom (55.09±(10.32)) vs cisgender males' (47.39±(7.53)), p=0.001. Of the TGD group, 17/32 (53.1%) met ICHD-3 criteria for migraine and overall had 2.5±[0.88-8.50] days headache/month vs the proportion of cisgender males with migraine at 15/37 (40.5%) and overall 2.0±[1.00-5.50] days headache/month. There were no significant differences between groups in either of these measures nor in prevalence of tension type headache. There was little to no headache disability (ranging to mild disability) in both groups with modified 30-day PedMIDAS scores of 0.50±[0.00-4.25] in the TGD youth and 1.00±[0.00-4.00] in the cisgender youth, and baseline disability did not significantly differ between groups. The proportion of TGD youth for whom we had pubertal staging and who were in early puberty was 7/29 (24.1%) vs 1/37 (2.7%) of the cisgender males and significantly differed, p=0.017. **Conclusions:** Our preliminary results show that although there is greater anxiety and depression in the TGD youth compared to controls at baseline, no significant differences were observed in number of headache days per month, or prevalence of migraine or tension type headache. Next steps will include analysis of longitudinal brain structural changes, changes in resting state functional connectivity, and change in number of headache days per month.

Enhancing and Ameliorating Light Avoidance in Mice with Photoreceptor Targeting and CGRP Sensitization
Presenting Author: ***Eric Kaiser, MD, PhD, University of Pennsylvania***
Co-Authors: Audrey Cavanah, BA; University of Pennsylvania; Geoffrey Aguirre, MD, PhD; University of Pennsylvania; Frances

Jensen, MD; University of Pennsylvania
Background: A growing body of literature implicates intrinsically photosensitive retinal ganglion cells (ipRGCs) as mediators of photophobia. In addition to encoding bright light via melanopsin stimulation, ipRGCs receive extrinsic input from cones. In humans, we have shown that melanopsin and cone stimulation in isolation or in combination elicit visual discomfort (McAdams, et al, 2020 - PNAS). These signals appear amplified in those with migraine with interictal photophobia. Prior work in mice has shown that calcitonin gene-related peptide (CGRP) administration leads to light avoidance, suggesting it could be one potential mechanism of amplifying ipRGC signals. Given our prior findings in humans, we hypothesized that light avoidance in mice may also be mediated by ipRGCs. Here, we measured whether spectral variation targeting melanopsin or specific cone types elicits light avoidance. **Methods:** We studied two transgenic mice with: 1) human red cone knock-in (RCKI, B6.129-Opn1mwtm1(OPN1LW)Nat/J), or 2) adult-onset ablated M1 ipRGCs (Opn4-/-, Opn4tm4.1(DTA)Saha/J). Light avoidance behavior was observed in a two-zone chamber illuminated by narrow-band LEDs targeting photopic opsins: 365 nm (UV; rodent S-cone), 460 nm (blue; melanopsin), and 630 nm (red; human L-cone). Mice were given a choice to spend time between zones with differing relative contrast levels (0.50, 0.75, or 1.00) for the targeted photoreceptor. Mice were studied without intervention or following priming with either peripheral CGRP (0.1 mg/kg, ip) or vehicle administration every-other-day for 9 days. A primary measure (mean +/- SEM) was the asymptotic ratio of time in the high versus low contrast zone, where a ratio of 1.0 indicates no preference. **Results:** RCKI mice avoided the high melanopsin (0.481 +/- 0.082, n = 18) and L-cone (0.697 +/- 0.113, n = 15) contrast zones but exhibited a significant preference for the higher S-cone (1.348 +/- 0.056, n = 16) contrast zone. These effects were contrast-dependent, where avoidance or preference decreased with less relative contrast. The addition of S-cone contrast offset avoidance to melanopsin (0.898 +/- 0.122, n = 14) or L-cone (1.158 +/- 0.071, n = 45) contrast. Ablation of ipRGCs in Opn4-/- mice diminished avoidance of melanopsin and preference for S-cone stimulation compared to control littermates. CGRP priming (0.373 +/- 0.092, n 14) increased avoidance of melanopsin stimulation as compared to vehicle priming (0.711 +/- 0.131, n = 14) by day 9. **Conclusions:** Our findings suggest that melanopsin stimulation alone can mediate light avoidance in mice consistent with our observations in humans. A novel finding is that extrinsic cone inputs to the ipRGCs can modulate these effects with excitatory input from L-cones and inhibitory input from S-cones. Furthermore, CGRP may potentially augment post-retinal ipRGC signals, leading to photophobia in migraine.

Health Services and Health Equity Research

Influences on Health Preventive Behaviors After Minor Stroke: Understanding Patient Perceptions and Practices in an Urban Underserved Population
Presenting Author: ***Imama Naqvi, MD, MS, Student, Columbia University***
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Background: Secondary preventive behaviors including blood pressure (BP) management reduces risk of stroke recurrence while physical activity (PA) facilitates recovery after stroke. Yet significant gaps exist between professional guideline recommendations and practice among patients discharged home after a minor stroke. Stakeholder perspectives are needed to inform implementation and sustainably improve outcomes. Social Cognitive Theory (SCT) is a theoretical framework which proposes that human behavior is the product of the interaction between personal factors, environmental influences, and behavioral patterns. This theory can inform the influences on an individuals behavior in development and maintenance of secondary stroke prevention behaviors. Objective: We sought to understand influences on preventive behaviors from stroke patients who reside in an urban underserved community. **Methods**: We conducted structured qualitative interviews with a purposive sample of minor stroke patients with hypertension (n=14) discharged home from a comprehensive stroke center. We assessed knowledge of recommendations, and perceived barriers and facilitators influencing preventive behaviors for community reintegration. Two separate interviews were conducted to assess BP management and PA. A combination approach to interview content analysis was used, inductive with open data coding, and deductive with predefined categories informed by SCT. We conducted data saturation assessment after each interview with a <5% new information threshold of all themes coded in the analysis as the point of saturation. Socio-demographics were collected at baseline. PA was monitored with wearable devices for one month. Patient-reported surveys included the Patient Reported Outcomes Measurement Information System-Physical Function (PROMIS-PF) Short Form, International Physical Activity Questionnaire (IPAQ) and Stages of Change - Continuous Measure (URICA-E2). **Results:** Participants included 57% Black, 29% Hispanic and 50% women with mean age 58.9 (Â±9.6) yrs. A third had â‰¤ high school education, and 43% had Medicaid or no insurance. Both the average daily step count 5147 Â± 2534 steps and PROMIS-PF mean score was also less than the general population average at 44.9 Â±9.8. However, 46% participants self-reported high PA levels in the IPAQ and 43% were in the contemplation

phase for exercise. Data saturation was reached at 10 interviews for Interview 1 and at 6 interviews for Interview 2. We identified three key themes as influencing preventive behaviors: 1. Positive outcome expectations, either affective, social, or physical, 2. Self-efficacy: confidence to navigate socio-structural challenges, and 3. Agency: being in charge of own actions, out of necessity or by choice. While all participants identified BP control with reduced recurrence risk and PA with recovery, there was limited knowledge of recommended goals and target levels. Home BP telemonitoring facilitated confidence in self-management and improved BP medication adherence. Psychological needs of autonomy were tied to environmental barriers specific to urban living such as navigating stairs, or neighborhood crime risk. Low balance confidence was the most frequently stated barrier to PA in the community, with two-thirds reporting fear of falling after returning home. **Conclusion**: Positive outcome expectations, self-efficacy, and agency influence preventive health behaviors after minor stroke. However, gaps in patients' knowledge together with environmental barriers must be addressed to improve health outcomes.

Movement Disorders

Quantitative Kinematic Assessment of X-linked Dystonia Parkinsonism Using Wearable Sensor Technology
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Background: X-linked dystonia parkinsonism (XDP) is a rare neurogenetic combined movement disorder, with prominent dystonia and parkinsonian features, resulting in complex, overlapping motor symptoms that challenge traditional assessment. Objective, rater-independent motor assessments are crucial for improving diagnosis and monitoring change for XDP and other forms of combined parkinsonism. We sought to create a quantitative, objective framework for assessing combined dystonia parkinsonism using kinematic data from wearable sensors combined with machine learning (ML), enabling clinician-independent identification and severity evaluation. **Methods:** 28 patients with manifest XDP and 5 healthy controls were assessed using 17 wearable inertial measurement unit sensors and motion sensor gloves with a standardized motor examination. Dystonia and parkinsonian features were assessed with the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) and Burke-Fahn-Marsden scale (BFM). We crafted feature extraction from sensor data to mirror clinicians' observations during assessments and applied the Synthetic Minority Over-sampling Technique to address class imbalance. Sammon mapping projection algorithms were applied to explore the feature space, and random forest algorithms were used to identify and quantify dystonic and parkinsonian features and predict clinical scores. **Results:** Across all tasks analyzed, including those involving the upper limbs (e.g., finger tapping), lower limbs (e.g., toe-tapping), and gait, the features obtained from sensor data demonstrated clear cluster differentiation between control participants and individuals with XDP. The use of a random forest regressor achieved an accuracy of up to 85% in differentiating between the two groups. Furthermore, projections identified distinct clusters of sensor-derived features corresponding to various MDS-UPDRS scores in the tasks assessed. The prediction of MDS-UPDRS scores using random forest regression algorithms displays an accuracy significantly and consistently above the chance level across tasks, indicating that the features extracted from sensor data provide a reliable basis for estimating clinical scores. **Conclusions:** This approach underscores the utility of wearable technology and ML in characterizing dystonic and parkinsonian motor features, paving the way for clinician-independent assessment in XDP and other causes of combined dystonia.

Detecting and Measuring the Clinical Impact of Concomitant Alpha-synuclein Pathology in Alzheimer's Disease
Presenting Author: ***Thomas Tropea, DO, MPH, MTR, University of Pennsylvania Perelman School of Medicine***
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Objective: The objectives are to determine associations between cerebrospinal fluid (CSF) aSyn seed amplification (SAA) and (1) concomitant Lewy body (LB) pathology and alpha-synuclein (aSyn) distribution in pathology confirmed Alzheimer's disease (AD), and (2) clinical and cognitive outcomes in AD, mild cognitive impairment (MCI). **Background**: aSyn containing LB typically associated with Parkinson's disease and dementia with Lewy bodies occur in the brains of ~40% of people with AD. Retrospective postmortem studies have shown that concomitant LB pathology in people with dementia due to AD associates with a faster rate of cognitive progression, earlier onset of disease, and signs of parkinsonism. SAA can detect aSyn in CSF collected during life. **Methods:** Pathologically confirmed cases of AD followed longitudinally prior to postmortem analysis from the UPenn Center for Neurodegenerative Disease Research CNDR cohort were included. Individuals with MCI and neurologically normal controls (NC) followed longitudinally were also included. All cases met diagnostic criteria for AD or MCI; AD cases were pathologically confirmed, DLB type assigned, and a semiquantitative aSyn burden based on immunohistochemical staining across 9 brain regions was assigned. CSF was collected at study entry and aSyn SAA was performed by Amprion. Clinical and neuropsychological assessments were performed at least at yearly intervals. Multivariate regression was used to determine the association of SAA with aSyn pathology and cognitive and functional performance. **Results:** 91 AD, 53 MCI, and 63 NC were included. MCI and NC participants were followed for up to 15 years, while AD were followed for up to 15 years prior to death. SAA detected aSyn in 33% AD, 15% MCI, and 7% N. SAA had a sensitivity of 1.0 in diffuse or neocortical predominant LB cases and 0.54 in amygdala predominant cases. Median (IQR) Global aSyn burden score was 0.1 (0-0.1) in the SAA negative groups and 1.7 (0.8-2.1) in the SAA positive group. In AD, a positive SAA associated with shorter disease duration at death and a faster time to death, and lower cognitive and functional performance at baseline. In MCI, a positive aSyn associated with faster cognitive decline. **Conclusions:** aSyn SAA performance varies with LB distribution and associates with global aSyn burden in AD brains. Concomitant aSyn detected during life associates with worse clinical symptoms in dementia due to AD and MCI.

Neurocritical Care and Traumatic Brain Injury

Highly Epileptiform EEG Trajectories and Functional Recovery Post-cardiac Arrest
Presenting Author: ***Edilberto Amorim, MD, University of California, San Francisco***
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Objective: To determine epileptiform activity trajectories associated with neurological recovery post-cardiac arrest. **Methods:** Multicenter cohort, partly prospective and partly retrospective involving seven academic or teaching hospitals from the U.S. and Europe. Individuals aged 16 or older who were comatose after return of spontaneous circulation (ROSC) following a cardiac arrest who had continuous EEG monitoring were included (all EEG data up to 84 hours). Automated spike frequency and artifact detection on EEG were calculated with 10-second resolution and summarized hourly. Participants were considered to have a highly epileptiform EEG and were included in the spike trajectory analysis if spike activity reached at least 0.5 Hz for one hour or longer. Expert visual review was pursued for validation. Trajectories were determined using dynamic time warping and k-means clustering using trajectories™ Euclidean distance. Functional outcome was determined at 3-6 months using the best Cerebral Performance Category (CPC) scale. A deep learning model (long short-term memory) using spike frequency and 94 additional EEG signal features measuring signal complexity, frequency, and amplitude was pursued to predict spike trajectory cluster and poor functional recovery (CPC 3-5) hourly. **Results:** 1,020 patients (56,676 hours) were analyzed and 320 (31.4%) had a highly epileptiform EEG based on automated analysis. After expert review, 247 (24%) met the criteria for periodic epileptiform activity or seizures. Two-hundred and one patients (81.4%) had poor functional recovery. Three spike frequency trajectory clusters were identified: cluster A (N=139) showed an increase in spike frequency after 24h from ROSC, cluster B (N=57) showed an increase in spike rate within 24h from ROSC, and cluster C (N=51) had a persistently elevated spike rate from the time of EEG initiation. Specificity for poor outcome in these clusters was 70.6%, 94.8%, and 96.1%, respectively. The deep learning model was able to separate cluster A from B and C with an AUC of 0.89 by 16h and 0.91 by 21h. Average AUC for poor functional recovery prediction was 0.84. **Conclusions:** Three dominant epileptiform activity trajectories post-cardiac arrest were identified. While nearly all patients with early epileptiform activity had poor functional recovery, almost a third of patients with delayed onset of highly epileptiform activity had good recovery."

Heterogeneity of Bmal1-dependence in NG2-glia
Presenting Author: ***Terry Dean, MD, PhD, Children's National Hospital***
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NG2-glia, also called oligodendrocyte precursor cells (OPCs) comprise the largest population of regenerative cells in the adult brain (~5%) and are critical in the response to injury and disease. We and others have recently shown that NG2-glia rhythmically express circadian clock genes and demonstrate diurnal variation in cellular functions, with the key clock component Bmal1 playing an integral role. Expanding on this work, we present here data suggesting that NG2-glia Bmal1 also regulates processes in a clock-independent manner. Unlike in cortex, white matter NG2-glia lack robust rhythmic expression of Bmal1, and Bmal1 CKO does not appear to affect white matter NG2-glia density. We also provide evidence that traumatic brain injury (TBI), alone, is capable of inducing NG2-glia Bmal1 expression in both mice and humans. Together, these data suggest that the clock-dependence and downstream regulation of BMAL1 may be subject to the local environment in health and disease. These data provide a starting point by which we may further uncover mechanisms regulating the brains™ inducible regenerative potential via NG2-glia. As such, it holds particular significance for CNS injuries lacking in targeted therapies, such as TBI.

Can the Incorporation of Quantitative Markers and Death Improve the Prediction of Post-Ischemic Stroke Epilepsy?
Presenting Author: ***Jennifer Kim, MD, PhD, Yale School of Medicine***
Co-Authors: Yilun Chen
Background: SeLECT, a validated post-ischemic stroke epilepsy (PISE) prognostic model, facilitates enrolling high-risk patients in anti-epileptogenic trials. While its positive predictive value (PPV) doubles PISE incidence, about 90% of SeLECT-predicted PISE remain false-positive predictions at the first-year post-stroke. We developed a new model to reduce the false-positive predictions of SeLECT to achieve more targeted trial enrollment. **Methods**: In this retrospective study (2014-2022), we included adult ischemic stroke patients at Yale-New Haven Hospital with neuroimaging and electroencephalography (EEG) assessments â‰¤7 days post-stroke. Outcomes included time from stroke to PISE, or death before PISE. In the training cohort (n=230), proportional cause-specific hazard models identified quantitative PISE biomarkers and Death predictors. A predictive model was built using a random survival forest with competing risk and was evaluated in a testing cohort (n=50). **Results:** Of 280 patients included, 53 developed PISE. Quantitative biomarkers predictive of PISE were identified, including 72h NIHSS (HRCS=PISE [95%CI] Î”3 units, 1.2 [1.1-1.4]), infarct volume (Î”10 mL, 1.06 [1.04-1.08]), epileptiform abnormality burden (Î”10%, 1.2 [1.1-1.3]), total power asymmetry (Î”10%, 2.0 [1.4-2.9]), and total rhythmicity asymmetry (Î”10%, 1.3 [1.07-1.6]). In the testing cohort, compared to SeLECT, SeQuant identified a more selective patient group (n=18 vs 44) with a higher PISE rate (39% vs 20%) <1-year post-stroke. **Interpretation:** The benefit of SeQuant is most prominent amongst patients with high SeLECT scores, suggesting that SeQuant may complement SeLECT in a two-stage risk stratification framework.

Quantitative Pupillometry Predicts Neurologic Deterioration in Patients with Large Middle Cerebral Artery Stroke
Presenting Author: ***Charlene Ong, MD, MPHS, Boston University Chobanian & Avedisian School of Medicine***
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Background: Abnormal pupil reactivity can accompany neurologic deterioration due to life threatening mass effect (NDltme) in patients with large ischemic stroke at risk for cerebral edema. However, the association of quantitative pupillometry prior to NDltme and the optimal quantitative pupillometric thresholds for identification of NDltme are less clear. **Methods:** We conducted a prospective single-center study of patients with large middle cerebral artery (MCA) stroke. We first used adjusted Cox proportional hazard models to assess the association of time to NDltme and longitudinal pupil measurements including the Neurological Pupil Index (NPi), constriction velocity (CV), and dilation velocity (DV). To determine whether pupil characteristics significantly declined prior to NDltme, we performed Tukey adjusted pair-wise analysis of variance to compare average pupil characteristics within 2-hour time windows from a total of 12 hours prior to NDltme. Finally, we used the Youden Index to investigate optimal thresholds for identifying ND at the time of occurrence. **Results:** Of 71 eligible patients (age 66.5 Â± 16.4 years, 40.8% women), 25 (35.2%) experienced NDltme. Cox models adjusted by age, sex and ASPECTs revealed a significant association between NPi and subsequent NDce (HR 0.34, 95% CI 0.21 to 0.53). NPi 2 hours before NDce was significantly lower than NPi 12 hours prior to NDltme (3.68 v. 4.35, p = 0.006). The optimal NPi threshold for detecting ND was 3.51 with 37% sensitivity and 77% specificity. DV <0.51 mm/s had the highest Youden Index for detecting ND with 58% sensitivity and 71% specificity. **Conclusions:** NPi is associated with time to NDltme and declines up to 12 hours prior in large MCA stroke patients. An NPi threshold of 3.51 improved sensitivity in identifying ND. DV may also be a promising and

previously overlooked pupillometric biomarker. Further study is necessary to determine the optimal pupillometric predictors of ND.

Automated Measurement of Cerebral Hemorrhagic Contusions and Outcomes after Traumatic Brain Injury: A TRACK-TBI STUDY

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Introduction: Because withdrawal of life sustaining therapy based on perceived poor prognosis is the commonest cause of death after moderate or severe traumatic brain injury (TBI), the accuracy of clinical prognoses is directly linked with mortality. Though the location of brain injury is known to be important for determining recovery potential after TBI, the best available prognostic models, like the IMPACT score, do not currently incorporate brain injury location. **Objective**: Here, we tested whether automated measurement of cerebral hemorrhagic contusion size and location improves the prognostic performance of the IMPACT score. Design: Observational cohort study. Setting: Multicenter. Participants: We included adult participants from the US-based TRACK-TBI study with moderate or severe TBI (GCS score 3-12) and contusions on brain CT. Exposures: We labeled contusions on CT scans with BLAST-CT, a validated, artificial intelligence algorithm. **Outcome:** The primary outcome was a Glasgow Outcome Scale-Extended (GOSE) score â‰¤4 at 6 months. We tested whether frontal or temporal lobe contusion volumes improved the performance of the IMPACTcore+CT score with logistic regression and AUC comparisons. Using sparse canonical correlation analysis, we generated a Disability Heat Map, representing the strongest brain-wide associations with outcome. **Results:** In a multi-center, prospective cohort of 291 patients with moderate or severe TBI and contusions (meanÂ±SD age: 42Â±18; 221 [76%] male; median [Q1,Q3] arrival GCS score: 5 [3,10]), only temporal contusion volumes improved the discrimination of the IMPACTcore+CT score (AUC: 0.86 vs 0.84; p=0.031). A data-derived map of contusion locations with the strongest association with unfavorable outcomes (Disability Heat Map) highlighted bilateral regions within the temporal and medial frontal lobes. **Conclusions:** We used a novel tool to demonstrate regional variation in the association between contusion volumes and unfavorable outcomes after TBI. Temporal, but not frontal, contusion volumes improved IMPACTcore+CT performance. CT-based automated contusion measurement is an immediately translatable strategy for improving TBI prognostic models.

Neurodegeneration and Cell Death

Rescuing Alpha-synuclein Toxicity Through Neuron-specific Enhancement of Autophagy

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Parkinson disease (PD) is a neurodegenerative movement disorder marked by progressive motor and non-motor symptoms that lead to profound disability. Neurodegeneration in PD relates to toxic aggregation of alpha-synuclein (asyn), and mounting evidence shows that asyn can be degraded through the conserved pathway of autophagy. However, multiple aspects of autophagy are impaired in PD, and available methods to modulate autophagy fail to confer clinical benefits in patients because of the intrinsic resistance of neurons to these methods. This resistance stems in part from MTMR5 (myotubularin-related phosphatase 5), a potent autophagy regulator that we previously identified to be selectively enriched in neurons. MTMR5 acts as an autophagy suppressor, and MTMR5 knockdown enhances degradation of multiple autophagy substrates. To overcome proteostatic barriers to ameliorate PD pathogenesis, we sought to determine whether knockdown of MTMR5 facilitates asyn turnover and rescues asyn proteotoxicity. To investigate how and to what extent MTMR5 manipulation modifies asyn degradation and cell viability, we established a novel human induced pluripotent stem cell (iPSC)-derived neuron model of PD expressing fluorescently labeled autophagy effectors and asyn. Our PD model combined with super-resolution microscopy enables high-content, non-invasive optical monitoring of asyn degradation by autophagy in human neurons. We found that knockdown of MTMR5 significantly augmented autophagic clearance of not only WT asyn, but also mutant variants of asyn associated with familial PD and that demonstrate enhanced aggregation. We also found that MTMR5 knockdown and pharmacologic stimulation of autophagy mitigated asyn-related neuronal death. We will next employ unbiased, genome-wide CRISPR-based screens to uncover key factors regulating MTMR5 in neurons. Collectively, our findings attest to the neuroprotective effects of targeting MTMR5 for restoring asyn proteostasis. These studies also establish a novel research platform leveraging neuronal autophagy and myotubularin biology to discover innovative mechanisms for therapy development in PD and related neurodegenerative disorders.

Tau Seeding from Brain Homogenate Samples Correlates with Histopathological Burden
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Background: Misfolded alpha-synuclein aggregates (aSyn-seeds) detected by seed amplification assay (aSyn-SAA) are an established biomarker in Parkinson's disease, dementia with Lewy bodies, and other synucleinopathies. Additionally, SAA methods to detect tau-seeds are currently under development. Comparisons of the seeding activity from these early tau directed assays with pathological tau histopathological burden is an important step in validating these new assays.
Objectives: Here we sought to examine seeding activity from brain homogenate samples using a tau-SAA from autopsy-validated cases of different types of tauopathies and compare seeding activity to degree of tau histopathological burden.
Methods: Middle frontal lobe frozen sections were obtained from 29 participants (2 aged control participants, 10 Alzheimer's disease (AD), 9 progressive supranuclear palsy (PSP), 8 corticobasal degeneration (CBD), representing a range of Braak tau stages (0: 5, I: 8, II: 2, V: 3, VI: 9). Brain homogenates were analyzed by tau-SAA using 0.7mg/mL untagged 0N3R as monomeric substrate in 10mM HEPES pH 7.4, 150mM NaCl, 20ÂµM heparin, and 10ÂµM ThT and incubated for 300 hours. The dilution factor needed to reach 50% of the replicates negative (SD50-DF) was determined by the Spearman-Karber method, taking into the calculation the signal from diluent alone as false signal according to Hamilton et al., 1977. Available contra-lateral formalin fixed frontal lobe samples were immunostained for phospho-tau (AT8 ThermoFisher) and AD related tau (GT38 Abcam) and % area occupied (%AO) of tau inclusions was calculated for grey matter regions as we have done previously. SD50-DF and %AO values were log transformed for parametric statistical analyses. **Results:** Middle frontal lobe SD50-DF values were higher in AD than control cases, PSP and CBD cases, often 100 times higher (F=4.8 p=0.009). Ascending Braak stages presented with exponentially higher seeding activity, 10-100 times higher in Braak VI than lower stages (F=8.6 p=0.0003). Correlations between frontal lobe log(SD50-DF) and contralateral frontal lobe log(%AO) of tau inclusions are noted (AT8 R2=0.42 p=0.005, GT38 R2=0.22 p=0.09).**Conclusions:** In agreement with structural evidence showing that the tau aggregate core for 4R tauopathies include all 4 repeated regions, this 0N3R tau-SAA was significantly more sensitive detecting 3R misfolded tau from AD than PSP and CBD. Exponential increases in tau seeding activity is observed in higher Braak tau stages, specifically V and VI when neurofibrillary tangle pathology is observed in the middle frontal lobe. Contralateral tau histopathology also correlates with tau seeding activity from this assay in this initial set of cases.

Tau Phosphorylation at Alzheimer's Disease Biomarker Sites Impairs Tau Cleavage by Lysosomal Proteases
Presenting Author: ***Courtney Lane-Donovan, MD, PhD, University of California, San Francisco***
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The need for biomarkers for early detection of AD has led to the identification of select tau phosphorylation sites that accumulate early in disease and before, such as p-tau181, p-tau205, and p-tau217, which are in the proline-rich domain of tau. It is currently unknown why these specific phosphorylation sites accumulate early in disease. In this study, we focused on the role of the lysosome and lysosomal dysfunction in processing phosphorylated tau by combining in vitro analysis of tau processing with human proteomics analysis. We show that while full-length tau is rapidly processed by lysosomal proteases, the proline-rich domain persists and takes much longer to be processed. Moreover, when tau is hyperphosphorylated, the proline-rich domain is processed even more slowly by lysosomal cathepsins. By using FRET analysis of specific short amino acid sequences of tau, we show that phosphorylation at AD biomarker sites impairs cleavage of tau by specific proteases, but only at higher pH, as may be seen in aging or disease states. Each of the AD biomarker sites directly precedes a proline residue, and phosphorylation would be predicted to promote a proline-like cyclic conformation of the phosphorylated residue. We propose a model whereby tau phosphorylation at these biomarker sites and resulting cyclization renders the site resistant to cleavage by proteases. The low pH of the lysosome allows the relative unfolding of this cyclization and thus clearance of tau. This suggests that lysosomal dysfunction may be a very early disease process that promotes accumulation of phosphorylated tau. By analyzing publicly available proteomics datasets, we find that p-tau181 but not NFL, another biomarker, correlates with changes in CSF levels of specific lysosomal cathepsins, highlighting the potential role of lysosomal dysfunction in disease. These results offer a potential new therapeutic approach to AD through either strengthening overall lysosomal function or targeting independent cathepsin activity.

Neonatal Mild Hypoxic-ischemic Encephalopathy: Persistently Elevated Programmed Neuronal Death for Weeks After Injury
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Objective: Mild hypoxic-ischemic encephalopathy (HIE) is common in neonates with 30-40% of patients experiencing adverse long-term outcomes. Mild HIE may progress in severity (Sarnats original description); however, the progression and pathophysiology of injury after mild HIE is poorly understood, and no therapies are currently available. To address these issues, we developed a novel in vivo system to measure individual neuronal activity and death in real-time after mild hypoxia-ischemia (HI). **Methods:** After P1 intracerebroventricular injection (AAV1-Syn1-mRuby2-GCaMP6s) and P8 cranial window placement, P10 mouse pups underwent right carotid ligation and 15 minutes of hypoxia (FiO2 0.08) vs. sham. Chronic, awake 2P calcium imaging of right somatosensory cortex was completed from P10-21. Neuronal death was quantified using the fluorophore quenching assay. Immunohistochemistry and ex-vivo 14T MRI was completed at P28. **Results:** Mild HI transiently suppresses cortical network activity for hours post-HI (vs. sham, n=13 pups/group; $p<0.01$). No post-HI seizures are seen. By 24 hours, network activity fully recovers and there is no disruption in normal maturational network desynchronization 4 days after HI (n=8 pups/groups; n.s.). Cortical activity remains intact for 11 days (n=8 pups/group; n.s.). Despite this, mild HI causes delayed, progressive neuronal loss maximal during the second week post-injury (n=8 pups/group; $p<0.01$). At baseline, 1-, 2-, and 4-days post-HI, network participation of individual neurons destined to die is indistinguishable from those that survive (n=8 pups; n.s.). 2 weeks post-HI, mild HI does not cause visible hemispheric atrophy or stroke by gross inspection (n=8) and no cortical or hippocampal atrophy was seen on ex-vivo MRI (n=3 pups/group; n.s.).
Conclusions: This is the first study to longitudinally measure neuronal death and network activity in real-time after mild perinatal HI in vivo. Like neonates with mild HIE, our model demonstrated re-constitution of cortical network activity, no post-HI seizures, and no moderate-severe injury. Despite this, neuronal loss is progressive. Critically, the neurons destined to die demonstrate multiple biomarkers of viability for days after injury, suggesting their later death can be modified. These data have important translational implications for patients with mild HIE. Therapies may need to be deployed at a different time and/or for a different duration compared to those used for moderate-to-severe HIE. This novel in vivo model will permit rapid, quantitative measurements with cellular resolution of the neuroprotective utility versus neurotoxicity of new interventions in future studies.

Neurodevelopment

Functional Connectivity within the Language Network at 4 to 6 Years of Age and Relationship to Later Language Performance at 8 to 12 Years in Extremely Preterm Children and Term Peers: Short Term Gains with Long Term Consequences?
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Preterm birth impacts 1 in 10 children. Preterm children are at increased risk for language delay or disorder compared to term children (TC). Children born extremely preterm (EPT, <28 weeks gestation) are at greatest risk. The neural basis for risk and resiliency in language functioning of EPT is poorly understood. This longitudinal study follows a cohort of 131 participants (67 children born preterm and 64 term developmental comparisons) from early school age (4-6 years) though later school age (8-12 years) with cognitive assessments and multimodal neuroimaging. The preterm group is further subdivided into those with a history of language delay or disorder (EPT-HLD, n=25) and those without (EPT, n=36). Previously, we reported this cohort of preterm children exhibited increased functional connectivity during verb generation in beta and gamma frequency bands. Subnetwork strength in the gamma band positively correlated with language scores for EPT. Our aim here is to assess the degree to which this same subnetwork strength during verb generation at 4-6 years relates to language scores at 8-12 years. Participants completed neuroimaging and standardized assessments of language at both study visits (4-6 years and 8-12 years). Here, we include functional connectivity metrics from fMRI-constrained magnetoencephalography (MEG) obtained while children completed a covert verb generation task at 4-6 years of age (Barnes-Davis et al 2021). In brief, fMRI was conducted using a 3T Philips Achieva scanner. MEG data were recorded at 1200 Hz using a 275-channel whole-head CTF system. Children performed the same task in MEG and fMRI. Task-based fMRI data were conventionally analyzed in SPM12, and verb generation minus noise (first-level) contrasts were produced for each participant. Because there were no group differences in first-level contrasts, a joint activation map was generated across groups (Figure 1). We applied a whole-brain

200-unit parcellation to the activation map. Parcels with >10% active voxels were retained, and their centroids served as "nodes" for MEG analyses. Timeseries of activity at each node was estimated with a linearly constrained minimum-variance beamformer (LCMV). Phase locking value (PLV) was computed at narrow frequency bins to assess functional connectivity (consistency of phase differences) between nodes. Frequency bands in which there were significant group differences in PLV were investigated using Network Based Statistics. Subnetwork strength was computed for significant subnetworks. Subnetwork strength at 4-6 years was then correlated with standardized assessments of Core Language (Clinical Evaluation of Language Fundamentals, CELF-5) and IQ (Kaufman Brief Intelligence Test, KBIT2) at 8-12 years. Differences between groups were assessed using ANOVA with post-hoc Tukey's HSD contrasts. 62 children have followed up (to date) at 8-12 years of age and had neuroimaging at 4-6 years (34 TC, 18 EPT, 10 EPT-HLD). There were no significant group differences in age at MRI/MEG, sex, race, parental education, family income, or language representation in fMRI. Both preterm groups had higher subnetwork strength versus TC in the beta band ($p<0.001$) and gamma band ($p<0.001$). There were significant group differences in IQ ($p=0.006$) and Core Language ($p=0.002$, Table 1) with post-hoc analyses showing TC performed higher than EPT and EPT-HLD. There were no significant correlations between subnetwork strength and performance between groups. Beta subnetwork strength at 4-6 years negatively correlated with Core Language scores at 8-12 years (rho=-0.529, $p<0.001$, Figure 2), after adjusting for group (TC, EPT, EPT-HLD) and age at MRI/MEG (adjusted rho=-0.311, $p=0.033$). Gamma band subnetwork strength negatively correlated with IQ (rho=-0.469, $p<0.001$, Figure 3). This persisted after adjusting for group and age at MRI/MEG (adjusted rho=-0.294, $p=0.045$). At 4-6 years of age, preterm children (EPT and EPT-HLD) exhibited increased functional connectivity versus their term developmental comparisons (TC) in beta and gamma bands. Network strength of the gamma subnetwork positively correlated with language scores for the preterm children at 4-6 years of age. However, it appears this short-term gain might have long-term consequences. Our current analyses, while preliminary, indicate that subnetwork strength at 4-6 years of age negatively correlates with later performance at 8-12 years. Specifically, strength of the gamma subnetwork negatively correlates with IQ, and strength of the beta subnetwork negatively correlates with Core Language scores. Future analyses will include the entire cohort of our longitudinal study and investigate the degree to which changes in functional connectivity over time relate to language development.

Loss of Function of EIF4A2 Leads to Neurodevelopmental Impairment in Zebrafish
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The DEAD-box family of RNA helicases is critical for neurodevelopment. We have previously shown that variants in the DEAD-box encoding gene Eukaryotic Initiation Factor-4A2 (EIF4A2) lead to a neurodevelopmental disorder (NDD) characterized by intellectual disability, epilepsy, and structural changes in the developing brain (Paul, Duncan et al AJHG, 2023). Modelling of missense variants in Drosophila demonstrates that both loss and gain of EIF4A2 function alter neurodevelopment. However, the mechanisms by which EIF4A2 loss or gain of function alter neurodevelopment have yet to be determined. EIF4A2 is an essential regulator of protein translation through the CCR4-NOT deadenylation complex and is important for stem cell pluripotency and differentiation. EIF4A2 interacts with multiple critical genes during development, including SOX2 and ARX. When EIF4A2 is knocked down in stem cells, SOX2 is reduced. In contrast, in the presence of hypomorphic ARX variants, overexpression of EIF4A2 is observed, leading to a reduction in cytoskeletal proteins. ARX and SOX2 are essential for interneuron differentiation and migration, suggesting that EIF4A2 also serves a critical role in interneuron development. To understand the importance of EIF4A2 in neurodevelopment, we created eif4a2-/- zebrafish with CRISPR/Cas9 gene editing. Since individuals with variants in EIF4A2 demonstrate hypotonia, motor delays and intractable seizures, we assessed hyperexcitability and motor function in eif4a2-/- zebrafish and compared to wild type (WT) control zebrafish. To assess EIF4A2â€™s role in interneuron development, acute F0 CRISPants were generated in a transgenic zebrafish line that labels GABAergic interneurons. Tail coiling assays were first performed at 17-24 hours post fertilization (hpf) to capture the muscle contractions that are generated by the primary motor neurons in zebrafish. In eif4a2-/- zebrafish, there was a significant increase in the number and duration of tail coil bursts generated when compared to WT controls (WT n=337, eif4a2-/- n=440, $p< 0.01$), suggesting that eif4a-/- zebrafish are hyperexcitable starting as early as 17 hpf. Swimming was then assessed at 5 days post fertilization (dpf) and the eif4a2-/- zebrafish consistently swim slower and shorter distances than WT (WT n=360, eif4a2-/- n=360, $p< 0.0001$). Since a majority of individuals with variants in EIF4A2 have intractable seizures, stage II seizures were recorded in zebrafish through a established Nodulus DanioVision protocol. At 6 dpf, eif4a2-/- zebrafish had increased spontaneous seizures when compared to WT (WT n=185, eif4a2-/- n=314, $p< 0.05$). In order to understand if the hyperexcitability phenotype was secondary to alterations in interneuron, preliminary studies using acute F0 CRISPants of eif4a2 were completed in a transgenic dual reporter zebrafish line that labels GABAergic interneurons. Preliminary data demonstrates a reduction in interneurons in eif4a2 acute F0 CRISPant zebrafish when compared to WT controls at 6 dpf (WT n=4, eif4a2-/- n=4, $*p<0.05$). This study demonstrates that eif4a2-/- zebrafish exhibit hyperexcitability and motor impairments, similar to the individuals with pathogenic variants in EIF4A2. Preliminary studies suggest that GABA interneurons are impacted by loss of eif4a2 function, suggesting that variants in EIF4A2 may lead to a novel interneuronopathy. Future studies

are needed to further characterize that impact of EIF4A2 loss of function on interneuron development.

The Timing of Purkinje Cell Silencing Determines Severity of Neurodevelopmental Outcomes
Presenting Author: ***Jason Gill, MD, PhD, Baylor College of Medicine***
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Cerebellar dysfunction has increasingly been implicated as a key component in a wide variety of neurodevelopmental disorders, ranging from cerebral palsy and autism to neuropsychiatric disease. Early life, from the third trimester through the toddler years, is a crucial time for psychosocial as well as physiologic brain development and includes the massive expansion and elaboration of the cerebellar cortex, which houses over 70-80% of the neurons in the mammalian CNS. As a result, understanding the impact of cerebellar dysfunction in early life on behavior and physiology is a crucial step in understanding the basis of an important group of neurodevelopmental disorders. Using the mouse as a model, which takes advantage of the evolutionary conservation of cerebellar cortical circuitry and first order cerebellar connectivity across vertebrates, we devised an inducible model of cerebellar dysfunction, by which removal of dietary doxycline leads to cre/flox mediated silencing of Purkinje cells through downregulation of vesicular GABA transporter protein expression. We hypothesize that the timing of cerebellar silencing is a crucial mediator of the severity of resulting behavioral perturbations. We find that early silencing, where there is a lack of Purkinje cell neurotransmission in the early postnatal days, leads to a pervasive phenotype characterized by severe motor impairment (footprinting assay, accelerating rotarod, qualitative video analysis) and functional impairment (including increased distance on open field assay and abnormal social interactions). By contrast, silencing at weaning (postnatal day 21) led to mild qualitative motor defects (and an absence of quantitative motor deficits). Interestingly, these “late silencing” mice displayed similar impairments in the open field assay and social assays compared to the “early silencing” cohort. Electrophysiology revealed that the cerebellar nuclear neurons had increased measures of irregularity as compared to control and “late silencing” phenotypes. Together our data reveal that the timing of cerebellar dysfunction is a crucial determinant of the resulting behavioral phenotype. Furthermore, abnormal cerebellar nuclear firing may be a component of the dysfunction associated with early silencing suggesting that there may be an early critical period for the entrainment of baseline characteristics of cerebellar nuclear neurotransmission and thus modulation of upstream networks. Interestingly, while we did not find significant motor or electrophysiologic abnormalities in the late silencing cohort, there were significant deficits in functional domains including hyperactivity and social interaction. This may reflect an ongoing role for cerebellar neurotransmission in the modulation of cortical network function. The importance of timing of cerebellar dysfunction on resulting neurologic function ought to help clarify how neurodevelopmental disorders produce such a wide spectrum of phenotypes. Expanding this analytic process to subregions of the cerebellar cortex and further evaluating cortical network form and function in the context of cerebellar developmental dysfunction will be important horizons for future research.

Sensory Gating Impairment in Adults with Chronic Tic Disorders
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Co-Authors: Andy Xue, BS, Vanderbilt University; Alexander Conley, PhD, Vanderbilt University Medical Center; Alexandra Key, PhD, Emory University School of Medicine
Background: More than 50% of children and 80% of adults with chronic tic disorders (CTDs) experience sensory over-responsivity (SOR). Severity of SOR correlates with severity of core psychiatric features of the CTD phenotype. Mechanisms underlying SOR in CTD are unclear, but impaired sensory gating is strongly implicated. We seek to identify electroencephalographic (EEG) signatures of SOR in adults with CTD. **Methods:** Adults with CTD and healthy controls complete scales assessing SOR (Sensory Perception Quotient, SPQ), tics, and co-occurring psychiatric symptoms. Participants are then monitored with dense-array EEG during sequential auditory and tactile sensory gating paradigms, during which stimulus pairs are repeatedly presented (stimulus duration 20 ms, inter-stimulus interval 400 ms for auditory paradigm and 500 ms for tactile paradigm, inter-trial interval 7-7.5 s). Using event-related spectral perturbation analysis, frequency band-specific sensory gating indices are calculated for 100-ms epochs following first and second stimuli (S1 and S2, respectively). Analyses focus on the central electrode cluster, overlying the midpoint of the scalp in the international 10-20 system. We conduct between-group contrasts (Wilcoxon rank-sum) of sensory gating indices and within-group multivariable regression analyses (adjusting for age) of band power with SPQ score. **Results:** To date, auditory paradigm data are available for 26 control and 29 CTD participants, and tactile paradigm data are available for 26 control and 26 CTD participants. In the auditory paradigm, the CTD group exhibited significantly ($p < 0.05$) smaller delta-band (1-4 Hz) gating in the 100-200 ms, 200-300 ms, and 300-400 ms epochs relative to the control group. Between-group differences were not evident for the other frequency band gating indices. After adjusting for age, post-S1 theta (4-8 Hz) power in each 100-ms epoch was significantly associated with SOR for the control group, such that increased theta power was associated with increased SOR; no such association was evident for the CTD group. In the tactile paradigm, the CTD group exhibited significantly smaller theta-band

gating in the 300-400 ms and 400-500 ms epochs relative to the control group. Between-group differences were not evident for the other frequency band gating indices. After adjusting for age and post-S1 band-specific power, post-S2 delta power for the 100-200 ms, 200-300 ms, and 300-400 ms epochs was significantly associated with SOR for the CTD group, such that increased band power was associated with increased SOR; no such association was evident for the control group. **Conclusion:** Preliminary results reveal band-specific differences in auditory and tactile gating between adults with CTD and controls. Additional enrollment is needed to conduct well-powered analyses that examine sensory gating differences in adults with CTD and the relationship of such gating differences with SOR.

Neurogenetics and Gene Therapy

Bi-allelic BORCS5 Variants Result in a Wide Spectrum of Progressive Neurodevelopmental Disorders via Lysosomal Dysfunction

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Objective: To characterize a new brain disorder associated with BORCS5 bi-allelic variants, elucidating their effect on lysosomal distribution and activity. **Background:** BORCS5 encodes a subunit of the BORC complex, which mediates through the interaction with ARL8b the kinesin-dependent anterograde lysosomal movement in axons. Despite its established role, the potential human traits associated with BORCS5 defects and the mechanisms whereby pathogenic variants may contribute to neuronal dysfunction remain undiscovered. **Methods:** Whole-exome sequencing was employed to identify BORCS5 variants in 6 independent families. Lysosomal trafficking and activity were assessed in mammalian cell lines, patients fibroblasts, and induced pluripotent stem cell (iPSC)-derived cortical neurons. **Results:**10 cases from 6 families were identified with bi-allelic BORCS5 pathogenic variants, including 4 predicted loss-of-function (LoF) alleles (c.203-1G>T;p.?; c.316delG;p.A106fs; c.382_383delAG;p.L128fs; c.417 C>G; p.Y139*) and two missense alleles (c.284G>A; p.R95Q and c.296A>C; p.H99P). Patients with homozygous LoF variants presented with pre- or early postnatally lethal massive hydrocephalus with arthrogryposis multiplex congenita, accompanied by pathological evidence of neuroaxonal dystrophy in one family. In contrast, subjects with at least one missense variant had a less severe clinical presentation, characterized by global developmental delay with epilepsy, severe intellectual disability, spasticity, progressive dystonia, and parkinsonism. Brain MRI showed diffuse hypomyelination and parenchymal atrophy. LoF alleles were associated with reduced protein expression and perinuclear clustering of lysosomes in all cellular models. Conversely, the missense variants R95Q or H99P were expressed and did not cause similar abnormalities in lysosome distribution. However, both LoF and missense variants were associated with lysosomal dysfunction, as suggested by reduced activity and maturation of lysosomal hydrolases. **Conclusions:** BORCS5 bi-allelic variants lead to a broad spectrum of brain disorders, ranging from perinatally lethal neuroaxonal dystrophy to a neurodevelopmental phenotype with progressive movement disorders. Our findings establish a genotype-phenotype correlation, revealing that missense variants associated with a less severe clinical phenotype do not significantly impact lysosomal distribution but exert a notable influence on lysosomal maturation and activity. This correlation implies additional roles for BORCS5 in lysosomal biology, contributing to our understanding of the diverse manifestations observed in individuals with BORCS5-related disorders.

Single Nucleus RNA Sequencing in the Chronic Phase of Perinatal Hypoxic-ischemic Encephalopathy Reveals a Novel Anti-inflammatory Therapeutic Target

Presenting Author: ***Jeffrey Russ, MD, PhD, Duke University***

Co-Authors: Alexa C. Stone, Kayli Maney, Lauren Morris, Caroline F. Wright, Jillian H. Hurst, and Jennifer L. Cohen

Objective: Up to one third of neurodevelopmental disorders (NDDs) are attributable to single-gene pathogenic variants. However, we have little understanding of how single gene variants contribute to neuronal pathophysiology. To begin to provide a cellular link between genotype and neurodevelopmental phenotype, we integrated large-scale phenotypic information from subjects with monogenic neurodevelopmental diagnoses with recently published large-scale human cortical single-nucleus RNA-sequencing (snRNAseq) data from across developmental stages. This allowed us to investigate cell type-specific biases in gene expression associated with distinct neurodevelopmental phenotypes. **Methods:** Phenotypic information was gathered from: 1) a single-institution Duke University cohort of 84 neonates with pathogenic single-gene variants, and 2) a cohort of 4,238 subjects with pathogenic single-gene variants enrolled in the United Kingdom/Ireland Deciphering Developmental Disorders (DDD) study. Variants were grouped by neurodevelopmental phenotype and their expression across cortical cell subtypes was compared within snRNAseq datasets from 86 human cortex samples spanning from 2nd trimester to

adulthood. **Results:** Pathogenic variants associated with speech/cognitive delay or seizures involved genes that are more highly expressed in excitatory neurons or in microglia than variants associated with other NDDs. Variants enriched in excitatory neurons that are associated with speech/cognitive delay without seizures tended to involve calcium regulatory pathways and were biased toward higher expression in extratelencephalic cortical neurons. Variants enriched in excitatory neurons that are associated with speech/cognitive delay with seizures tended to involve synaptic regulatory machinery and were biased toward higher expression in intratelencephalic cortical neurons. Both subsets of pathogenic variants showed highest expression in the 2nd trimester of gestation but with increased with neuronal differentiation. Variants enriched in microglia were primarily driven by rare variants involved in mitosis and transforming growth factor beta (TGFB) signaling. **Conclusions:** By combining large-scale phenotypic data from subjects with single gene-related NDDs with massive, recently published human cortical snRNAseq datasets across developmental stages, we identified cell-specific expression biases for genes in which pathogenic variants are associated with speech/cognitive delay and seizures. The involvement of genes with enriched expression in excitatory neurons or microglia highlights the unique role both cell types play in sculpting the developing brain and potentially mediating neurodevelopmental symptoms.

Parvalbumin-positive Interneuron Alterations in a Mouse Model of Pcdh19 Clustering Epilepsy
Presenting Author: ***Julie Ziobro, MD, PhD., University of Michigan***
Co Authors: Noor Daddo, BS, University of Michigan, Joy Huang, BS, University of Michigan, Sheetal Jahagirdar, PhD, University of Michigan, Jack M. Parent, MD, University of Michigan
Introduction: Protocadherin-19 (PCDH19)-clustering epilepsy (PCE) is a severe developmental and epileptic encephalopathy (DEE) and one of the most common monogenic epilepsies. It is characterized by cognitive impairment and intractable seizure clusters with onset in the first few years of life. PCDH19 is an X-linked gene that encodes a transmembrane cell adhesion molecule critical for cell-cell interactions during brain development. PCE affects females and rare mosaic males, while hemizygous males expressing only mutant PCDH19 do not develop epilepsy. A leading hypothesis to explain this phenomenon is that it occurs due to cellular interference associated with random X-inactivation (or mosaic mutations) in which cells expressing only wild type and those expressing only mutant PCDH19 fail to interact properly during brain development. This is demonstrated in our mouse model in which we see a striking pattern in which the Pcdh19+ and null neurons (after random X-inactivation) segregate from one another in the cortex, hippocampal CA1 region, and in interneuron progenitors in the ganglionic eminences. Given the essential role of GABAergic signaling in neuronal development and the key role of inhibitory interneurons in many genetic epilepsies, we sought to examine interneuron distribution and relation to seizure susceptibility in a mouse model of PCE. **Methods:** Female Pcdh19+/- mice crossed with X-GFP males or female Pcdh19+/-; parvalbumin (PV)-cre females crossed with X-GFP; tdTomato cre-reporter males were used. Female offspring express GFP on approximately half of their neurons, while males do not express GFP. All PV-cre x tdTomato offspring expressed tdTomato on PV-positive interneurons. As fever is a common trigger for seizure clusters in patients with PCE, we sought to evaluate seizure susceptibility to hyperthermia in our model. The body temperature of P15-16 mice was gradually raised with a heat lamp and maintained at 42.5Â°C for 15 minutes. Seizures were scored on a modified Racine scale by an observer blinded to genotype. Brains were then harvested and processed for immunohistochemical analysis of GFP pattern and parvalbumin positive interneuron density and distribution. **Results:** Female Pcdh19+/- mice had a lower seizure-threshold and more severe seizures than wild-type control female littermates when exposed to hyperthermia, but did not show a significant difference in seizure threshold compared to Pcdh19-/y males. Histological evaluation revealed the known segregation pattern of GFP+ neurons in Pcdh19+/- females, in which GFP was expressed on the wild-type allele and no fluorescent marker on the Pcdh19-null allele. Brains of Pcdh19+/+ females showed a random distribution of GFP+ neurons. Evaluation of tdTomato+ interneurons revealed a lower density of PV-positive interneurons in the CA1 region of the hippocampus in Pcdh19+/- females when compared to Pcdh19+/+ controls. **Conclusions**: Juvenile Pcdh19+/- mice have a lower seizure threshold and more severe seizures when exposed to hyperthermia than wild-type controls in addition to a lower density of parvalbumin positive interneurons within the CA1 region of the hippocampus. These findings suggest that alterations in interneuron distribution may be an underlying factor in the phenotypic spectrum of PCE. Ongoing studies will evaluate potential synaptic and functional alterations of the inhibitory system in our mouse model of PCE.

Understanding mtDNA Variant Segregation in Single Cells: How T Cell Activation Contributes to Purifying Selection Against the MELAS-associated m.3243A>G Pathogenic Variant in Blood
Presenting Author: ***Melissa Walker, MD, PhD, Massachusetts General Hospital/ Harvard Medical School***
Unlike nuclear variants, mitochondrial (mt)DNA variants can coexist with the wildtype allele in a percentage across hundreds or thousands of copies of mtDNA present in a cell, a state called heteroplasmy, and a course of great variability between and within affected kindreds and tissues within the same individual. While the somatic segregation of the m.3243A>G pathogenic variant (MT-TL1, associated with Maternally Inherited Diabetes and Deafness [MIDD], Mitochondrial Encephalomyopathy and

Lactic Acidosis [MELAS]) is notoriously variable, trends have historically been observed with apparent concordance with clinical phenotypes: the most severely affected tissues (brain, muscle) often have the highest heteroplasmy burden. Intriguingly, these tissues are also largely composed of nondividing cells. Conversely, hematologic symptoms are comparatively rare and blood has long been recognized to maintain lower m.3243A>G heteroplasmy levels compared to other tissues. We have shown at the single cell level that T cells maintain a lower percentage (heteroplasmy) of the m.3243A>G. The mechanism(s) underlying this purifying selection, however, remain unknown. We now report data supporting a model of cell fitness in the maintenance of lower heteroplasmy distributions in the T cell compartment. Specifically, we have observed that purified patient memory CD4+ T cells have lower bulk m.3243A>G heteroplasmy compared to naÃ¯ve CD4+ T cells. In vitro activation of naÃ¯ve CD4+ m.3243A>G patient T cells results in lower bulk m.3243A>G heteroplasmy after proliferation. Finally, m.3243A>G patient T Cell Receptor (TCR) repertoire sequencing reveals relative oligoclonality compared to controls. These data support a role for T cell activation as a bottleneck for cell level selection against high heteroplasmy cells, in a likely cell-autonomous fashion. This model is consistent with findings of relative T cell oligoclonality in other genetically encoded deficits of cell fitness, mouse models of distinct mtDNA variants, and in cell lines edited to introduce mtDNA variants. Further work will be required to elucidate precise metabolic underpinnings and potential clinical consequences of this finding.

Neuroinflammation and Neuroinfection

Vascular Inflammation in Neuropsychiatric Long COVID
Presenting Author: ***Lindsay McAlpine, MD, Yale University***
Co-Authors: Jennifer Chiarella, Allison Nelson, Benjamin Orlinick, Allison Grubman, Bibhuprasad Das, A Shelli Farhadian, Serena Spudich
Biomarkers of platelet and endothelial dysfunction are elevated in patients with acute COVID-19 and predict mortality in critically ill patients. Biomarkers of coagulopathy and endothelial dysfunction are elevated 60 days after COVID-19 and correlate inversely with a 6-min walk test. Evidence of 'microclotting on blood testing after COVID-19 has unclear clinical implications. It is unknown if vascular inflammation persists in individuals with neuropsychiatric Post-COVID-19 Conditions (N-PCC). We investigated for vascular inflammation in 3 groups: individuals with acute COVID-19, N-PCC, and post-COVID-19 controls with no PCC. Participants with N-PCC (new or worsening neuropsychiatric symptoms >3 months after COVID-19) and post-COVID-19 controls with no PCC underwent a cross-sectional clinical assessment (surveys, chart review) and blood collection. Participants with acute COVID-19 were enrolled while hospitalized due to COVID-19. Plasma samples were tested via multiplex bead-based ELISA for the following analytes: Î±1-acid glycoprotein (AGP), Î±2 macroglobulin, ADAMTS13, C-reactive protein (CRP), D-dimer, Fetuin A36, fibrinogen, haptoglobin, L-selectin, platelet factor 4 (PF4), serum amyloid protein (SAP) A, serum amyloid A (SAA), soluble intercellular adhesion molecule-1 (sICAM-1), soluble platelet selectin (sP-Selectin), and soluble vascular cell adhesion molecule-1 (sVCAM-1) (Eve Technologies). All results were log transformed for normality except fibrinogen, L-selectin, SAP, and ADAMS13. ANOVA testing was used with a False Discovery Rate adjustment to address for multiple comparisons. Kruskal-Wallis and Fishers exact tests were used to compare demographics. Exclusion Criteria: <18 years old, pregnant, acute thrombotic event, and history of dementia, stroke, or other major neurologic/psychiatric illness. The acute COVID-19 (A; #28), N-PCC (N; #50), and control groups (C; #29) were similar demographically, in terms of age, gender, race, and most vascular risk factors. The acute COVID-19 group had higher BMI (p=0.008), more hypertension (p=0.03), and were enrolled prior to widespread vaccine availability (p=0.0007). The post-COVID-19 groups had similar time from acute COVID-19 to study visit (N:325 days, C:418, p=0.95). N-PCC symptoms included cognitive issues (72%), new or worsening anxiety or depression (67%), and headache (61%). The results are as follows (median [IQR]): a-2 Macroglobulin (A: 1,001,295 [801,219-1,301,925] N: 1,742,400ng/mL [1,409,950-1,977,275] C: 1,513,700 [1,351,300-1,805,900]; p<0.0001), AGP (A: 1,914,050 [1,617,325-2,149,450] N: 1,484,800 ng/mL [1,132,300-1,790,400] C: 1,124,650 [886,355-1,405,075]; p<0.0001), CRP (A: 147,390,000 pg/mL [76,652,500-274,410,000] N: 12,306,500 [3,929,625-30,898,500] C: 5,882,300 [3,128,100-9,523,175]; p<0.0001), Fetuin A36 (A: 189,142 ng/mL [173,775-208,482] N: 283,256 [224,859-341,091] C: 230,007 [192,167-260,028]; p<0.0001), Fibrinogen (A: 844,531ng/mL [743,837-1,158,234] N: 1,723,500 [1,594,800-2,105,850] C: 1,928,650 [1,612,550-2,299,900]; p<0.0001), Haptoglobin (A: 2,734,350 ng/mL [1,155,775-5,498,775] N: 1,324,850 [832,471-1,650,850] C: 961,743 [612,410-1,201,375]; p<0.0001), L-Selectin (A: 596,697 pg/mL [514,247-721,467] N: 772,704 [657,702-907,725] C: 650,522 [517,830-801,486]; p=0.0035), PF4 (A: 1,406ng/mL [1,033-1,674] N: 666 [483-1,020] C: 820 [483-1,181]; p<0.0001), SAP (A: 7,719,050 pg/mL [6,268,650-9,884,438] N: 7,430,550 [5,807,025-8,215,275] C: 5,268,300 [4,652,100-5,952,375]; p<0.0001), ADAMTS13 (A: 533 ng/mL [481-597] N: 448 [381-528] C: 358 [315-400]; p<0.0001), D-Dimer (A: 1,899 ng/mL [1,446-2,564] N: 725 [520-1421] C: 511 [399-1,150]; p<0.0001), SAA (A: 30,381 ng/mL [15,783-45,539] N: 7773 [3514-14627] C: 5,012 [2,766-10,205]; p<0.0001), sICAM-1 (A: 87 ng/mL [80-100] N: 87 [75-102] C: 73 [66-84]; p=0.0037), sP-Selectin (A: 82 ng/mL [70-89] N: 52 [42-62] C: 39 [35-45]; p<0.0001), and sVCAM-1 (A: 686 ng/mL [431-1,064] N: 433 [376-512] C: 399 [330-461]; p<0.0001). We found no evidence of coagulopathy in the N-PCC group. All acute phase proteins were elevated in acute COVID-19 and two remain persistently elevated in N-PCC, AGP and

haptoglobin. Markers of leukocyte adhesion to the endothelium and endothelial dysfunction were persistently elevated in N-PCC compared to controls, including L-selectin, ADAMTS13, sP-selectin, sICAM-1, and sVCAM-1. sICAM-1 (endothelial adhesion) and SAP (vascular remodeling) remained elevated in the N-PCC group at acute COVID-19 levels. Three markers were higher in N-PCC group compared to the acute COVID-19 group, including Fetuin A36 (vascular calcification), L-selectin (endothelial adhesion), and Î±2 macroglobulin (endothelial adhesion) suggesting a distinct pathophysiology from acute COVID-19. Overall in the N-PCC group, there is elevation of markers related to leukocyte adhesion to the endothelium, endothelial dysfunction, and vascular remodeling. Several markers were higher in the N-PCC group compared to the acute COVID-19 group suggesting a distinct pathophysiology from acute COVID-19. Further studies will longitudinally investigate endothelial adhesion and dysfunction in individuals with N-PCC.

Neuromuscular Disease

Utilization of Humanized Drosophila Models to Evaluate Mechanisms for Disrupted Autophagy in TBK1-ALS
Presenting Author: ***Sarah Berth, MD, PhD, Baylor College of Medicine***
Co-Authors: Hyun-Jun Choi, PhD, Baylor College of Medicine, Amara Gammon, BS, An Bui, BS, Baylor College of Medicine, Thomas Lloyd, MD PhD, Baylor College of Medicine,
One of the most common genetic causes of ALS/FTD overlap is mutations in TBK1, a gene encoding TANK-binding kinase 1 (TBK1), a kinase that regulates autophagy and the innate immune system. Thus far mutations are thought to cause ALS through haploinsufficiency, although many are missense mutations and have not been comprehensively characterized. Development of models of TBK1-mediated ALS/FTD have been challenging due to homozygous loss-of-function of TBK1 being lethal, but heterozygous loss-of-function of TBK1 has not shown a phenotype. We have generated and begun characterization of an in vivo model of TBK1-ALS in Drosophila with mutant alleles and RNA interference to knockdown the TBK1 fly orthologue ik2. Utilizing CRIMIC technology to replace the ORF for ik2 by a Kozak-Gal4 cassette, we show the endogenous expression pattern of ik2 in neurons and glia, and show functional complementation between human TBK1and fly ik2. Further, we show that loss of function of ik2 produces phenotypes consistent with ALS, including impaired locomotion, survival, loss of neuromuscular junction boutons, and disrupted autophagy. These data show the feasibility of in vivo modeling of TBK1-ALS in Drosophila. Future directions will be characterization of TBK1-ALS mutations in motor neurons in vivo utilizing live imaging techniques in Drosophila.

Defining the Role of BMP4/Smad8/miRNA Axis as a Disease-Driving Pathway in Duchenne Muscular Dystrophy
Presenting Author: ***Michael Lopez, MD, PhD, The University of Alabama at Birmingham***
Co-Authors: Hanna Sothers, University of Alabama at Birmingham, Xianzhen Hu, University of Alabama at Birmingham, David Crossman, PhD, University of Alabama at Birmingham, Ying Si, University of Alabama at Birmingham, Matthew Alexander, PhD, University of Alabama at Birmingham, Merry-Lynn McDonald, PhD, University of Alabama at Birmingham, Peter King, MD, University of Alabama at Birmingham
Background: Duchenne muscular dystrophy (DMD) is a fatal X-linked recessive disease due to loss-of-function mutations in the DYSTROPHIN gene. DMD-related skeletal muscle wasting is typified by an aberrant immune response involving upregulation of TGFβ family of cytokines. We previously demonstrated that bone morphogenetic protein 4 (BMP4) is increased in DMD and BMP4 stimulation induces a 20-fold upregulation of Smad8 transcription. However, the role of BMP4 in severely affected DMD skeletal muscle is unknown. We hypothesized that BMP4 signaling could drive aberrant gene expression in severely affected human DMD skeletal muscle detectable as a transcriptomic signature. **Methods:** Transcriptomes from skeletal muscle biopsies of late-stage DMD vs. non-DMD controls and C2C12 muscle cells with or without BMP4 stimulation were generated by RNA-Seq. They were then analyzed for single transcript differential expression followed by Ingenuity Pathway Analysis and weighted gene co-expression network analyses. **Results**: A total of 2,328 transcripts in the human muscle and 5,291 transcripts in C2C12 muscle cells were differentially expressed. We identified an overlapping molecular signature of 1,027 genes dysregulated in DMD muscle that were induced in BMP4-stimulated C2C12 muscle cells. Highly upregulated DMD muscle transcripts that overlapped with BMP4-stimulated C2C12 muscle cells included ADAMTS3, HCAR2, SERPING1, SMAD8, and UNC13C. **Conclusions:** In summary, the DMD transcriptome was characterized by dysregulation of pathways involving immune function, extracellular matrix remodeling, and metabolic/mitochondrial dysfunction. We additionally define a late-stage DMD skeletal muscle transcriptome that substantially overlaps with the BMP4-induced molecular signature in C2C12 muscle cells. This supports BMP4 as a disease-driving regulator of transcriptomic changes in late-stage DMD skeletal muscle and expands our understanding of the evolution of dystrophic signaling pathways and the associated gene networks which could be explored for therapeutic development.

Myotonic Dystrophy Type 2: Phenotypic Variability Patterns in a Neuromuscular Referral Center-Based Cohort
Presenting Author: ***Paloma Gonzalez Perez, MD, PhD, Massachusetts General Hospital***
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Objective: We aimed at investigating the presence of patterns that account for the phenotypic variability in a myotonic dystrophy type 2 (DM2) retrospective cohort at the Mass General Brigham Neuromuscular Centers. **Methods:** We collected the presence or absence of 23 clinical variables at symptom onset, diagnosis, and last follow-up from 67 DM2 patients. We first identified set/s of variables (factors or cluster/s) representative of the large research data pool at onset by performing factor analysis and principal component analysis, then assigned each patient to the cluster for which they had the highest computed total factor score. Twelve variables grouped into two distinct clusters that, based on their variable content, we named as proximal myotonic myopathy (PROMM)- DM2 or non-PROMM-DM2. Eleven variables, even when frequent in the cohort, did not cluster to any identified set of variables. Patients assigned to non-PROMM-DM2 more frequently had clinical myotonia and positive family history, and less frequently multiorgan involvement. Most patients (67.2%) remained assigned to same cluster during disease course and 11 non-PROMM eventually transitioned to PROMM-DM2. Item theory response analysis was conducted to determine which variables were more common at milder stage of the disease (of note, lower number of present variables was considered mild form of the disease, and higher number of present variables was considered severe form of the disease). Dyslipidemia and early cataracts (both belonging to PROMM-DM2 cluster) were the earliest extramuscular manifestations that occurred during disease course and their presence accounted for the conversion of most of the non-PROMM to PROMM converters. Deciphering phenotypic variability patterns may help in determining prognosis and selecting best clinical trial candidates in this multiorgan and relatively unpredictable muscular dystrophy.

Neuro-oncology

T Cell Exclusion in Medulloblastoma – Exploring the Role of Immune Checkpoints
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Background: Medulloblastoma, the most common embryonal brain tumor of childhood, has one of the coldest tumor microenvironments (TMEs) even amongst brain tumors. While well established that lymphocytes poorly infiltrate the tumor, the specific mechanisms of T-cell exclusion are underexplored. We and others have shown that although medulloblastoma has poor expression of tumoral PD-L, it highly expresses a different B7-family molecule, B7-H3, which has been negatively correlated with patient survival. Further, we show high infiltration of myeloid cells within the tumor microenvironment, with high expression of the inhibitory immune checkpoint molecule VISTA. VISTA has been shown to inhibit T-cell activation upon interacting with its binding partners VSIG3 and VSIG8. Finally, analysis of a human database of medulloblastoma tumors identified VSIG8 expression to positively correlate with B7-H3 expression. Thus, we hypothesize that VISTA and its binding partners are expressed in the tumor microenvironment of medulloblastoma in a B7-H3 dependent manner to facilitate T cell exclusion, which contributes to poor survival in this tumor. **Methods:** An established murine medulloblastoma cell line, mCB DNp53 MYC, was implanted orthotopically into BL6/J mice and evaluated for immune cell infiltration by multicolor flow cytometry and immunohistochemistry. mCB DNp53 MYC cells were co-cultured with naÃ¨ve CD4 lymphocytes from BL6/J mice stimulated with CD3/CD28 beads and supplemented with recombinant mouse IL-2 for 5 days. T-cell proliferation was measured using Cell Trace Violet dilution by flow cytometry. VSIG3 and VSIG8 expression were evaluated on mCB DNp53 MYC in vitro by western blot and flow cytometry. Immunohistochemistry was performed on a 60 human medulloblastoma tissue microarray using a human B7-H3 antibody (R&D), which was subsequently given a tertile expression score. Bulk RNA seq database of human tumor samples maintained by Caris Molecular Intelligence was queried for medulloblastoma cases. Log2 transform of transcripts per million was analyzed to identify correlation between immune checkpoint molecules using a FDR of 2. **Results:** mCB DNp53 MYC cells were found to highly express B7-H3, similar to human medulloblastoma. Further, VSIG3 and VSIG8 were identified on both human and murine medulloblastoma cell lines in vitro. IHC on tumors harvested from tumor-bearing mice revealed poor infiltration by CD3+ lymphocytes, but high infiltration of CD11b+ myeloid cells displaying high levels of VISTA expression. Interestingly, a number of myeloid cells clustered at the tumor border, a

phenotype that has been associated with T cell exclusion in other tumors. Co-culture analysis revealed that murine medulloblastoma cells were able to inhibit the proliferation of bead activated CD4 T-cells. Increased expression of VISTA was preliminarily found on non-proliferating CD4 T-cells following co-culture. Experiments to determine whether antibody blockade with B7-H3, VISTA, VSIG3, or VSIG8 can rescue CD4 T cell proliferation are ongoing. In our human medulloblastoma tissue microarray, >90% of samples were positive for B7-H3 consistent with other studies. Analysis of bulk RNA-seq data in medulloblastoma revealed strong associations between B7-H3 and VISTA/VSGI8. **Conclusions:** These results support the hypothesis that multiple immune suppressive mechanisms are contributing to T-cell exclusion in medulloblastoma. Tumor infiltrating myeloid cells that cluster at the tumor border have been associated with T-cell exclusion in other tumors and thought to possibly represent an immune barrier to their infiltration. Since human medulloblastoma samples typically do not include adjacent normal brain tissue, this phenotype may be difficult to confirm in humans but add to the novelty of this finding in our model. Furthermore, we have shown for the first time that medulloblastoma tumor cells can directly inhibit the proliferation of CD4 T cells in vitro, overriding strong external stimuli. Given the paucity of lymphocytes in medulloblastoma, this effect has long been hypothesized but not previously demonstrated. The high expression of B7-H3 in medulloblastoma and the correlation with VISTA and its binding partners in human tumors suggests that the interplay of these molecules may be important in contributing to this phenotype.

Characterization of Methionine Dependence in IDH-mutant Glioma
Presenting Author: ***Julie Miller, MD, PhD, Massachusetts General Hospital***
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Mutations in the metabolic enzyme, Isocitrate dehydrogenase (IDH) 1 or 2, are found in 20% of adult diffuse gliomas. This mutation causes high levels of the metabolite D-2- hydroxyglutarate (2-HG), which leads to extensive epigenetic changes, widespread alterations in metabolism and tumor formation. While IDH-mutant gliomas are responsive to upfront treatment with radiation, chemotherapy and IDH inhibitors, these tumors inevitably recur, leading to progressive neurologic impairment and untimely death.
Mutant IDH-induced changes in metabolic programs create tumor-specific metabolic vulnerabilities that have therapeutic potential. Strategies to target aberrant tumor metabolism may use drugs to exploit cell-intrinsic properties or employ dietary interventions, which can have a profound effect on the availability of metabolites within the tumor microenvironment. Different cancer types depend on specific nutrients for survival, yet these dependencies have not been fully elucidated for IDH-mutant glioma. Based on
this, we explored the interplay between metabolism, diet, and IDH-mutant glioma growth. Using patient-derived gliomasphere cultures and orthotopic mouse models, we found an improvement in survival times of animals with IDH-mutant gliomas put on an intermittent fasting diet. Using metabolomics, we discovered that the survival advantage was associated with depletion of the amino acid methionine in the fasted tumors. We observed a similar impairment in IDH-mutant glioma cell line viability in vitro under methioninerestricted conditions. We note a profound dependence on methionine cycle metabolism and production of S-adenosylmethionine (SAM), the universal methyl donor. As a consequence, IDH-mutant gliomas are sensitive to inhibition of MAT2A, a key enzyme involved in SAM production. Altogether these data show the importance of methionine for IDH-mutant glioma survival and reveal a metabolic vulnerability that is amenable to targeting.

Neuro-opthalmology and Neurovestibular Disease

Estrogen-induced NFÎºB Activation Mediates IL-1Î² Production in Murine Optic Glioma
Presenting Author: ***Yunshuo Tang, PhD, Washington University in Saint Louis***
Co-Authors: Na-Keysha Berry, BS, Stephanie Bozeman, BS, David Gutmann, MD, PhD
Introduction: Vision loss is one of the most significant morbidities associated with optic pathway glioma (OPG), which is a low-grade astrocytoma seen in 15-20% of children with the neurofibromatosis type 1 (NF1) cancer predisposition syndrome. While not fatal, up to 50% of children with NF1-OPG develop retinal ganglion cell (RGC) death, retinal nerve fiber layer (RNFL) thinning, and eventual visual impairment, which occurs three times more frequently in girls than boys. Leveraging a validated preclinical murine model of Nf1-OPG, we previously demonstrated that estrogen mediates RGC death by inducing glial production of IL-1Î², an inflammatory cytokine that is neurotoxic to Nf1-mutant RGC. Herein, we present evidence that estrogen-induced IL-1Î² production is mediated through activation of the NFÎºB pathway, and NFÎºB inhibition leads to durable neuroprotection. **Methods**: Female Nf1-OPG mice were treated with 3 mg/kg/day of acetylsalicylic acid (ASA) in drinking

water or vehicle (water) from 4 weeks to 12 weeks of age, during the window of tumor initiation and growth. ASA prevents NFÎºB activation by inhibiting degradation of the natural NFÎºB inhibitor IÎºB. After the conclusion of treatment at 12 weeks of age, mice were euthanized and perfused either immediately, or at 16 weeks of age. a third cohort of mice were treated with 3 mg/kg/day of ASA from 8 weeks to 12 weeks of age (window of tumor growth), and harvested at the end of treatment. Eyes and optic nerves were processed for paraffin (optic nerves) or cryo (eyes) embedding. immunohistochemical analysis of RGCs (Rbpms) and retinal nerve fiber layer thickness (Smi32) were performed on 10-Âµm retina sections, while immunohistochemistry using IL-1Î², Iba1 (tumor-associated monocytes), and Ki67 (proliferation marker) antibodies was performed on 5-Âµm optic nerve sections. Statistical analysis of two groups was performed using a nonparametric Student's t test, while analysis of three or more groups was performed using a nonparametric one-way ANOVA with Dunn's multiple comparison correction. Statistical significance was defined as $P < 0.05$. **Results:** Inhibition of NFÎºB activation reduced IL-1Î² expression in the optic nerve and protected female Nf1-OPG mice against RGCs death and RNFL thinning. Inhibition of NFÎºB from 4 to 12 weeks of age and 8 to 12 weeks of age were found to be equally effective at preventing RGC death and RNFL thinning. The neuroprotective effect conferred by ASA treatment was also durable, as RGC number and RNFL thickness measured 4 weeks after cessation of treatment were similar to that maintained on ASA treatment. Consistent with the previous discovery that IL-1Î² neutralization is neuroprotective but not antitumor, ASA treatment had no effect on optic nerve volume, tumor proliferation (%Ki67+ cells), or content of tumor associated monocytes (%Iba1+ cells). **Conclusion:** We demonstrated that estrogen-induced IL-1Î² expression in Nf1-OPG is dependent on NFÎºB activation. In a proof-of-concept study, we demonstrated that inhibition of NFÎºB activation using an FDA-approved pharmacological agent (ASA) reduces IL-1Î² production and protects against retinal pathology in a preclinical murine model of Nf1-OPG. These results suggest that estrogen activates the NFÎºB signaling cascade to induce IL-1Î² expression in glial cells in the setting of Nf1-OPG, and pharmacological inhibition of NFÎºB may be a novel therapeutic strategy to attenuate vision loss in children with NF1-OPG.

Neurorecovery and Neuroplasticity

Parvalbumin Interneurons Regulate Circuit Plasticity in the Healthy and Injured Somatosensory Cortex
Presenting Author: ***William Zeiger, PhD, University of California, Los Angeles***
Co-Author: Baruc Campos, PhD, University of California - Los Angeles, Brenda Vasquez, BS, University of California - Los Angeles, Carlos Portera-Cailliau, University of California - Los Angeles
Abstract: Circuits in the central nervous system have the capacity for plasticity and reorganization. Circuit remapping occurs during development, learning, and in response to sensory experience. This capacity for plasticity might also offer an avenue for recovery after an injury to the brain. For example, based largely on human macroscopic brain mapping studies (e.g., fMRI), it has been widely hypothesized that plasticity and remapping of circuits underlies recovery after stroke. However, how specific changes in neuronal circuits mediate improvement in function and recovery after stroke remains a major gap in our understanding. Using a mouse model of focal cortical stroke, we previously performed longitudinal two-photon calcium imaging (2PCI) of neurons in the peri-infarct somatosensory cortex (S1) after stroke. We found that sensory-evoked activity was reduced for a prolonged period after stroke and that spontaneous remapping was absent. We also found that whisker trimming-induced circuit remapping, a well-established paradigm for experience-dependent plasticity in the healthy somatosensory cortex, was impaired. These results suggest that plasticity in the peri-infarct cortex may be maladaptive and limit recovery. We are now exploring potential mechanisms of this maladaptive plasticity by studying the role of Parvalbumin (PV) inhibitory interneurons in the healthy and injured cortex. PV cells play important roles in regulating the spatial and temporal encoding of sensory information in the cortex, and their activity has been hypothesized to gate critical periods of plasticity. Here, we used longitudinal 2PCI to record the activity of individual PV cells in the healthy S1 before, during, and after inducing experience-dependent plasticity by whisker trimming. We find that the spatial distribution of sensory-evoked responses in PV cells mirrors that of pyramidal cells. Whisker trimming leads to recruitment of PV cells responsive to the spared whisker in deprived cortical barrels, and there are long-lasting shifts in responsivity to the spared whisker in the spared barrel even after whisker regrowth. Furthermore, chemogenetic inhibition of PV cells during experience-dependent plasticity blocks whisker trimming-induced remapping. In the peri-infarct cortex, sensory-evoked responses to the principal whisker of the infarcted barrel are selectively impaired after stroke, similar to the effects observed in pyramidal cells. Together, these results suggest that proper functioning of PV cells is essential for adaptive plasticity in the healthy and injured cortex. Understanding the details of how cortical circuits change after injury will be essential for designing pharmacologic and neuromodulatory approaches to promote functional remapping and improve recovery from brain injury in the future.

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Zeiger, William	38, K-S1.007
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Friday, September 13, 2024
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Edilberto	Amorim	Children's National Hospital	5	4
Maria	Barnes-Davis	Cincinnati Children's Hospital Medical Center	6	6
Sarah	Berth	Baylor College of Medicine	3	1
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Jason	Chua	Johns Hopkins University	6	2
David	Coughlin	University of California San Diego	6	1
Terry	Dean	Children's National Hospital	5	1
Anna	Duncan	Massachusetts General Hospital	6	3
Joline	Fan	University of California, San Francisco	2	4
Thomas	Foutz	Washington University in St. Louis	2	7
Jason	Gill	Baylor College of Medicine	6	2
Paloma	Gonzalez Perez	Massachusetts General Hospital	3	6
James	Gugger	University of Rochesteer	2	7
Elan	Guterman	University of California, San Francisco	2	7
Chloe	Hill	University of Michigan	2	7
Jennifer	Hranilovich	University of Colorado School of Medicine	1	5
David	Isaacs	Vanderbilt University Medical Center	6	5
Michelle	Johansen	Johns Hopkins University School of Medicine	5	7
Eric	Kaiser	University of Pennsylvania	1	2
Gunisha	Kaur	Weill Cornell Medicine	1	6
Jennifer	Kim	Yale School of Medicine	5	7
Courtney	Lane-Donovan	University of California, San Francisco	6	3
Michael	Lopez	The University of Alabama at Birmingham	3	5
Allison	Martin	Albert Einstein College of Medicine	4	2
Lindsay	McAlpine	Yale University	4	4
Melanie	McNally	Massachusetts General Hospital	6	2
Niccolo	Mencacci	Northwestern University	7	1
Julie	Miller	Massachusetts General Hospital	4	2
Imama	Naqvi	Columbia University	1	4
Charlene	Ong	Boston University Chobanian & Avedisian School of Medicine	5	6
Archana	Patel	Boston Children's Hospital, Harvard Medical School	1	5
Sam	Payabvash	Yale University	5	5
Jeffrey	Russ	Duke University	7	1
Ranmal	Samarasinghe	University of California, Los Angeles	2	3
Rani	Sarkis	Brigham and Women's Hospital, Harvard Medical School	2	7
Samuel	Snider	Brigham and Women's Hospital	5	6
David	Soleimani-Meigooni	University of California, San Francisco	4	5

Christopher	Stephen	Massachusetts General Hospital and Harvard Medical School	3	4
Yunshuo	Tang	Washington University in Saint Louis	4	2
Regina	Triplett	Washington University in St. Louis	2	5
Thomas	Tropea	University of Pennsylvania Perelman School of Medicine	3	4
Melissa	Walker	Massachusetts General Hospital/ Harvard Medical School	7	3
William	Zeiger	University of California - Los Angeles	7	3
Julie	Ziobro	University of Michigan	7	3

Saturday, September 14, 2024 – Breakout #1 Assignments

First Name	Last Name	Saturday Breakout #1	Room Name	Saturday Breakout #1 (Mentors)
Joline	Fan	1	Lake Sheen A	Liu, Poduri
Thomas	Foutz	1	Lake Sheen A	Liu, Poduri
James	Gugger	1	Lake Sheen A	Liu, Poduri
Chloe	Hill	1	Lake Sheen A	Liu, Poduri
Regina	Triplett	1	Lake Sheen A	Liu, Poduri
Jason	Chua	2	Lake Sheen A	Berman, Carmichael
David	Isaacs	2	Lake Sheen A	Berman, Carmichael
Courtney	Lane-Donovan	2	Lake Sheen A	Berman, Carmichael
Yunshuo	Tang	2	Lake Sheen A	Berman, Carmichael
Terry	Dean	3	Lake Sheen B	Schor, Brooks-Kayal
Anna	Duncan	3	Lake Sheen B	Schor, Brooks-Kayal
Niccolo	Mencacci	3	Lake Sheen B	Schor, Brooks-Kayal
Jeffrey	Russ	3	Lake Sheen B	Schor, Brooks-Kayal
Julie	Ziobro	3	Lake Sheen B	Schor, Brooks-Kayal
Paloma	Gonzalez Perez	4	Lake Sheen B	Skolarus, Geocadin
Jennifer	Hranilovich	4	Lake Sheen B	Skolarus, Geocadin
Lindsay	McAlpine	4	Lake Sheen B	Skolarus, Geocadin
Imama	Naqvi	4	Lake Sheen B	Skolarus, Geocadin
Samuel	Snider	4	Lake Sheen B	Skolarus, Geocadin
Maria	Barnes-Davis	5	Lake George A	Paredes, Jensen
Jason	Gill	5	Lake George A	Paredes, Jensen
Archana	Patel	5	Lake George A	Paredes, Jensen
Ranmal	Samarasinghe	5	Lake George A	Paredes, Jensen
William	Zeiger	5	Lake George A	Paredes, Jensen
Edilberto	Amorim	6	Lake George A	Stacey, Hamilton
Jennifer	Kim	6	Lake George A	Stacey, Hamilton
Rani	Sarkis	6	Lake George A	Stacey, Hamilton
Christopher	Stephen	6	Lake George A	Stacey, Hamilton
Nick	Brenton	7	Lake George B	Mowry, Ances
Gunisha	Kaur	7	Lake George B	Mowry, Ances
Charlene	Ong	7	Lake George B	Mowry, Ances
David	Soleimani-Meigooni	7	Lake George B	Mowry, Ances
Eric	Kaiser	8	Lake George B	Becher, Poduri
Allison	Martin	8	Lake George B	Becher, Poduri
Julie	Miller	8	Lake George B	Becher, Poduri
Melissa	Walker	8	Lake George B	Becher, Poduri
Sarah	Berth	9	Lake George B	Paulson, Nelson
David	Coughlin	9	Lake George B	Paulson, Nelson
Michael	Lopez	9	Lake George B	Paulson, Nelson
Thomas	Tropea	9	Lake George B	Paulson, Nelson
Elan	Guterman	10	Lake George A	Landsness, McCullough
Michelle	Johansen	10	Lake George A	Landsness, McCullough
Melanie	McNally	10	Lake George A	Landsness, McCullough
Sam	Payabvash	10	Lake George A	Landsness, McCullough

Saturday, September 14, 2024 – Breakout #2 Assignments

First Name	Last Name	Saturday Breakout #2	Room Name	Saturday Breakout #2 (Mentors)
Edilberto	Amorim	1	Lake Sheen A	Sansing, Standaert
Maria	Barnes-Davis	1	Lake Sheen A	Sansing, Standaert
Sarah	Berth	1	Lake Sheen A	Sansing, Standaert
Jason	Chua	1	Lake Sheen A	Sansing, Standaert
David	Coughlin	1	Lake Sheen A	Sansing, Standaert
Terry	Dean	2	Lake Sheen A	Carmichael, McCullough
Anna	Duncan	2	Lake Sheen A	Carmichael, McCullough
Joline	Fan	2	Lake Sheen A	Carmichael, McCullough
Thomas	Foutz	2	Lake Sheen A	Carmichael, McCullough
Jason	Gill	3	Lake Sheen B	Renthal, Brooks-Kayal
James	Gugger	3	Lake Sheen B	Renthal, Brooks-Kayal
Elan	Guterman	3	Lake Sheen B	Renthal, Brooks-Kayal
Chloe	Hill	3	Lake Sheen B	Renthal, Brooks-Kayal
David	Isaacs	3	Lake Sheen B	Renthal, Brooks-Kayal
Jennifer	Hranilovich	4	Lake Sheen B	Poduri, Paulson
Michelle	Johansen	4	Lake Sheen B	Poduri, Paulson
Eric	Kaiser	4	Lake Sheen B	Poduri, Paulson
Jennifer	Kim	4	Lake Sheen B	Poduri, Paulson
Courtney	Lane-Donovan	4	Lake Sheen B	Poduri, Paulson
Allison	Martin	5	Lake George A	Liu, Berman
Lindsay	McAlpine	5	Lake George A	Liu, Berman
Melanie	McNally	5	Lake George A	Liu, Berman
Niccolo	Mencacci	5	Lake George A	Liu, Berman
Imama	Naqvi	5	Lake George A	Liu, Berman
Charlene	Ong	6	Lake George A	Leslie-Mazwi, Hamilton
Archana	Patel	6	Lake George A	Leslie-Mazwi, Hamilton
Sam	Payabvash	6	Lake George A	Leslie-Mazwi, Hamilton
Jeffrey	Russ	6	Lake George A	Leslie-Mazwi, Hamilton
Rani	Sarkis	6	Lake George A	Leslie-Mazwi, Hamilton
Samuel	Snider	7	Lake George B	Skolarus, Greer
David	Soleimani-Meigooni	7	Lake George B	Skolarus, Greer
Christopher	Stephen	7	Lake George B	Skolarus, Greer
Yunshuo	Tang	7	Lake George B	Skolarus, Greer
Thomas	Tropea	7	Lake George B	Skolarus, Greer
William	Zeiger	8	Lake George B	Landess, Vickrey
Julie	Ziobro	8	Lake George B	Landess, Vickrey
Nick	Brenton	8	Lake George B	Landess, Vickrey
Paloma	Gonzalez Perez	8	Lake George B	Landess, Vickrey
Gunisha	Kaur	9	Lake George B	Geocadin, Stacey
Michael	Lopez	9	Lake George B	Geocadin, Stacey
Julie	Miller	9	Lake George B	Geocadin, Stacey
Ranmal	Samarasinghe	9	Lake George B	Geocadin, Stacey
Regina	Triplett	9	Lake George B	Geocadin, Stacey
Melissa	Walker	9	Lake George B	Geocadin, Stacey

Saturday, September 14, 2024
Poster Tour Group Assignments & Poster Numbers

First Name	Last Name	Abstract Title	Poster Group	Poster Number	Mentor
Edilberto	Amorim	Highly Epileptiform EEG Trajectories and Functional Recovery Post-Cardiac Arrest	1	1	McCullough
Michelle	Johansen	Proteomics and the Risk of Incident Embolic and Thrombotic Stroke in the Atherosclerosis Risk in Communities Study	1	17	McCullough
Jennifer	Kim	Can the Incorporation of Quantitative Markers and Death Improve the Prediction of Post-Ischemic Stroke Epilepsy?	1	19	McCullough
Melanie	McNally	Neonatal Mild Hypoxic-ischemic Encephalopathy: Persistently Elevated Programmed Neuronal Death for Weeks After Injury	1	23	McCullough
Charlene	Ong	Quantitative Pupillometry Predicts Neurologic Deterioration in Patients with Large Middle Cerebral Artery Stroke	2	27	Leslie-Mazwi
William	Zeiger	Parvalbumin Interneurons Regulate Circuit Plasticity in the Healthy and Injured Somatosensory Cortex	2	38	Leslie-Mazwi
Imama	Naqvi	Influences on Health Preventive Behaviors after Minor Stroke: Understanding Patient Perceptions and Practices in an Urban Underserved Population	2	25	Leslie-Mazwi
Sam	Payabvash	Deep-learning Model for Prediction of Hematoma Growth after Intracerebral Hemorrhage from Admission Head CT	2	29	Leslie-Mazwi
Maria	Barnes-Davis	Functional Connectivity within the Language Network at 4 to 6 Years of Age and Relationship to Later Language Performance at 8 to 12 Years in Extremely Preterm Children and Term Peers: Short term gains with long term consequences?	3	2	Paredes
Anna	Duncan	Loss of Function of EIF4A2 Leads to Neurodevelopmental Impairment in Zebrafish	3	7	Paredes
Jason	Gill	The Timing of Purkinje Cell Silencing Determines Severity of Neurodevelopmental Outcomes	3	11	Paredes
Niccolo	Mencacci	Bi-allelic BORCS5 Variants Result in A Wide Spectrum of Progressive Neurodevelopmental Disorders via Lysosomal Dysfunction	3	24	Paredes
Jeffrey	Russ	Single Nucleus RNA Sequencing in the Chronic Phase of Perinatal Hypoxic-ischemic Encephalopathy Reveals a Novel Anti-inflammatory Therapeutic Target	4	30	Brooks-Kayal
Regina	Triplett	Epilepsy and Neurodevelopmental Risk Stratification in Very Preterm Infants with Intraventricular Hemorrhage	4	47	Brooks-Kayal
Melissa	Walker	Understanding mtDNA Variant Segregation in Single Cells: How T Cell Activation Contributes to Purifying Selection Against the MELAS-associated m.3243A>G Pathogenic Variant in Blood	4	48	Brooks-Kayal

Thomas	Foutz	Insights from Centromedian Thalamic Stimulation Evoked Responses to Improve Brain Stimulation Therapies	5	10	Poduri
James	Gugger	Structural Neuroimaging Phenotypes of Post-Traumatic Epilepsy	5	12	Poduri
Julie	Ziobro	Parvalbumin-positive Interneuron Alterations in a Mouse Model of Pcdh19 Clustering Epilepsy	5	39	Poduri
Chloe	Hill	Developing a Clinic-Based Priority Communication Tool to Improve Outcomes for Patients with Drug-Resistant Epilepsy	5	14	Poduri
Rani	Sarkis	Late Onset Unexplained Epilepsy is Associated with Verbal Memory Impairment and Lower Amydala Volumes	6	31	Stacey
Elan	Guterman	Evaluating the Feasibility of Prehospital Point-of-care EEG: The Prehospital Implementation of Rapid EEG (PHIRE) Study	6	13	Stacey
Ranmal	Samarasinghe	Fusion Brain Organoid Studies to Uncover Circuit Dysfunction in Genetic Epilepsy	6	46	Stacey
Joline	Fan	Global Network Disruption Across Sleep-wake States in Focal Epilepsy	6	9	Stacey
Jennifer	Hranilovich	Baseline Clinical Characteristics from a Prospective Multiple Cohort Study of Headache in Transgender/Gender Diverse Youth and Their Cisgender Male Comparators: Preliminary Findings	7	15	Renthal
Eric	Kaiser	Enhancing and Ameliorating Light Avoidance in Mice with Photoreceptor Targeting and CGRP Sensitization	7	18	Renthal
Gunisha	Kaur	Chronic Somatic Pain in Refugee Torture Survivors in the United States	7	43	Renthal
Thomas	Tropea	Detecting and Measuring the Clinical Impact of Concomitant Alpha-synuclein Pathology in Alzheimer's Disease	8	37	Paulson
David	Coughlin	Tau Seeding from Brain Homogenate Samples Correlates with Histopathological Burden	8	5	Paulson
Courtney	Lane-Donovan	Tau Phosphorylation at Alzheimer's Disease Biomarker Sites Impairs Tau Cleavage by Lysosomal Proteases	8	20	Paulson
Jason	Chua	Rescuing Alpha-synuclein Toxicity Through Neuron-specific Enhancement of Autophagy	9	4	Hamilton
David	Soleimani-Meigooni	Synaptic Loss in Relapsing and Progressive Multiple Sclerosis: An In Vivo Exploratory Study using SV2A-PET	9	33	Hamilton
Nick	Brenton	Obesity as a Driver of Inflammation and Brain Volume Loss in Pediatric Multiple Sclerosis	9	40	Hamilton
Allison	Martin	T Cell Exclusion in Medulloblastoma – Exploring the Role of Immune Checkpoints	10	21	Becher, Schor
Yunshuo	Tang	Estrogen-induced NFÎºB Activation Mediates IL-1Î² Production in Murine Optic Glioma	10	36	Becher, Schor

Julie	Miller	Characterization of Methionine Dependence in IDH-mutant Glioma	10	45	Becher, Schor
Sarah	Berth	Utilization of Humanized Drosophila Models to Evaluate Mechanisms for Disrupted Autophagy in TBK1-ALS	11	3	Nelson
Paloma	Gonzalez Perez	Myotonic Dystrophy Type 2: Phenotypic Variability Patterns in a Neuromuscular Referral Center-Based Cohort	11	42	Nelson
Michael	Lopez	Defining the Role of BMP4/Smad8/miRNA Axis as a Disease-Driving Pathway in Duchenne Muscular Dystrophy	11	44	Nelson
David	Isaacs	Sensory Gating Impairment in Adults with Chronic Tic Disorders	12	16	Berman
Christopher	Stephen	Quantitative Kinematic Assessment of X-linked Dystonia Parkinsonism Using Wearable Sensor Technology	12	35	Berman
Lindsay	McAlpine	Vascular Inflammation in Neuropsychiatric Long COVID	13	22	Ances, Geocadin
Archana	Patel	The Impact of Malaria on the Central Nervous System - Does ComaReally Matter?	13	28	Ances, Geocadin
Terry	Dean	Heterogeneity of Bmal1-dependence in NG2-glia	13	6	Ances, Geocadin
Samuel	Snider	Automated Measurement of Cerebral Hemorrhagic Contusions and Outcomes after Traumatic Brain Injury: A TRACK-TBI STUDY	13	32	Ances, Geocadin