

Amanda E. Hernan, Ph.D.
CURRICULUM VITAE

Position: Research Scientist/Lab Head
Division of Neuroscience, Nemours Children's Health

Affiliated Assistant Professor
Department of Psychological and Brain Sciences, University of Delaware

Affiliated Assistant Professor
Department of Neurological Sciences, University of Vermont

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Division of Neuroscience
Nemours Children's Health
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EDUCATION

2008-2013	Dartmouth College, Hanover, NH	Ph.D., Experimental and Molecular Medicine
2003-2007	Case Western Reserve University, Cleveland, OH	B.S., B.A., Biology, Psychology

LICENSES, CERTIFICATION

Year	License/Certification
2012	SYNERGY Certificate Program in Clinical and Translational Research Methods, The Dartmouth Clinical and Translational Science Institute, Hanover, NH

FACULTY POSITIONS HELD

Years	Institution	Academic Title	Department
2019-2021	University of Vermont, Burlington, VT	Assistant Professor (tenure pathway)	Neurological Sciences

OTHER POSITIONS AND MAJOR ADMINISTRATIVE POSITIONS HELD

Years	Location/Program Name	Role
2013-2019	Department of Neurological Sciences, University of Vermont Larner College of Medicine, Burlington, VT	Postdoctoral Associate
2007-2013	Department of Neurology Research, Geisel School of Medicine at Dartmouth, Hanover, NH	Graduate Research Assistant
2004-2007	Department of Psychiatry, Case Western Reserve University, Cleveland, OH	Research Technician

HONORS AND AWARDS

Year	Name of Award
2006	Howard Hughes Baccalaureate Fellow
2005-2007	Dean's High Honors, Case Western Reserve University

2011 Graduate Travel Awardee, Dartmouth College
2016 American Epilepsy Society Fellow
2017 NIH NINDS K22 Transition to Independence Award
2018 Gordon Research Seminar Chair
2020 LCOM Gender Equity in Medicine and Science Rising Star Nominee
2020 NIH NINDS Curing the Epilepsies 2021 Conference Travel Awardee
2021 Citizens United for Research in Epilepsy Continuity Funding Awardee

KEYWORDS/AREAS OF INTEREST

Epilepsy, early life seizures, neuropsychiatric disease, cognition, neural networks, prefrontal cortex, hippocampus, neuropeptides

SUMMARY OF PROFESSIONAL ACTIVITIES- OVERALL

I am a translational neuroscientist with interest in understanding neural network damage after early life seizures. I have been conducting epilepsy-focused neuroscience research focused for the past 11 years as a graduate student at the Geisel School of Medicine at Dartmouth and as a postdoctoral associate in the Department of Neurological Sciences at the University of Vermont Larner College of Medicine. In fall 2019, I accepted a position as an Assistant Professor (tenure pathway) in the Department of Neurological Sciences in the Larner College of Medicine. I am now transitioning to the role of Research Scientist/Lab Head at in the Neuroscience Division of Nemours Children's Hospital and Assistant Professor in the Department of Psychological and Brain Sciences at the University of Delaware. I will also serve as the core director of the electrophysiology core at Nemours.

In 2017, I was awarded with a NIH NINDS Advanced Postdoctoral Career Transition award to study the mechanisms for improving cognitive outcome in pediatric epilepsy with ACTH. In September 2019, I was awarded phase II, the independent phase, of that award. My long-term career goals are to build an epilepsy research program designed around understanding the potential neuroprotective role of neuropeptide signaling during development on improvement of outcome in pediatric epilepsy.

My work is poised to challenge a particular dogma of pediatric epilepsy treatment, namely that treating seizures is the only effective way to prevent deleterious cognitive outcomes. The potential findings of this research, therefore, have huge implications for the way physicians treat epilepsy in children. My immediate research project seeks to understand the mechanisms underlying a neuropeptide-based intervention, using cellular, behavioral, and network modeling techniques. This combination of approaches is designed to maximize the translatability of these results to other neurodevelopmental insults that affect cognition in children.

A particular strength of this work is that I will be able to observe neural networks, both at rest and during behavioral tasks, simultaneously in multiple brain regions subserving cognition. Traditionally, the hippocampus has been the focus of study when looking at the effects of ELS on cognition. Since clinical evidence indicates that multiple neural networks are likely affected by generalized ELS, particularly executive function networks of the PFC, I am interested in examining LFP and single-unit firing in the hippocampus and PFC simultaneously during tasks that require careful crosstalk between these structures. As an extension of this, I am also interested in understanding dynamic signaling between astrocytes and neurons in this context, and the role neuropeptide modulation of this signaling may play in cognitive impairment. There are currently very few, if any, pharmaceutical treatment options for executive dysfunction in epilepsy. It is therefore paramount that the mechanism by which ACTH is able to prevent executive function deficits after ELS is understood.

SUMMARY OF ACCOMPLISHMENTS

- Published 14 peer-reviewed papers, including 9 first author and 2 last author publications with two last author publications in preparation
- Received NIH NINDS Transition to Independence Award, K22NS104230-01 (2017-2019 mentored phase I; 2019-2022 independent phase II)
- Course director for NSCI 381, recurring guest lecturer in 2 additional graduate/undergraduate courses and a recurring lecture series for Neurological Sciences medical residents
- Thesis advisor and direct mentor for 8 undergraduates, 4 graduate students (PhD and Master's)
- Co-chaired an international Gordon Research Seminar in the Mechanisms of Neuronal Synchronization in Epilepsy
- Session chair for the Aetiology in Epilepsy Session of the National Center for Young People with Epilepsy Annual Research Retreat (UK)
- 15 invited national and international oral presentations
- Presenting author on 19 abstracts
- Postdoctoral representative of the Vermont Chapter of the Society for Neuroscience
- Faculty representative of the Vermont Chapter of the Society for Neuroscience
- American Epilepsy Society Postdoctoral Fellow
- Involved in a number of community outreach organizations to improve female and underrepresented minority visibility in science and to increase science literacy among the public.

PROFESSIONAL SERVICE

DEPARTMENTAL SERVICE

Years	Department	Committee	Role
2020-	Neurological Sciences	Diversity, Equity and Inclusion	Research faculty committee member

COLLEGE SERVICES

None to date.

MEDICAL CENTER SERVICE

None to date.

UNIVERSITY SERVICE

Years	Service Committee	Role
2014-2019	Vermont Chapter of the Society for Neuroscience	Postdoctoral Representative
2015	Upward Bound	Neuroscience course co-leader
2019-	Faculty Senate	Faculty Senator
2019-2022	Vermont Chapter of the Society for Neuroscience	Faculty Representative

GOVERNMENT

None to date.

SOCIETY MEMBERSHIPS

2006-present	Society for Neuroscience
2010-present	American Epilepsy Society
2013-present	F1000 Prime Associate Faculty Member
2013-present	500 Women Scientists
2016-present	International League Against Epilepsy: Young Epilepsy Section
2019-present	Association for Women in Science

SERVICE TO PROFESSIONAL ORGANIZATIONS

2013-2019	Vermont Chapter of the Society for Neuroscience	Postdoctoral representative
2016-2018	Gordon Research Seminar: Mechanisms of Epilepsy and Neuronal Synchronization	Elected co-chair
2020-2022	Vermont Chapter of the Society for Neuroscience	Faculty representative

SERVICE TO PROFESSIONAL PUBLICATIONS

2010, 2013	Journal of Neuroscience
2018-present	Neuropharmacology
2016-present	PLoS One
2015-present	Pharmaceutics, Brain Sciences, Antioxidants, Molecules
2014	Brain and Development
2012-present	Naunyn-Schmiedeberg's Archives of Pharmacology
2011-present	Epilepsy and Behavior
2020-present	Journal of Central Nervous System Disease
2020-present	Nature Communications
2021-present	Psychoneuroendocrinology
2021-present	Review Editor on the Editorial Board of Epilepsy, Frontiers in Neurology

PUBLIC SERVICE

2014-present	Involved in the "request a scientist" program through 500 Women Scientists organization, which is a resource designed to amplify female voices in STEM fields
2018-present	AAAS SciLine registered expert. A program designed to connect scientists to journalists and other science communicators with the goal of creating a better-informed public.
2019-present	STEM Role Model and FabFem mentor. These national registry programs are designed to connect STEM and female STEM mentors to younger generations of students with interest in STEM fields.

SUMMARY OF SERVICE ACTIVITIES

I have been elected and served as the postdoctoral representative of the Vermont Chapter of the Society for Neuroscience for the past 5 years, a role which I will continue as the currently elected Faculty Representative for the Chapter in the future. I am also a member of a number of professional societies. In 2016, I was elected as co-chair of the 2018 Mechanisms of Epilepsy and Neuronal Synchronization Gordon Research Seminar (GRS); the GRS is a unique forum for graduate students, post-docs, and other scientists with comparable levels of experience and education to present and exchange new data and cutting-edge ideas. Offered bi-annually, this conference is in conjunction with the Gordon Research Conference, which together attract the most influential epilepsy researchers and trainees in the field.

I have also served as an instructor in the Upward Bound program. Through this program, I had the opportunity to give hands-on didactic instruction to high school students through the Upward Bound program. I serve as a UVM Faculty Senator, and am recently serving as a faculty representative for the Neurological Sciences Diversity, Equity and Inclusion Committee.

Over the past few years, I have been invited to review several manuscripts from mid- and top-tier journals in the fields of neuroscience, and look forward to continuing to contribute to the peer review process and promote rigorous, hypothesis-driven research. I was recently asked to peer review NIH applications for the NICHD loan repayment program.

Finally, I have had the opportunity to serve as a mentor for young people, particularly young women and other underrepresented groups in STEM fields, on a number of national and international registries.

TEACHING

FORMAL SCHEDULED CLASSES

Year	Course Title	Course		Hours	Number of Learners	Learner Level
		R	E			
2016-2020	NSCI 381 and 382 Seminar in Neuroscience: Sem in Anatomy & Neuroscience	X		1 credit	15-20	G
2016-present	NSCI 222 Cellular Neurophysiology (3 lectures)		X	3 credits	15-20	UG/G
2018-2019	NSCI 295 Advanced Special Topics: Complex Network Systems in Biology		X	3 credits	5-10	G
2019-present	NSCI 280 Glia: Not just neuron glue (1 lecture)		X	3 credits	15-55	UG/G

R-required; E-elective; Hours-approx. per semester; G-graduate studies (instruction as per the LCOM Teaching Academy Portfolio)

CURRICULUM DEVELOPMENT

None to date.

POSTGRADUATE AND OTHER COURSES

Years	Department	Responsibility
2014	Neurological Sciences; NSCI 306	Guest Lecturer
2014, 2015	Neurological Sciences; NSCI 323	Guest Lecturer
2016-present	Neurological Sciences; NSCI 222	Guest Lecturer
2017-present	Neurological Sciences; Basic Science of Epilepsy Resident Lecture Series	Guest Lecturer

2018-2019 Neurological Sciences; NSCI 295
 2019-present Neurological Sciences; NSCI 280

Guest Lecturer
 Guest Lecturer

PREDOCTORAL STUDENTS SUPERVISED OR MENTORED

Dates	Name	Program School	Role	Current Position
2011	Abigail Alexander	Undergraduate, Bates College	Research Advisor	Research Assistant, McLean Hospital
2012-2013	David Lerner	Undergraduate, Dartmouth College	Research Advisor	Research Assistant, UPenn School of Medicine
2014	Michael Onwukaeme	Summer Neuroscience Undergraduate Research Fellow, University of Vermont	Research Advisor	Research Intern, National Institute of Health
2013-2014	Andrew Massey	Undergraduate Intern, University of Bath	Research Advisor	Development officer, Royal Shakespeare Company
2015	Madonna Enwe	Summer Neuroscience Undergraduate Research Fellow, University of Vermont	Research Advisor	Medical student, Ohio State University
2015-2016	Laura Powers	Undergraduate Researcher, University of Vermont	Research Advisor	Laboratory technician, Sanofi Pharmaceuticals
2017-2018	Umesh Acharya	Summer Neuroscience Undergraduate Research Fellow, University of Vermont	Research Advisor	Teen Director at Sara Holbrook Community Center
2018-2019	Colin Villarín	Summer Neuroscience Undergraduate Research Fellow/Honors Thesis Student, University of Vermont	Research Advisor Thesis Advisor	Clinical Research Coordinator, Massachusetts General Hospital
2019	Kelly Lee	Summer Neuroscience Undergraduate Research Fellow, University of Vermont	Research Advisor	Undergraduate at Trinity Washington University
2018-2021	Tyra Martinez	Master's Program in Biology, University of Vermont	Research Advisor	former student
2018-present	Montana Kay Lara	Neuroscience Graduate Program, University of Vermont	Co-advisor	current student
2020	Paul Lehmann	Thesis Student, University of Vermont	Research Advisor	current student
2020-present	Emily Dean	Summer Neuroscience Undergraduate Research Fellow, University of Vermont	Research Advisor	current student

2020-present	Corttney Feldman	Thesis Student, Honors College, University of Vermont	Research Advisor	current student
2020-present	Jake Spiegler	Undergraduate Researcher, University of Vermont	Research Advisor	current student
2020-present	Trevor Wolf	Cellular and Molecular Biology Graduate Program, University of Vermont	Dissertation co-advisor	current student
2020-present	Mohamed Khalife	Neuroscience Graduate Program, University of Vermont	Dissertation research advisor	current student

DISSERTATION/THESIS COMMITTEE MEMBERSHIP

2018 Chair, Colin Villarin, Honors College at the University of Vermont
2019 Primary Advisor, Tyra Martinez, Graduate College at the University of Vermont
2020 Member, Noelle Michaud, Graduate College at the University of Vermont
2020 Member, Montana Kay Lara, Graduate College at the University of Vermont
2020 Member, Erin Cullen, Graduate College at the University of Vermont
2020 Member, Callum Thomas, Graduate College at the University of Vermont
2020 Primary Advisor, Khalil Abed Rabbo, Graduate College at the University of Vermont
2020 Chair, Corttney Feldman, Honors College at the University of Vermont

POSTDOCTORAL FELLOWS AND RESIDENTS DIRECTLY SUPERVISED OR MENTORED

None to date.

INFORMAL TEACHING

2013-present Attend and present in Epilepsy, Cognition and Development Group biweekly meetings to undergraduate, graduate and postdoctoral trainees
2017-2018 Participated in Complexity and Medicine journal club, presenting research to faculty, graduate students and postdocs with an interest in Complex Systems
2020-present Participate in the international “N2: The Network Network” continuing seminar series hosted at University College London.

FACULTY MENTORED

None to date.

OTHER VISITING FACULTY SUPERVISED

2019-present	Tsuyoshi Tsukada	Kanazawa Medical University, Ishikawa, Japan	Research Co-supervisor
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TEACHING AIDS

None to date.

TEACHING AWARDS AND NOMINATIONS

None to date.

SUMMARY OF TEACHING ACTIVITIES

Formal Teaching. During my time at UVM, I have served as a faculty coordinator and course co-director for the Neuroscience Graduate Program (NGP) Journal Club, NSCI 381/382. This course is a year-long, weekly mandatory component of graduate education for all NGP students designed to teach students how to read, critically evaluate and effectively communicate scientific literature. I serve as a guest lecturer for NSCI 295/395C, 222, and 280.

Research mentor. While I enjoy teaching in a classroom setting, I feel that I excel and am most effective mentoring in a laboratory setting. Through my twelve years of academic research experience, I have served as a formal and an informal mentor for numerous graduate and undergraduate students, as well as lab technicians and postdoctoral fellows. Most recently, I have served formally the faculty mentor for a Summer Undergraduate Neuroscience student Colin Vilarin, who continued his honors thesis in my lab, finishing up in Spring 2019. Colin is now a Clinical Research Coordinator at Massachusetts General Hospital and has several interviews for MD/PhD programs. I have also accepted Khalil Abed Rabbo, my technician, who will be doing his Masters in Pharmacology; Montana Kay Lara, a PhD student in the NGP program is being co-supervised by Rod Scott and me; Trevor Wolf, a PhD student in the CMB program is being co-supervised by James Stafford and me; and Mohamed Khalife, an NGP PhD graduate student, is rotating through my lab currently and will likely join my lab in the fall.

RESEARCH AND SCHOLARLY ACTIVITIES

RESEARCH AWARDS AND GRANTS

Ongoing Research Support

2019-2022 NIH NINDS K22NS104230-03 (Phase II)

PI, Title: Mechanisms for Improving Cognitive Outcome in Pediatric Epilepsy with ACTH

2020-2020 Citizens United for Research in Epilepsy, Epilepsy Research Continuity Fund Award,

PI

2020-2021 NIH NIGMS P30GM118228-05S1, Budd, Ralph (PI)

Co-I, Title: Vermont Immunobiology / Infectious Diseases Center: Alzheimer's-focused administrative supplement

Completed Research Support

2020-2020 Mallinkrodt Pharmaceuticals Investigator-Initiated Award

Co-I, Title: Genetic and Neural Dynamic Mechanisms of Cognitive Improvement with Acthar Gel After Early Life Seizures

2017-2019 NIH NINDS K22NS104230-02 (Phase I)

PI, Title: Mechanisms for Improving Cognitive Outcome in Pediatric Epilepsy with ACTH

2011-2013 Questcor Pharmaceuticals Investigator-Initiated Grant,

Co-PI, Title: The Effects of ACTH in Prevention of Autism

Selected Unfunded Grant Submissions

NIH NINDS R21

PI, Title: Leveraging genetic diversity to identify astrocytic modifiers of TSC phenotypes

NIH NINDS R21

PI, Title: Circuit-based targeting of neural and epigenetic networks underlying cognitive comorbidities in pediatric epilepsy

Brain Research Foundation Seed Grant Program, UVM-selected LOI

PI, Title: Exploring the Role of Astrocyte-Neuronal Communication in Epilepsy: Neuropeptide Treatment Strategies and Cognitive Outcome

SCHOLARSHIP

Peer Reviewed Publications

Original Research

Kleen JK, Sesque A, Wu EX, Miller FA, **Hernan AE**, Holmes GL, Scott R. Early-life seizures produce lasting alterations in the structure and function of the prefrontal cortex. *Epilepsy and Behavior*. 2011; 2(22):214-219.

Iseava E, **Hernan A**, Iseav D, Holmes GL. Thrombin facilitates seizures through activation of persistent sodium current. *Annals of Neurology*. Aug 2012;72(2):192-8.

Hernan AE, Holmes GL, Isaev D, Scott R, Isaeva E. Altered Short-Term Plasticity in the Prefrontal Cortex After Early Life Seizures. *Neurobiology of Disease*. Oct 2012; 50:120-126.

Hernan AE, Scott RC. F1000Prime Recommendation of NS Narayanan, JF Cavanagh, MJ Frank and M Laubach. *Nat Neurosci* 2013 16(12):1888-95. Nov 27 2013; DOI: 10.3410/f.718148986.793487469.

Hernan AE, Alexander A, Holmes GL, Scott RC. Attention Deficit Caused by Early Life Interictal Spikes is Improved by ACTH. *PLoS One*. Feb 2014; 9(2):e89812. DOI: 10.1371/journal.pone.0089812.

Hernan AE, Alexander A, Jenks K, Barry J, Isaeva E, Lenck-Santini PP, Holmes GL, Scott RC. Focal Epileptiform Activity in the Prefrontal Cortex is Associated with Long-term Attention and Sociability Deficits. *Neurobiology of Disease*. March 2014; 63:25-34. DOI: 10.1016/j.nbd.2013.11.01.

Pehek, EA, **Hernan AE**. Stimulation of glutamate receptors in the ventral tegmental area is necessary for serotonin-2 receptor-induced increases in mesocortical dopamine release. *Neuroscience*. April 2015. 290(2):159-164.

Holmes GL, Tian C, Camp DR, **Hernan AE**, Flynn SP, Barry JM. Early-Life Seizures Result in Marked Alteration in Sociability and Functional Brain Connectivity is Reversed by Bumetanide. *Neurobiology of Disease*. May 2015. 77:204-219.

Mahoney JM, Titiz AS, **Hernan AE**, Scott RC. Short-range temporal interactions in sleep; hippocampal spike avalanches support a large milieu of sequential activity including replay. *PLOS One*. Feb 11 2016. 11(2):e0147708.

Hernan AE, Holmes GL. Antiepileptic Drug Treatment Strategies in Neonatal Epilepsy. *Progress in Brain Research*. April 20 2016. DOI: 10.1016/bs.pbr.2016.03.011.

Massey AT, Lerner D, Scott RC, Holmes GL, **Hernan AE**. ACTH Improves Anxiety After Early Life Seizures. *Frontiers in Neurology*. April 2016. 7(65) DOI: 10.3389/fneur.2016.00065.

Hernan AE, Schevon CA, Worrell GA, Galanopoulou AS, Kahane P, de Curtis M, Ikeda A, Quilichini P, Williamson A, Garcia-Cairasco N, Scott RC, Timofeev I. Methodological standards and functional correlates of depth in vivo electrophysiological recordings in control rodents. A TASK1-WG3 report of the AES/ILAE Translational Task Force of the ILAE. *Epilepsia*. 2017. DOI: 10.1111/epi.13905

Hernan AE, Mahoney JM, Curry WJ, Richard G, Lucas MM, Massey AT, Scott RC. Environmental Enrichment Normalizes Hippocampal Timing Coding in a Malformed Hippocampus. *PLoS One*. 2018. 13 (2), e0191488

Hernan AE, Mahoney JM, Mawe SM, Scott RC. Abnormal fine spike timing in hippocampal-prefrontal ensembles predicts poor encoding and underlies behavioral performance in healthy and malformed brains. *Cerebral Cortex*. 2020. *In Press*.

In Preparation

Villarin C, Martinez TM, Curry WJ, **Hernan AE**. Behavioral impairments in a recurrent early life seizure mouse model and modification with ACTH. *In Preparation*.

Non-Peer Reviewed Publications

Review Articles

None to date.

Books and Chapters

None to date.

Other Scholarly Publications

None to date.

Abstracts

- 2006 The Effects of Stress on Rat Prefrontal Cortex Function and Neurochemistry: Serotonin-Dopamine Interactions.
SOURCE Poster Symposium. Case Western Reserve University. Cleveland, OH.
- 2007 Subcellular Localization of Glutaredoxin2.
Biology Poster Symposium. Case Western Reserve University. Cleveland, OH.
- 2007 Serotonin-2A receptor regulation of mesocortical dopamine release in the rat: mediation by AMPA receptors.
Society for Neuroscience. San Diego, CA.
- 2008 Amyotrophic Lateral Sclerosis: Does the Tetanus Vaccine Alter Pathogenesis of the Disease in a Rat Model?
Dartmouth Neuroscience Day. Lebanon, NH.
- 2010 Increased Short-Term Synaptic Plasticity After Early Life Seizures.
Mechanisms of Epilepsy and Neuronal Synchronization Gordon Conference. Waterville, ME.
- 2010 Increased Short-Term Synaptic Plasticity After Early Life Seizures.
American Epilepsy Society. San Antonio, TX.
- 2011 Early Life Seizures Cause Altered Short-Term Synaptic Plasticity.
Dartmouth Neuroscience Day. Lebanon, NH.
- 2011 Alterations in Short-Term Synaptic Plasticity After Early Life Seizures.
Society for Neuroscience. Washington, DC.
- 2012 The Effect of Epileptiform Activity in the Prefrontal Cortex During Development.
Dartmouth Neuroscience Day. Hanover, NH.
- 2012 Epileptiform Activity in the Prefrontal Cortex During Development: Plasticity and Behavioral Alterations.
Program in Experimental and Molecular Medicine Retreat. Fairlee, VT.
- 2012 The Effect of Focal Interictal Spikes During Development on Short-Term Plasticity and Cognition.
American Epilepsy Society. San Diego, CA.
- 2013 The Effect of Focal Interictal Spikes During Development.
Society for Neuroscience. San Diego, CA.

- 2014 Environmental enrichment improves hippocampal networks in animals with malformations of cortical development. Society for Neuroscience. Washington, DC.
- 2015 The role of ACTH in improving cognitive outcomes in rodent models. Neurobiology of epilepsy: From genes to networks Symposium. Montreal, QC, Canada.
- 2016 Hippocampal and Prefrontal Timing Coding and Cognition in a Malformed Brain. Gordon Research Seminar and Gordon Research Conference. Girona, Spain.
- 2018 Hippocampal and Prefrontal Timing Coding and Cognition in a Malformed Brain. Gordon Research Seminar and Gordon Research Conference. West Dover, VT.
- 2018 Administration of ACTH Prevents Development of Cognitive Deficits in Early Life Seizure Model. Gordon Research Seminar and Gordon Research Conference. West Dover, VT.
- 2019 Distributed dynamic coding for spatial working memory in hippocampal-prefrontal networks. Society for Neuroscience. Chicago, IL.

Patents Issued or Pending

None to date.

Other Creative Activities

None to date.

Quality Improvement and Patient Safety Activities

None to date.

SUMMARY OF SCHOLARLY ACTIVITIES

The effect of early life seizures on the prefrontal cortex and cognition: Children who have experienced early life seizures (ELS) are at increased risk for cognitive impairments and behavioral disorders including depression, anxiety, hyperactivity and deficits in attention. The level of alteration of behavior and cognitive performance depends on the age of seizure onset, type, number and severity of epileptic episodes. The majority of clinical and animal data strongly indicates that neonatal seizures lead to deficits that are associated with frontal cortical dysfunction. The goal of my work is to understand extent to which ELS affects frontocortical aspects of cognition and to identify potential mechanisms for such dysfunction in the context of ELS. To this end, I examined a variety of frontocortical behavioral paradigms and found deficits in behavioral flexibility, attention and sociability occur after ELS. I then began to examine short-term plasticity (STP) as a potential network-level mechanism for PFC-associated deficits after ELS, and found significant alterations in STP in two networks in the PFC after ELS.

The effect of focal early life epileptiform activity without seizures on the prefrontal cortex and cognition: Often children with epilepsy have infrequent ictal EEG events, but frequent Interictal abnormalities as well. It has previously been shown that epileptiform activity in the form of interictal spikes is associated with transient cognitive deficits, presumably because the aberrant coordination of large populations of neurons transiently disengages these neurons from normal neural processing, leading to brief disturbances in cognitive functions. However, what was not yet known is whether focal alterations in excitability leading to epileptiform activity, like that seen in children with syndromes like Landau-Kleffner or epilepsy with continuous spike and wave during sleep, is associated with alterations in *developing* cognitive neural networks in such a way as to lead to long-lasting deleterious cognitive consequences. To this end, I developed a model of focal epileptiform activity during development in the PFC and tested the cognitive and neural network level STP outcomes during adulthood. I found that, similarly to generalized ELS, animals with a history of early life epileptiform activity had deficits in attention and sociability, as well as long-term changes in STP in the PFC. Interestingly, we were then able to treat some of these deficits without alteration of the epileptiform activity itself.

The effect of epilepsy-related factors other than seizures on neural networks. Elucidating the systems level correlates of cognitive deficits associated with etiologies that underlie epilepsy in patients is important from both a clinical and basic science perspective. From a clinical perspective, it may facilitate finding successful treatment strategies outside of the classical approach of simply treating seizures, which can dramatically improve quality of life for patients; from a basic science perspective, it provides a greater understanding of mechanisms underlying cognitive deficits in general. To this end, we have been using a clinically-relevant model of malformations of cortical development (MCDs) *without* seizures. In our MCD model, we found alterations in hippocampal pyramidal cell firing and local field potentials that would be expected to underlie some of the cognitive deficits seen in these animals. These alterations are partially ameliorated by early environmental manipulations, suggesting that neural networks alterations and corresponding cognitive deficits can be improved or prevented in animals with MCDs. In order to explore this finding further, we are currently developing novel neural network modeling approaches to decode single unit activity in behaving animals order.

The role of neuropeptide modulation in neuroprotection after early life seizures. I am also interested in the neuroprotective role a specific subtype of neuropeptides, the melanocortins, can have on developing networks that underlie cognition in epilepsy. I have shown that ACTH, a naturally-occurring agonist of melanocortin receptors, prevents cognitive deficits in two rat models and more recently a mouse model of early life epileptiform activity. My current research goals are to continue to explore this finding by 1) identifying the specific melanocortin receptor subtype and cell population, neuron or astrocyte, responsible for this action and 2) dissecting the specific alterations in rate and temporal coding of neurons within and between the hippocampus and prefrontal cortex that are responsible for this improved cognitive outcome with ACTH treatment.

INVITED PRESENTATIONS

Regional

2012	International Epilepsy Symposium, “Epileptiform Activity in the Prefrontal Cortex During Development: Plasticity and Behavioral Alterations.”	Lebanon, NH
2013	Neurology Special Donor Seminar, “What Do Interictal Spikes Do to the Developing Brain?”	Lebanon, NH
2015	Neuroscience, Behavior and Health Forum, “The Role of ACTH in Preventing Cognitive Deficit in Rodent Models of Pediatric Epilepsy.”	Burlington, VT
2015	Neurological Sciences Grand Rounds, UVM College of Medicine, “Improving Cognitive Outcomes in Pediatric Epilepsy.”	Burlington, VT
2016	UVM Basic Science Lecture Series, “The Role of Melanocortins in Improving Cognitive Outcome in Pediatric Epilepsy.”	Burlington, VT
2016	Northern New England Neurological Society, “New Approaches to Improving Cognitive Outcome in Epilepsy.”	Essex Junction, VT
2018	UVM Larner College of Medicine Research Showcase Selected Speaker, “National Firing Dynamics in a Model of Malformation of Cortical Development.”	Burlington, VT
2018	American Association for Laboratory Animal Science, “Towards a Treatment for Cognitive Deficits in Epilepsy.”	Burlington, VT
2019	Neurological Sciences Research Retreat, “Melanocortin Peptides as Novel Therapeutic Targets for Behavioral Impairments in Epilepsy.”	Burlington, VT
2020	Neuroscience, Behavior and Health Forum, “Asynchrony, Astrocytes and ACTH”	Burlington, VT
2021	Biology Department Seminar Series, “Asynchrony to Astrocytes: therapeutic strategies for cognitive dysfunction in pediatric epilepsy and beyond”	Burlington, VT

National

2018	Department of Biological Sciences Seminar at Kent State University, “Toward a treatment for neuropsychiatric comorbidities in epilepsy: Melanocortin peptides, neural dynamics and cognition”	Kent, OH
2019	Psychology Department Seminar at University of Illinois, “Neural Network Mechanisms of Behavioral Impairment in Epilepsy.”	Urbana, IL
2019	Biology and Biotechnology Seminar at Worcester Polytechnic Institute, “Neural Network Mechanisms of Behavioral Impairment in Epilepsy.”	Worcester, MA
2019	Comparative Biosciences Seminar at University of Illinois, “Neural Network Mechanisms of Behavioral Impairment in Epilepsy.”	Urbana, IL
2019	American Epilepsy Society, Basic Science Skills Workshop, Chronic In Vivo Recording: Single Unit to iEEG	Baltimore, MD
2021	Nemours Childrens Healthcare Seminar, Asynchrony to Astrocytes: therapeutic strategies for cognitive dysfunction in pediatric epilepsy	Wilmington, DE

International

2012	National Center for Young People with Epilepsy, “Altered Short-term Plasticity and Excitation in the Prefrontal Cortex After Early Life Seizures.”	East Grinstead, UK
2013	National Center for Young People with Epilepsy, “The Cognitive Impact of Frequent Epileptic Discharges During Development on the Prefrontal Cortex.”	East Grinstead, UK
2015	National Center for Young People with Epilepsy, “The Role of ACTH in Improving Cognitive Outcomes.”	East Grinstead, UK
2015	National Center for Young People with Epilepsy, “Aetiology in Pediatric Epilepsy.”	East Grinstead, UK
2016	National Center for Young People with Epilepsy, “Hippocampal-prefrontal Network Abnormalities in MCD.”	East Grinstead, UK