

ICARE: Interagency Collaborative to Advance Research in Epilepsy
2016 Member Reports

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National Institute of Neurological Disorders and Stroke (NINDS), NIH

Primary Representative: Vicky Whittemore, PhD, Program Director, Channels Synapses and Circuits Cluster, NINDS

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Mission: The mission of NINDS is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease.

Major Topics of Interest:

NINDS supports a broad range of research studies and training awards related to the epilepsies, and on the cognitive, behavioral, and emotional impairments that often accompany epilepsy. The majority of these studies are funded through the standard investigator-initiated application process, and include studies on basic mechanisms of the epilepsies, seizures and co-occurring conditions, translational projects to develop new therapeutics, and clinical studies and trials involving human subjects with epilepsy. All epilepsy related studies funded by NINDS (or other NIH institutes) can be found by searching the NIH RePORTER database at <http://projectreporter.nih.gov/reporter.cfm>.

- Basic mechanisms: NINDS supports studies on causes of the epilepsies, including genetics, infection, injury, metabolism, and structural defects. Basic mechanisms of epileptogenesis and ictogenesis are also major areas of study. Additional projects are focused on better understanding causes of co-occurring conditions and their relationship to epilepsy and seizures.
- Translational efforts: NINDS supports several exploratory R21 awards to develop or better characterize new models of epilepsy for therapeutic development, optimize candidate therapeutics, or otherwise prepare for a translational development U01 award. Several U01 awards related to epilepsy have also been funded in recent years, including device and biologics development efforts. In August of 2014, The NINDS Office of Translational Research (OTR) issued revised funding programs for investigators interested in translational research. These include Innovation Grants to Nurture Initial Translational Efforts (IGNITE), which has replaced previous translational R21 awards, and the NINDS Cooperative Research to Enable and Advance Translational Enterprises (CREATE) program for biologics and devices, which has replaced the previous U01 program. Additional information and a decision tree to help guide investigators to the appropriate funding opportunity can be found on the NINDS OTR homepage here http://www.ninds.nih.gov/funding/areas/translational_research/index.htm
- The Epilepsy Therapy Screening Program (ETSP) is a long-standing contract supported by NINDS to provide assistance to academic or industry groups through free *in vivo* seizure model screening to identify promising anti-seizure agents. The ETSP is also incorporating new screening approaches to differentiate compounds that may be better tolerated than existing drugs, or more effective for the population of patients with medication-resistant epilepsy.
- Clinical studies and trials: NINDS supports a number of observational clinical studies to evaluate the development of epilepsy in those at risk, to better localize the seizure onset zone and evaluate surgical risks and prognosis, to evaluate the effects of AED treatment on pregnant women and on the developing brain, and to assess the outcomes of children and adolescents with epilepsy over the long-term. NINDS is currently supporting a clinical trial to determine the best anticonvulsant for individuals with status epilepticus who have failed first line therapy. In recent years, NINDS has supported clinical trials testing new surgical approaches, best medical treatment of childhood

absence epilepsy, best treatment of neurocysticercosis (a parasitic infection of the brain that causes epilepsy), and best treatment of status epilepticus by emergency medical services personnel.

Research Support:

NINDS supports investigator initiated projects in basic, translational and clinical research related to epilepsy. The Institute also supports individual career development awards, training programs, conference grants, and small business awards related to epilepsy. See the NINDS Epilepsy Research Web for additional information: <http://www.ninds.nih.gov/research/epilepsyweb/>.

Examples of Recent Activities:

- BPN project: NINDS will support a Blueprint Neurotherapeutics project to develop new medications for epilepsy. The grant is still in negotiations.
- Epi4K Gene Discovery in Epilepsy Center Without Walls(CWoW) <http://www.epgp.org/epi4k/>
- Sudden Death in the Young Registry (SDY) - <http://www.nih.gov/news/health/oct2013/nhlbi-24.htm>
- Center for SUDEP Research (CSR) - http://csr.case.edu/index.php/Main_Page
- T32s for epilepsy training

Resources Available:

- NINDS Common Data Elements for Epilepsy Research <http://www.commondataelements.ninds.nih.gov/#page=Default>
- NINDS Epilepsy Therapy Screening Program (ETSP) <http://www.ninds.nih.gov/research/asp/index.htm>
- NIH Blueprint resources (animal models, gene expression, research reagents, cell/tissue/DNA, clinical resources, translational resources) <http://neuroscienceblueprint.nih.gov/index.htm>
- International Epilepsy Electrophysiology Portal <https://www.ieeg.org/>
- Neurological Emergencies Treatment Trials (NETT) network: <http://nett.umich.edu/nett/welcome>
- NIH Stroke Trials Network: http://www.ninds.nih.gov/research/clinical_research/NINDS_stroke_trials_network.htm
- NeuroNEXT Phase II/Biomarker network: http://www.ninds.nih.gov/news_and_events/proceedings/20101217-NEXT.htm
<http://www.neuronext.org/>
- Federal Interagency Traumatic Brain Injury Research Informatics System (FITBIR): <http://fitbir.nih.gov/>
- NINDS Office of Clinical Research website resources: http://www.ninds.nih.gov/research/clinical_research/index.htm
- NINDS Office of Translational Research website resources: http://www.ninds.nih.gov/funding/areas/translational_research/

Priorities and/or Plans for Future Activities:

In general, the NINDS looks to the Epilepsy Research Benchmarks for priorities identified by the epilepsy community. Plans for future epilepsy research activities include intent to support Epilepsy Centers without Walls on Disease Modification and Prevention (RFA-NS-16-012) in FY2016.

National Institute on Alcohol Abuse and Alcoholism (NIAAA), NIH

Primary Representative: Qi-Ying Liu, M.D., MSc., Program Director, Division of Neuroscience and Behavior

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Mission: NIAAA provides leadership in the national effort to reduce alcohol-related problems by conducting and supporting alcohol-related research in a wide range of scientific areas including genetics, neuroscience, behavior, epidemiology, prevention, and treatment; by coordinating and collaborating with other research institutes and federal programs on alcohol-related issues; by collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work; and by translating and disseminating research findings to health care providers, researchers, policymakers, and the public. The goals of NIAAA are: to better understand the health risks and benefits of consuming alcohol, as well as why it can cause addiction, to reveal the biological and socio-cultural origins of why people respond to alcohol differently, to remove the stigma associated with alcohol problems, and to develop effective prevention and treatment strategies that address the physical, behavioral, and social risks that result from both excessive drinking, and underage alcohol consumption.

Major Topics of Interest:

- Both alcohol use disorders and epilepsy affect large numbers of Americans. Alcohol use disorders affect 18 million Americans and cost an estimated \$185 billion annually, and the epilepsy affects nearly 3 million Americans and 50 million people worldwide.
- Chronic alcohol exposure induces complex adaptive changes in the central nervous system, allowing the brain to function in an allostatic state in the presence of alcohol. Quick withdrawal from or reduction of alcohol consumption produces a hyper-excitability state and causes an alcohol withdrawal syndrome. Severe and life-threatening symptoms associated with alcohol withdrawal, including seizures, often make it difficult for an individual to quit drinking because of these negative aspects of withdrawal.
- Epileptic seizures and alcohol withdrawal seizures may share similar neurobiological mechanisms and respond to similar therapeutic treatments.
- Studies suggest that alcohol abuse, dependence and withdrawal may decrease seizure threshold and increase the frequency and severity of seizures in epilepsy patients. Alcohol consumption may also impair seizure control due to neurobiological, nutritional and/or pharmacokinetic mechanisms.
- A recent meta-analysis found that a strong and consistent association between alcohol consumption and epilepsy/unprovoked seizures exists, and that the probability of the onset of epilepsy increases with the amount of alcohol consumed daily in a dose-dependent manner. Further studies are necessary to make any conclusions.
- A remarkably high prevalence of epilepsy and seizure was found in patients with fetal alcohol spectrum disorders. Animal studies reveal a possible role of genetic background in such perinatal effects of alcohol. Conflicting results were reported in this area and additional studies are required.

Research Support:

NIAAA supports basic, translational and clinical research and training in the area of alcohol-related seizures. NIAAA also sponsors meetings and workshops in the areas of alcohol-related neural plasticity, adaptation, excitability and modulation that are relevant to seizures and epilepsy.

Examples of Recent Activities: NIAAA has no active grants studying epilepsy. However, NIAAA is funding training and research grants investigating mechanisms and management of alcohol use-related

(particularly alcohol withdrawal-induced) seizures. These include: Hippocampal neurotoxicity induced by ethanol withdrawal; Mechanisms of Alcohol Withdrawal; Neurosteroid Modulation of Ethanol Withdrawal Severity; Mechanisms of Alcohol Withdrawal Seizures: Role of L-type Ca^{2+} Channels; Alcohol withdrawal and tonic inhibition in the thalamus; An optogenetic investigation of CNS sensitization following alcohol withdrawal.

Priorities and/or Plans for Future Activities: NIAAA will continue to support research and training on the molecular, cellular, neurocircuit and genetic mechanisms of alcohol-related seizures and epileptogenesis. Depending on the availability and quality of datasets, NIAAA may carry out a cross-sectional study of seizures related to alcohol withdrawal. NIAAA will sign on to appropriate epilepsy research initiatives of other NIH institutes or centers if they are relevant to NIAAA mission.

Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), NIH

Primary Representative: Tracy M. King, MD, MPH, Medical Officer, Intellectual and Developmental Disabilities Branch

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Mission: The mission of NICHD is to ensure that every person is born healthy and wanted, that women suffer no harmful effects from reproductive processes, and that all children have the chance to achieve their full potential for healthy and productive lives, free from disease or disability, and to ensure the health, productivity, independence, and well-being of all people through optimal rehabilitation.

Major Topics of Interest:

- Intellectual and developmental disorders, including genetic, mitochondrial, and other inborn errors of metabolism and autism
- Rare diseases that impact intellectual function and may include epilepsy as a co-morbidity
- Research related to head injury, concussion, and trauma, including rehabilitation research
- Neonatal and birth injury with hypoxic-ischemic encephalopathy and/or seizures
- Congenital brain malformations and other structural birth defects that impact intellectual function
- Validation of assays for conditions that could be added to newborn screening panels and development of treatments for new and existing newborn screening disorders, many of which have intellectual disability and/or seizures as a symptom

Research Support: NICHD supports basic, translational, and clinical research via research grants and contracts. Research supported also includes training awards, meetings, networks, infrastructure, and other resources.

Examples of Recent Activities:

- There are 14 Intellectual and Developmental Disorders Research Centers (IDDRCs) across the country that support a wide array of projects pertaining to neurodevelopmental diseases that include epilepsy-based research. The IDDRC at Boston Children's Hospital has provided support in the form of core infrastructure to some of the Tuberous Sclerosis Complex (TSC)-related projects in particular. These include studies to identify risk factors and biomarkers for infantile spasms in TSC, as well as studies of sleep in this disorder.
- NICHD co-supports the Rare Disease Consortium on Rett Syndrome, *MECP2* duplications, and Rett-related disorders with mutations in *CDKL5* and *FOXG1*. Studies supported by this consortium include natural history studies of Rett and related disorders, for which seizures are a prominent clinical feature, as well as a study of neurophysiological biomarkers of abnormal synaptic activity in Rett syndrome, *MECP2* Duplication disorder, and the Rett-related disorders.
- NICHD also co-supports the Rare Disease Consortium focused on Mitochondrial disorders (North American Mitochondrial Disease Consortium, or NAMDC) that includes natural history studies of mitochondrial disorders such as MERRF (Myoclonic Epilepsy with Ragged Red Fibers) in which epilepsy is a relatively common finding. Of note, NINDS is the lead institute for this consortium.

- NICHD supports a number of studies that examine hypoxic stress and hypoxic/ischemic injury to the developing brain, particularly in neonates who may have had a prenatal or birth trauma. For these infants, the chance of epilepsy secondary to such an injury is quite high. Several of these studies are using animal models and histologic and imaging data to assess the degree of brain damage related to hypoxic ischemic injury and test potential neuroprotective agents. In addition, the NICHD-funded Neonatal Network has been instrumental in the development of standardized protocols involving head cooling to reduce the neurological sequelae and mortality secondary to hypoxic-ischemic injury in neonates.
- NICHD supports several R01 and P01 grants to identify genetic causes of structural brain malformations, many of which are associated with seizures.
- NICHD, along with the other NIH institutes that form the Autism Coordinating Committee, supports a number of Autism Centers of Excellence (ACE) grants and other autism-related programs, several of which pertain to epilepsy as a co-morbidity in this condition.
- NICHD, under the auspices of the Best Pharmaceuticals for Children Act, has supported a study comparing lorazepam versus diazepam for the treatment of pediatric status epilepticus. Benzodiazepines are considered first-line therapy for pediatric status epilepticus. Some studies suggested that lorazepam may be more effective or safer than diazepam, but lorazepam is not FDA-approved for this indication. The results of the study revealed that among pediatric patients with convulsive status epilepticus, treatment with lorazepam did not result in improved efficacy or safety compared with diazepam.

Resources Available:

- NICHD, NIMH, and NINDS have joined together to establish the NIH NeuroBioBank, an initiative to improve and coordinate human brain and tissue repositories supported by NIH. Five contracts were awarded in FY2013 through this program, which aims to increase access to high-quality biospecimens for research on epilepsy and other brain diseases. An additional contract was awarded in FY2014 to increase the acquisition of tissues with an emphasis on pediatric developmental disorders, and a data coordination contract was awarded to create a common informatics platform. See <https://neurobiobank.nih.gov/>
- The Newborn Screening Translational Research Network (NBSTRN) has as its purpose to improve the health outcomes of newborns with genetic or congenital disorders by means of an infrastructure that allows investigators access to robust resources for newborn screening research, including a virtual repository of dried blood spots, a data management tool, and a long-term follow-up data repository. See <https://www.nbstrn.org/>
- Jackson Laboratories Cytogenetic Models Resource. This resource maintains and distributes chromosome aberration stocks, which provide mouse models primarily for Down syndrome research. See <http://www.jax.org/cyto/index.html>

Priorities and/or Plans for Future Activities:

- Intellectual and developmental disorders, including common and rare genetic, metabolic, and mitochondrial diseases and newborn screening conditions that impact intellectual function and may include epilepsy as a co-morbidity
- Research related to head injury, concussion, and trauma, including rehabilitation research to improve quality of life for those with brain injuries
- Neonatal and birth injury associated with hypoxic-ischemic encephalopathy and seizures

- Research on autism as related to epilepsy
- Congenital and/or structural brain malformations that impact intellectual function and may predispose to epilepsy conditions
- Research on pediatric-specific labeling for anticonvulsants and other epilepsy-related treatments

National Institute of Nursing Research (NINR), NIH

Primary Representative: Lois Tully, Ph.D., Program Officer, Office of Extramural Programs

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Mission: The mission of the National Institute of Nursing Research (NINR) is to promote and improve the health of individuals, families, communities, and populations. The Institute supports and conducts clinical and basic research and research training on health and illness across the lifespan to build the scientific foundation for clinical practice, prevent disease and disability, manage and eliminate symptoms caused by illness, and improve palliative and end-of-life care. Building on NINR's Strategic Plan, past scientific accomplishments, and current research, four key themes have evolved. These include: 1) Symptom Science: Promoting Personalized Health Strategies, 2) Wellness: Promoting Health and Preventing Illness, 3) Self-Management: Improving Quality of Life for Individuals with Chronic Illness, and 4) End-of-Life and Palliative Care: The Science of Compassion

Research Support:

NINR supports clinical, biological, and translational research in many areas, including chronic illness, symptom management, disease prevention, and patient-focused health programs that encourage and enable individuals to become guardians of their own well-being. NINR also invests in training strategies and programs that support ongoing development of investigators at all stages of their research careers. For additional information, see <http://www.ninr.nih.gov/researchandfunding>

Fogarty International Center (FIC), NIH

Primary Representative: Kathleen Michels, Program Director, Division of International Training and Research (kathleen.michels@nih.gov)

Mission: FIC supports and facilitates global health research conducted by U.S. and international investigators, builds partnerships between health research institutions in the U.S. and abroad, and trains the next generation of scientists to address global health needs

Major Topics of Interest:

- Epilepsy impacts low and middle-income countries (LMICs) disproportionately with 85% of the epilepsy cases occurring in LMICs. Frequently, these cases remain untreated because of the stigma associated with epilepsy.
- In these LMIC settings, seizure disorders may have an underlying neuro-infectious origin (eg. cerebral malaria) that must be controlled and treated to prevent the onset of seizure activity. FIC is interested in studying the tropical infections that have the potential for progressing towards epilepsy and seizure activity.

Research Support:

FIC supports both basic and translational research and research training in the area of epilepsy and seizures of infectious origin. Our grants examine the etiology of epilepsy and seizures disorders and also focuses on prevention, early detection, and treatment of epilepsy and seizure activity in LMIC settings. A critical component of these projects is to emphasize building research capacity at the LMIC site in order to enhance how epilepsy and seizure research is conducted.

Examples of Recent Activities:

FIC has three research grants funded through our [Global Brain and Nervous System Disorders Research Across Lifespan](#) programs that involve epilepsy and seizure activity. A Johns Hopkins grantee partnering with the University of Zambia is involved in examining whether the blood brain epithelium is an appropriate therapeutic target for mitigating or preventing the neurologic sequelae stemming from cerebral malaria, a clinical syndrome that produces impaired consciousness, coma, delirium, intracranial hypertension, and seizures. Another project in the Congo is partnering with the Oregon Health and Science University to investigate the neurodevelopmental deficits and risk factors for epilepsy among populations suffering from river blindness. A third project in Mexico, working in collaboration with the University of Rhode Island, is developing a non-invasive transcutaneous focal stimulation (TFS) neuromodulation system for epilepsy treatment and a tripolar concentric ring electrode to improve upon the conventional diagnosis techniques that use traditional EEG.

Priorities and/or Plans for Future Activities: FIC will continue to fund research and training on prevention, management and treatment of epilepsy and seizure disorders in LMIC settings. The emphasis is on research questions relevant to LMIC specific priorities and context. Our key related funding opportunities under the [Global Brain and Nervous System Disorders Research Across Lifespan](#) (R21/R01) FOA will remain active until at least 2017.

National Center for Advancing Translational Sciences (NCATS), NIH

Primary Representative: David J. Eckstein, Ph.D., Senior Health Scientist Administrator, Office of Rare Diseases Research

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Mission: NCATS' mission is to catalyze the generation of innovative methods and technologies that will enhance the development, testing and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

Research Support: NCATS' organization of divisions and offices spans the entire spectrum of translational science. Through programs in its Division of Pre-Clinical Innovation, the Center drives advances in early stages of the translational process, from target validation to first-in-human studies. Through its Division of Clinical Innovation, NCATS supports clinical and translational research, creating and sharing the expertise, tools and training needed to develop and deploy effective treatments in people. Our cross-cutting programs in rare diseases, translational technologies, strategic alliances and other emerging areas address common scientific and organizational barriers to enable faster and more effective interventions that tangibly improve human health.

Examples of Recent Activities: The Bridging Interventional Development Gaps (BrIDGs) program assists researchers in advancing promising therapeutic agents through late-stage pre-clinical development toward an Investigational New Drug (IND) application and clinical testing. BrIDGs is not a grant program. Instead of receiving grant funds, selected investigators partner with NIH intramural scientists to complete pre-clinical therapy development studies at no cost to the investigator. Collaborators leverage BrIDGs expertise and resources to generate data for Investigational New Drug applications to a regulatory authority such as the Food and Drug Administration. The average small molecule project has a 2-3 year lifecycle and costs, on average, \$2,500,000. There are 2 currently active epilepsy BrIDGs projects. <https://ncats.nih.gov/bridgs/projects/active>

Resources Available: NCATS is distinct in many ways; it focuses not on specific diseases, but on what is common among them and the translational science process. The Center emphasizes innovation and deliverables, relying on the power of data and new technologies to develop, demonstrate and disseminate improvements in translational science. In these ways, NCATS is serving as an adaptor to enable other parts of the research system to work more effectively. NCATS complements other NIH ICs, the private sector and the nonprofit community.

NCATS 3Ds:

- **Developing** new approaches, technologies, resources and models
- **Demonstrating** their usefulness
- **Disseminating** the data, analysis and methodologies to the community

Collaborations among government, academia, industry and nonprofit patient organizations are crucial for successful translation; no one organization can succeed alone. To this end, NCATS leads innovative and collaborative approaches in translational science that are cross-cutting and applicable to the broad scientific community. The Programs and Initiatives that provide opportunities to work with NCATS can be found at <https://ncats.nih.gov/programs>.

Centers for Disease Control and Prevention (CDC) Epilepsy Program

Centers for Disease Control and Prevention (CDC)

National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)

Arthritis, Epilepsy and Well-Being Branch (AEWB)

Epilepsy Program

Primary Representative: Niu Tian, MD, PhD, Medical Officer

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Mission: CDC works 24/7 to protect America from health, safety and security threats, both foreign and in the U.S. CDC increases the health security of our nation.

NCCDPHP works to help people and communities prevent chronic diseases and promote health and wellness for all.

NCCDPHP's work targets four key action areas:

- Epidemiology and surveillance systems that track chronic diseases and their risk factors and provide data for action.
- Environmental approaches that improve community policies and design to make healthy choices easier.
- Health care system interventions that help doctors diagnose health threats earlier and manage them better.
- Community programs linked to clinical services that help people prevent and manage their chronic diseases and improve their quality of life.

The CDC Epilepsy Program within NCCDPHP works to improve the health and well-being of people with epilepsy. To accomplish this, the CDC Epilepsy Program:

- Leads self-management research, program implementation, and dissemination, including:
 - Researching new self-management programs
 - Disseminating our work
- Establishes and expands surveillance and data collection to:
 - Describe the burden of epilepsy
 - Identify risk and protective factors
 - Evaluate prevention efforts
 - Prioritize program development
- Prevents known risk factors for epilepsy by:
 - Developing specific interventions (e.g. to detect cysticercosis infection)
 - Promoting the health promotion and disease prevention efforts of others (e.g. traumatic brain injury, stroke prevention); and
- Develops and promotes programs that create a more supportive environment for people with epilepsy by:
 - Elevating epilepsy as a public health issue to motivate action
 - Complementing activities of key partners such as the Epilepsy Foundation

Major Topics of Interest:

The NCCDPHP Epilepsy Program research interests focus on population and epidemiologic studies of epilepsy burden, prevention research, and studies on epilepsy stigma. These research activities address the spectrum of epilepsy, are inclusive of all ages, and are often national or community-based in scope.

Population and epidemiologic studies of epilepsy include:

- Studies of epilepsy burden (prevalence, incidence, risk factors, comorbidities, quality of life; access to care, health disparities, and related factors) using established surveillance systems or other population studies
- Population-based epilepsy mortality surveillance, including sudden unexpected death in epilepsy (SUDEP), suicide, and all-cause mortality

Prevention Research includes:

- Advancing epilepsy self-management research by conducting research in collaboration with community stakeholders including people with epilepsy, and disseminating research findings
- Development and validation of an antigen detection method to screen for and monitor treatment of pork tapeworm infection, a leading cause of epilepsy and seizures in some developing countries and some US immigrant populations (supported in collaboration with CDC's Center on Global Health)

Epilepsy Stigma research includes:

- Developing and testing new communication strategies to combat epilepsy stigma
- Examining attitudes toward epilepsy in the U.S. population

Research Support:

The CDC Epilepsy Program supports public health surveillance, and both intramural and extramural research. The program leads surveillance studies using national and/or state surveillance systems, and supports other epidemiologic studies and prevention research by providing grants, contracts, or cooperative agreements to academic investigators or contractors.

Examples of Recent Activities:

Public health surveillance:

- Supporting epilepsy questions on the 2010, 2013, 2015, 2017 National Health Interview Survey (NHIS)
- Supporting, in collaboration with NIH and CDC's Division of Reproductive Health, the Sudden Death in the Young (SDY) Registry
- Supporting, in collaboration with CDC's School Health Program, questions on epilepsy on the School Health Profiles surveys

Intramural research underway:

- Analysis of 2010, 2013, 2015 NHIS data to assess epilepsy burden
- Analysis of National Violent Death Reporting System data to identify suicide burden in people with epilepsy
- Analysis of NCHS National Vital Statistics Systems Multiple Cause of Death data to identify possible SUDEP cases
- Analysis of 1993-2012 National Inpatient Sample /Healthcare Cost and Utilization Project data to examine trends in hospitalizations in people with epilepsy or seizure diagnosis

Extramural research underway (select examples):

Epidemiologic research:

Rare Epilepsies in New York City: Improving Surveillance with Text Processing of Clinical Notes in Electronic Health Records. (Weill Medical College of Cornell University)

This research team will use text processing of electronic health records from multiple academic medical centers in NY to improve surveillance and epidemiology of the rare epilepsies. They will describe the incidence, prevalence, comorbidities, mortality, and quality of ambulatory care for individuals with rare epilepsies. The text searching specifications will help centers identify rare epilepsies to support surveillance, research, quality improvement, care management, and referral to advocacy organizations.

Prevention research:

Managing Epilepsy Well (MEW) Network - The MEW Network was established in 2007 to advance the science on epilepsy self-management by conducting research across a network of universities, collaborating with community stakeholders to implement activities, and broadly disseminating research findings. The MEW Network is currently comprised of one Coordinating Center and seven Collaborating Center members.

MEW Network Coordinating Center (Dartmouth College and Emory University)

This team will facilitate communication and collaboration across the MEW Network in the development, evaluation, and dissemination of epilepsy self-management programs. Dartmouth will also evaluate HOBSCOTCH (Home Based Self-management and Cognitive Training Changes Lives), an evidence-based self-management program for adults with epilepsy and memory problems. Delivered by phone, HOBSCOTCH will be disseminated to adults with epilepsy living in rural New England to eliminate their barriers to care. Dartmouth will also examine the cost-effectiveness of HOBSCOTCH.

MEW Network Collaborating Centers

Case Western University- SMART (Self-management for people with epilepsy and a history of negative health events) will be developed to improve self-management and quality of life for adults with epilepsy with recent (past 6 months) negative health events (e.g., seizure, hospitalization, ED visit, accident/traumatic injury, self-harm attempt). The SMART study will enroll participants from lower-income urban locations, safety-net health systems, and a Veterans Health Care System. SMART will be delivered online, but will also include one or more group sessions, telephone coaching, and peer support.

University of Arizona - Evaluation of MINDSET (Management Information Decision Support Epilepsy Tool) for Hispanic-American adults with epilepsy. MINDSET was developed as a tablet-based clinical aid for both the patient and health-care provider to improve communication about self-management. The goal of this project is to develop and test a Spanish version of MINDSET. Both the English and Spanish version of MINDSET will be tested with patients attending four clinic sites on the Arizona and Texas border.

University of Illinois (Chicago) - PAUSE (Personalized Internet Assisted Underserved Self-management of Epilepsy). In partnership with the Epilepsy Foundation, PAUSE will provide patients with epilepsy with free access to a computer tablet and Internet service. Patients will test epilepsy educational information based on epilepsy.com content and real-time (web-based) video conferencing with a health educator.

Morehouse School of Medicine - Adapting Evidence-Based Epilepsy Self-Management Programs for Blacks in Georgia. Using a Community Advisory Committee, focus groups, and interviews with epilepsy stakeholders, this project seeks to promote the adoption and replication of evidence-based MEW Network self-management programs in underserved communities, and to understand the features that facilitate dissemination, replication, and adoption of these programs among African-American adults with epilepsy and their providers.

New York University - Evaluation of Project UPLIFT (Using Practice and Learning to Increase Favorable Thoughts) for Hispanic adults with epilepsy and depression. To address the unmet mental health needs of medically underserved Spanish-speaking adults with epilepsy, New York University will adapt UPLIFT for Hispanic adults with epilepsy. Project activities will include conducting focus groups with Spanish-speaking adults to understand how UPLIFT might be modified to account for cultural differences and to meet the needs of this group. UPLIFT content will be modified as necessary, content will be translated, and the Spanish-version of UPLIFT will be tested to assess its effectiveness in reducing depressive symptoms in Hispanic adults with epilepsy.

University of Minnesota – YESS (Youth, Epilepsy, and Successful Self-Management). The purpose of this study is to develop an online self-management program for youth and young adults (ages 13-19) with epilepsy that is grounded in behavioral science and youth development theory. The project will include a systematic review of the literature related to pediatric self-management; a series of focus groups with youth with epilepsy, parents/guardians of youth with epilepsy, and key informants; the creation of an advisory group comprised of youth with epilepsy to assist with program design and content; and intervention evaluation.

University of Washington - PACES in Epilepsy: Replication, Extension, and Dissemination. PACES (Program for Active Consumer Engagement in Self-Management) was developed to improve self-management and related health outcomes in adults with epilepsy. The goals of this study are to adapt PACES for telephone delivery; support both in-person and telephone group delivery of the program; and evaluate the effectiveness of PACES in both rural and veteran subpopulations in the Pacific Northwest. If effective, the PACES team will collaborate with the University of Washington Training Xchange staff in order to build a sustainable model of training recruitment, training options, and national dissemination (in-person and e-learning).

*CDC is also funding dissemination activities related to MEW Network Programs. For more information, please see: <http://web1.sph.emory.edu/ManagingEpilepsyWell/programs/uplift.php>

For additional information, see <http://www.cdc.gov/epilepsy/research/index.htm>)

Resources Available:

- The CDC Managing Epilepsy Well Network serves as a community-of-practice facilitating collaboration with external partners interested in studying epilepsy self-management and associated outcomes.
- Opportunities for collaboration on analysis of CDC surveillance system data exists.

Priorities and/or Plans for Future Activities:

Sustain relevant research activities aligned with IOM recommendations for CDC, including:

- Population and epidemiological studies of epilepsy addressing: (a) incidence; (b) prevalence; (c) risk factors and etiology; (d) comorbidities; (e) access to care; and (f) quality of life;

- Surveillance of mortality (SUDEP, suicide, other causes) in people with epilepsy (all ages);
- Advancing and disseminating self-management research and programs to improve quality of life for people with epilepsy through the Prevention Research Centers' Managing Epilepsy Well (MEW) Network

National Center on Birth Defects and Developmental Disabilities (NCBDDD)
Centers for Disease Control and Prevention (CDC)

Primary Representative: Stuart K. Shapira, MD, PhD, Chief Medical Officer and Associate Director for Science

Email: sshapira@cdc.gov

Mission:

- NCBDDD works to advance the health and well-being of our nation's most vulnerable populations.
- NCBDDD's focus on women, children, and people with a range of disabilities and complex disabling conditions positions the Center as a resource within public health that is unique and vital.
- Center Priorities:
 1. Enhancing the monitoring and tracking of autism and other developmental disabilities, and advancing research into the risk factors for these conditions
 2. Preventing major birth defects associated with maternal risk factors
 3. Preventing death and disability associated with venous thromboembolism (VTE)
 4. Preventing and controlling complications from bleeding disorders like hemophilia
 5. Identifying and reducing disparity in key health indicators, including obesity, among children, youth and adults with disabilities
 6. Incorporating disability status as a demographic variable into all relevant CDC surveys, policies, and practices

Major Topics of Interest: NCBDDD's research interests involve the evaluation of individuals with epilepsy co-occurring with neurologic, developmental, and genetic disorders, including attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder, cerebral palsy, fragile X syndrome, muscular dystrophy, spina bifida, and Tourette syndrome. The research primarily entails the use of existing national surveys or surveillance systems and linked datasets to characterize for these disorders, the prevalence of and treatment for epilepsy, health among persons with epilepsy (functional status and co-occurring mental and behavioral conditions), health insurance coverage, medical care costs, health services use, quality of health care, disparities in access to health care and ease of care, use of developmental services, school enrolment, and family financial and employment impact.

Examples of Recent Activities:

- Project to Learn about Youth – Mental Health (PLAY-MH): PLAY-MH is a set of cross-sectional epidemiologic studies within school districts with diverse populations from varied geographical settings to allow for a better understanding of mental, emotional, and behavioral disorders among a range of racial and ethnic groups. The goal of PLAY is to characterize the underlying community-based prevalence, diagnosed prevalence, and treated prevalence of children's mental, emotional, and behavioral disorders. The data are also being used to examine the relationships between diagnoses, services needed and received, and demographic information. NCBDDD included seizure disorders, including epilepsy, in the diagnosis and treatment questionnaires, and will be able to describe community-based diagnosis and treatment patterns within the 2014-2015 sites and 2015-2016 sites.
- CDC and the multidisciplinary Managing Epilepsy Well (MEW) Network are currently collaborating to synthesize the current literature on pediatric epilepsy self-management interventions, and develop a pediatric epilepsy self-management questionnaire.

- Under a previous Cooperative Agreement with the New York State Institute for Basic Research (IBR), the Fragile X Clinical and Research Consortium (FXCRC) has worked on a number of “consensus” documents. These are not guidelines or recommendations, as they didn’t go through the processes that would be required, however the work to develop the consensus documents did include a number of clinicians who specialize in the care of individuals with FXS. FXCRC put out a consensus document on seizures in the FXS population, http://fxcrc.org/images/stories/document-library/Seizures_in_Fragile_X_Syndrome.pdf. FXCRC plans to update the consensus document and look at data collected through the Fragile X Online Registry With Accessible Research Database (FORWARD), which contains clinician and parent reported data collected through 25 fragile X specialty clinics across the country. Four new awards have been made under a 5 year RFA, titled *Using Longitudinal Data to Characterize the Natural History of Fragile X Syndrome to Improve Services and Outcomes*. Data collection will build on the previous work developing the Fragile X Online Registry With Accessible Research Database (FORWARD). Awardees will be collecting longitudinal data on participants already enrolled and enrolling new participants of all ages. The questions related to seizures on the Clinician Report Form used in FORWARD include:

14. Does/did the child have seizures? (check one)

- ☐ Yes, currently
- ☐ Yes, but only in the past
- ☐ No (SKIP to 19.)
- ☐ Don’t know (SKIP to 19.)

15. If Yes, what type of seizures? (check one)

- ☐ Generalized ☐ Partial ☐ Febrile ☐ Unknown

16. What was the age of onset? _____ Years _____ Months (e.g. 3 years, 4 months) (Please provide best estimate if exact age unknown)

17. What was the age at last seizure? _____ Years _____ Months (e.g. 3 years, 4 months) (Please provide best estimate if exact age unknown)

18. Is the child currently on medication for seizures? (check all that apply)

- ☐ valproic acid (Depakote, Depakene)
- ☐ carbamazepine (Tegretol)
- ☐ oxcarbazepine (Trileptal)
- ☐ levetiracetam (Keppra)
- ☐ topiramate (Topamax)
- ☐ lamotrigine (Lamictal)
- ☐ phenytoin (Dilantin)
- ☐ phenobarbital
- ☐ zonisamide (Zonegran)
- ☐ lacosamide (Vimpat)
- ☐ rufinamide (Banzel)
- ☐ gabapentin (Neurontin)
- ☐ pregabalin (Lyrica)
- ☐ other (please specify): _____
- ☐ none

Priorities and/or Plans for Future Activities:

- There is significant potential for collaboration on future research activities when resources permit:
 - Expansion of surveillance activities using existing national surveys in order to focus on childhood epilepsy and co-morbidities that affect quality of life and wellbeing:
 - National Survey of Children's Health (NSCH) can be used to assess the prevalence of epilepsy and seizure disorders, health (functional status and co-occurring mental and behavioral conditions), health insurance, quality of health care, disparities in health care access and ease of care, use of developmental services, time use, school enrolment, and family financial and employment impact of epilepsy.
 - As an example, a manuscript has been submitted, but not yet published, on the prevalence of childhood anxiety and depression that included co-occurrence of a number of conditions, including epilepsy, which was about 3x more common among children with anxiety and depression than in those without.
 - Provider-based surveys, such as National Health Care Surveys administered by National Center for Health Statistics can be used to study both ambulatory care and hospital care for epilepsy.
 - Administrative databases, such as MarketScan database or Centers for Medicare & Medicaid Services (CMD) data, can be used to study the prevalence, medical care cost and co-morbidities for persons with epilepsy at a national level.
 - Multiple Cause Mortality Files can provide trend of death rate where epilepsy was recorded as a cause of death. The most frequently recorded other causes of death for those deaths associated with epilepsy can also be evaluated.
- NCBDDD could conduct surveillance of epilepsy as an independent condition in 8-year-old children in four Autism and Developmental Disability Monitoring (ADDM) Network sites. Based on the average number of 8-year old children in an ADDM site, and an estimated prevalence of epilepsy in 8 year olds of 6-10 per 1000, the expected number of 8-year-old children identified with epilepsy would be 210-350 per ADDM site (total among 4 sites of 840-1400). In addition to records already reviewed for ASD, CP and ID (autism spectrum disorder, cerebral palsy, and intellectual disability) surveillance, these ADDM sites would review records from neuroimaging, neurophysiology, and neurology sources, including descriptions of epilepsy or seizures, results from diagnostic testing, age of onset, etiology, medications, and other pertinent medical conditions. The abstracted information would then be reviewed and coded at each site by a pediatric neurologist to determine case status using the International League Against Epilepsy (ILAE) standard case definition and classification of epilepsy. The information that would potentially result from the data collected through this study would include:
 - Prevalence of epilepsy among 8-year-olds in the study population
 - Prevalence of epilepsy in the study population, by race, sex and type of epilepsy, including epilepsy syndromes (ILEA classification), and characterization of difference between groups.
 - Linkage to birth certificates for additional birth variables: e.g., birth weight, maternal age, maternal education
 - Linkage to birth defects data in sites that conduct birth defects surveillance (e.g., the Metropolitan Atlanta Congenital Defects Program conducts surveillance in the same region covered by the GA ADDM site (i.e., the Metropolitan Atlanta Developmental Disabilities Surveillance program)).
 - Mean age of diagnosis of epilepsy and factors that affect age of diagnosis
 - Prevalence of specific co-occurring conditions (e.g., autism, cerebral palsy, intellectual disability, hearing loss, visual impairment, etc.)

- School placement
- Medical services use

The ADDM Network currently conducts surveillance on 8-year-old children. Although 8 years may not be the optimal age for conducting independent epilepsy surveillance, routinely identifying epilepsy among 8-year-old children is a first step in leveraging ADDM Network infrastructure to develop a more comprehensive Epilepsy Monitoring Network among children and adolescents.

- Evaluate the prevalence of and relationship between medication use during pregnancy for the treatment of epilepsy and birth outcomes, including birth defects, preterm birth, low birth weight, and infant mortality using established CDC studies and surveys (e.g., the National Birth Defects Prevention Study [NBDPS], the Birth Defects Study to Evaluate Pregnancy exposureS [BD-STEPS], and the Pregnancy Risk Assessment Monitoring System [PRAMS]).

Congressionally Directed Medical Research Programs (CDMRP) Epilepsy Research Program (ERP)

Primary Representative: Anthony Pacifico, Ph.D.

Email: Anthony.M.Pacifico.civ@mail.mil

Mission: Responsibly manage collaborative research that discovers, develops, and delivers health care solutions for Service Members, Veterans and the American public.

Activities and Topics of Interest: The ERP was initiated in 2015 to develop an understanding of the magnitude of post-traumatic epilepsy (PTE) within the military and to expand research into the basic mechanisms by which traumatic brain injury (TBI) produces epilepsy. To this end, and to satisfy the ERP's Mission and Vision, the ERP has identified the following research Focus Areas for FY 15:

- **Epidemiology:** Epidemiological characterization of, and identification of risk factors for developing PTE following TBI including different variables such as race and ethnicity; age; gender; organic head injury factors; type of insult; latency to epilepsy; and comorbidities.
- **Markers and Mechanisms:** Identifying markers or mechanisms (via clinical prospective or preclinical models) that address PTE:
 - Early detection
 - Diagnosis
 - Prognosis
 - Comorbidity
 - Risk stratification
- **Models of PTE:** Development of new models or better characterization of existing etiologically relevant models for PTE including repetitive TBI.

Research Support:

Award Mechanism	Eligibility	Key Mechanism Elements	Funding	Submission Deadlines
Idea Development Award Go to: <ul style="list-style-type: none"> • Program Announcement • General Application Instructions Grants.gov Funding Opportunity Number: W81XWH-15-ERP-IDA	Assistant Professor level or above (or equivalent)	<ul style="list-style-type: none"> • Intent: Solicit research to understand the magnitude and underlying mechanisms of Post Traumatic Epilepsy (PTE), especially in Service members and Veterans while benefitting the civilian community. • Level I: <ul style="list-style-type: none"> ○ Intended to support investigator-initiated research that may be high-risk and/or high-gain. • Level II: <ul style="list-style-type: none"> ○ Intended to support advanced studies that may be multidisciplinary in nature, and/or have multiple collaborators. • Both Funding Levels are seeking applications in the Focus Areas described below: <ul style="list-style-type: none"> ○ Epidemiology: Epidemiological characterization and identification of risk factors for developing PTE following Traumatic Brain Injury (TBI) including different variables such as race and ethnicity; age; gender; organic head injury factors; type of insult; latency to epilepsy; and comorbidities. ○ Markers and Mechanisms: Identifying markers or mechanisms (via clinical prospective or preclinical models) that support PTE: <ul style="list-style-type: none"> • Early detection • Diagnosis • Prognosis • Comorbidity • Risk stratification ○ Models of PTE: Development of new or better characterization of existing etiologically relevant models for PTE including repetitive TBI. • Applications should provide relevant preliminary data to support the application's research hypothesis (or hypotheses). • Preproposal submission is required; application submission is by invitation only • Important Note: Research under any FY15 Focus Area can be used to compare and contrast psychogenic non-epileptic seizures (PNES) with PTE. 	<ul style="list-style-type: none"> • Level I: <ul style="list-style-type: none"> ○ Funding limit is \$500,000 direct costs. ○ Maximum period of performance is 3 years. ○ Indirect costs may be proposed in accordance with the institution's rate agreement. • Level II: <ul style="list-style-type: none"> ○ Funding limit is \$2.2M total costs. ○ Maximum period of performance is 4 years. ○ Indirect costs may be proposed in accordance with the institution's rate agreement. 	Pre-Application (Preproposal): August 19, 2015 5:00 p.m. Eastern time Full Application: November 24, 2015 11:59 p.m. Eastern time

Examples of Recent Activities: The program was inaugurated in the spring of 2015. The ERP will be making its first funding decisions in the spring of 2016.

Resources available: Our project selection process brings together individuals from government, academia and non-profits. It's through this collaborative process that we select projects that will help us address the ERP's mission, while coordinating the ERP's activities with other funders in this space.

Priorities and/or Plans for Future Activities: Any or all new initiatives will be announced in the spring of 2016.

Department of Veterans Affairs (VA) Epilepsy Centers of Excellence (ECoE)

Primary Representative: Paul Rutecki, MD, Acting Director VA ECoE

Email: Rutecki@neurology.wisc.edu or paul.rutecki@va.gov

Mission: The VA Epilepsy Centers of Excellence's mission is to improve the health and well-being of Veteran patients with epilepsy and other seizure disorders through the integration of clinical care, outreach, research and education.

The Epilepsy Centers of Excellence are charged with: (1) establishing a national system of care to all veterans with epilepsy, (2) educating veterans and others in their lives impacted by epilepsy about high quality epilepsy care, (3) providing health professional education and training in order to deliver the highest quality of standard of care to veterans with epilepsy, (4) utilizing national VA and other databases in order to inform providers and policy makers in Central Office about health care delivery and health policy decisions, (5) conducting state-of-the-art research about epilepsy, and (6) implementing an informatics backbone to meet the above objectives.

Major Topics of Interest:

- Psychogenic Non-Epileptic Seizures
- Post-Traumatic Epilepsy
- Genetic factors in epilepsy (utilizing Million Veteran Program)
- Psychological co-morbidities
- Quality of life
- Epidemiology of epilepsy in Operation Enduring Freedom (OEF)- Operation Iraqi Freedom (OIF) veterans
- SUDEP
- Epileptogenesis , posttraumatic epilepsy as model for intervention
- Comorbid psychiatric illness
- Novel therapeutic approaches to medically refractory epilepsy and refractory status epilepticus (responsive neurostimulation, new AEDs, etc.)
- Novel approaches to epilepsy diagnosis, including neurophysiology & neuroimaging
- Quality of epilepsy care
- Epidemiology & epilepsy surveillance
- Outcomes specific approaches to epilepsy care

Research Support:

- Types of research include basic science, clinical, translational and outcomes research studies
- Sources of funding include:
 - VA Office of Research & Development
 - Other Federal agencies (DoD, FDA, NIH, etc.)
 - Not-for-profit foundations
 - Pharmaceutical companies
 - American Epilepsy Association
- Infrastructure: The VA Epilepsy Centers of Excellence are clinically funded by VA Central Office and include 16 centers within four administrative regions. The ECoE has workgroups that focus on both basic science research and clinical research, allowing for collaboration and information sharing among the ECoE sites. These workgroups help to organize national efforts and provide guidance on potential collaborative studies.

Examples of Recent Activities:

The epidemiology of posttraumatic epilepsy in Veterans has been addressed in two recent publications. Penetrating head trauma was associated with a high risk of epilepsy (adjusted odds risk of over 18 times control) and mild TBI also had a small but increased risk (1.28, Pugh et al J Head Trauma and Rehab 30:29-37, 2015). The percentages of comorbid TBI and PTSD were 15.8% and 24.1%, respectively for Veterans of all ages with epilepsy receiving care at a VA hospital. For OIF/OEF/OND Veterans, these percentages increased to 52.6% and 70.4%, respectively (Rehman et al JRRD 52:751-62, 2015).

A VA based study on using an online patient community strategy showed that users had improved self-management and self-efficacy (Hixson et al Neurology 85: 129036, 2015).

Non-epileptic psychogenic seizures occur in Veterans and represent about 25% of patients admitted to epilepsy monitoring units. TBI was identified as a cause by patients more commonly those with psychogenic non-epileptic seizures (Salinsky et al, J Head Trauma and Rehab 30: E65-70, 2015). There is an ongoing collaborative study of prospectively evaluating patients undergoing epilepsy monitoring to characterize their psychological co-morbidities as they relate to the epilepsy monitoring final diagnosis (epilepsy versus psychogenic non-epileptic seizures).

Currently funded projects through the VA research and development office are diverse and include

- Posttraumatic epilepsy treatment
- Juvenile myoclonic epilepsy
- Hippocampal interneuron changes during epileptogenesis
- GABA signaling recurred for new born neuron incorporation
- GABA transporters and epilepsy
- New anti-epileptic drug mechanisms
- Psychogenic non-epileptic seizures
- Vagus nerve stimulation to augment recovery from traumatic brain injury
- Traumatic brain injury and pathologic l-glutamate synaptic plasticity
- Treatment of status epilepticus
- Epilepsy health care delivery

Resources Available:

- Basic Science Research Workgroup and Clinical Research Workgroup (monthly calls and open to others that want to collaborate, may inquire through Nikolai Dembrow (ndembrow@uw.edu) or Alan Towne (alan.towne@va.gov) respectively
- Epilepsy Monitoring Unit Database: clinical database of Epilepsy Center EMU diagnoses for use in understanding the Veteran population
- Computerized Patient Record System linked clinical database: database that is populated by a standardized template within the VA's CPRS EHR

Priorities and/or Plans for Future Activities:

- Build collaborative research projects amongst ECoE basic scientists
- Develop proposals for joint DoD/VA award: Chronic Effects of Neurotrauma Consortium (CENC)
- Develop viable protocol for post-traumatic epilepsy (PTE) and vagus nerve stimulation therapy (VNS) multi-site study
- Expand use of EMU database and explore potential research opportunities
- Explore potential to collaborate with Integrated Neurology Project for quality/ efficacy research

- Expand PNES Tele-mental health initiative to other ECoE's and the Integrated Neurology Project
- Explore genomic partnerships between ECoE and the Million Veteran Program (MVP)
- Expand collaboration between the ECoE's and the National Polytrauma Centers
- Explore the effect of TBI on sleep patterns
- Determine whether the mild TBI (mTBI) case group differs from the non-TBI control group and the effects of single versus multiple mTBIs
- Measure ERPs (specifically multimodal working memory, long-term memory access, & auditory cortical potentials) to seek additional physiologic evidence of neurodegeneration, clarify functional significance of changes in neurobiological variables through real-time measure of neural coordination, and characterize the neurocognitive mechanisms of impairments shown on cognitive performance tests.
- Epilepsy epidemiology & surveillance project
- Examining social network of physicians on care provided to Veterans with PNES/ epilepsy
- Identify targets for interventions to improve care based on findings from ongoing Reconstructin Epilepsy Care: Organizational Dynamics (RECORD) Quality project
- Basic mechanisms of epilepsy and mechanisms of novel anti-epileptic therapies

American Epilepsy Society (AES)

Primary Representative: Michael D. Privitera, M.D., PRESIDENT (2016); University of Cincinnati

Email: PRIVITMD@UCMAIL.UC.EDU

Mission: The mission of the American Epilepsy Society is to advance research and education for professionals dedicated to the prevention, treatment and cure of epilepsy.

Topics of Interest: Topics of AES-supported research represent the diversity of the AES membership and cover all aspects of epilepsy research, including basic; translational (treatment development); and clinical (neuropsychology, neurosurgery, nursing, psychiatric, clinical studies and clinical trials) research on the many different forms of epilepsy.

Research Support:

Research Grants:

- Early Career Research Funding: Predoctoral and Postdoctoral Research Fellowships, Research and Training Fellowships for Clinicians, Junior Investigator Research Awards (for recently independent epilepsy researchers); joint support for the Susan S. Spencer Clinical Research Training Fellowship in Epilepsy, with the American Academy of Neurology, the Epilepsy Foundation, and the American Brain Foundation
- Seed Grants: small grants to established investigators to pursue new research directions that may lead to larger subsequent support from other sources
- Workshop Grants: support for scientific conferences focused on epilepsy research

Other research training:

- The Epilepsy Patient Oriented Research Training Program (EpiPORT) pairs 10 clinical epilepsy fellows with mentors for a year-long program that includes the development and review of mock research proposals and a twice monthly webinar series on various aspects of clinical research, including research methods, topics of interest in clinical research, and practical resources for successful research management.

AES Annual Meeting:

- premiere venue for presenting important findings in epilepsy research through symposia, Investigator Workshops, Special Interest Groups, Skills Workshops, and platform presentations and posters
- mentoring and career development opportunities for junior investigators
- Travel Awards recognizing meritorious abstract submissions
- Research Recognition Awards presented recognizing outstanding records of achievement in basic and clinical epilepsy research

AES also provides administrative support and coordination for the Epilepsy Leadership Council (ELC)

Examples of Recent Activities:

Early Career Research Funding:

- In FY2014-2015, AES supported six postdoctoral and three predoctoral fellowships, one clinical fellowship, three junior investigator research grants, and one new and one continuing Susan S. Spencer Clinical Research Training Fellowship. ([See list of recipients.](#))
- Research projects recently supported included basic and translational research on mechanisms underlying seizure susceptibility and epileptogenesis, SUDEP, and pharmacoresistance, as well clinical studies on molecular markers associated with disease severity in TSC, epileptogenic focus localization based on non-invasive interictal recordings, and memory alterations in pediatric epilepsy.
- Applications are under review for our FY2015-2016 funding (support begin in July 2016). These include applications solicited through a new partnership with Wishes for Elliott to support research specifically focused on SCN8A-related epilepsy.

Seed Grants:

- Four projects supported in FY2014-2015, including basic research on disease mechanisms in temporal lobe epilepsy, diabetes-induced postischemic seizures, and Dravet syndrome, as well as a clinical imaging study on neurodegeneration in chronic epilepsy.

AES supported the following workshops in FY2014-2015:

- ADD Program Symposium, Park City, UT (May 2015)
- Epilepsy Course: From the Laboratory to the Clinic, Mexico City, MEXICO (July 2015)
- Seventh International Workshop on Seizure Prediction (IWSP7), Melbourne, Australia (August 2015)
- Neurobiology of Disease Symposium on Epileptic Encephalopathy, Washington, DC (October 2015)

AES Epilepsy Benchmarks Committee:

- This Committee works to track progress and research opportunities related to the NINDS Epilepsy Research Benchmarks. The Stewards have submitted a mid-course progress review of the 2014 Benchmarks for publication in the May/June 2016 issue of Epilepsy Currents.

Resources Available:

- [Epilepsy Currents](#): the bi-monthly review journal provides commentary on recent publications in basic and clinical epilepsy research
- [Basic Science Toolkit](#): directory of experts and other resources for basic epilepsy research
- [Q-PULSE](#): Quantitative Practical Use-Driven Learning Survey in Epilepsy, a survey of leading epileptologists on issues in clinical care with relevance to informing research opportunities
- Epilepsy Grants Awards Database (EGAD) Survey update
- AES Annual Meeting (see above), including access to archived abstracts and other content
- AES Special Interest Groups and Committees focused on areas of epilepsy research
- Professional education and clinical resources

Priorities and/or Plans for Future Activities:

- Increase annual research funding to \$1M over the next 3-5 years, with continued emphasis on supporting research training and early career investigators

- Partner with interested organizations to advance science, address strategic funding needs, and minimize fragmentation and overlap
- Strengthen mentoring and career development support for early career investigators
- Conduct a revised survey to assess AES research funding outcomes (EGAD)

The NINDS/AES Benchmark Stewards Committee

Primary Representative: Ray Dingledine (Committee Chair, Emory University)

Email: rdingle@emory.edu

Mission: The Benchmarks Stewards Committee tracks and promotes progress related to the NINDS Benchmarks for Epilepsy Research, which are community-wide research priorities updated periodically in conjunction with NINDS Curing the Epilepsies Conferences. As a primary task, the Stewards will publish interim and final progress reviews for the 2014 Benchmarks in 2016 and 2019, in advance of the next Curing the Epilepsies Conference.

Major Topics of Interest:

2014 NINDS Benchmarks for Epilepsy Research

- I. Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.
 - A. Identify new genes and pathways associated with the epilepsies and epilepsy-related conditions.
 - B. Identify new infectious, immune, age-related, environmental, or other causes and risk factors associated with the epilepsies and epilepsy-related conditions.
 - C. Determine whether factors related to age, gender, race/ethnicity, socioeconomic status, and other features of specific populations affect risk and mechanisms of epilepsy and epilepsy-related conditions.
 - D. Determine whether the bi-directional relationships that exist between the epilepsies and several co-occurring conditions (e.g., neuropsychiatric or neurodevelopmental disorders) result from the same underlying causal mechanisms, interacting mechanisms, or are a consequence of the first presenting condition.
- II. Prevent epilepsy and its progression.
 - A. Understand epileptogenic processes involved in epilepsies with neurodevelopmental origins, including those due to genetic or presumed genetic causes.
 - B. Understand epileptogenic processes involved in the development of epilepsy following traumatic brain injury, stroke, brain tumor, infections, neurodegeneration, or other insults to the brain.
 - C. Identify biomarkers that will aid in identifying, predicting, and monitoring epileptogenesis and disease progression, including markers early after injury/insult that identify those people at risk for epilepsy.
 - D. Develop or refine models aligned with the etiologies of human epilepsies to enable improved understanding of epileptogenesis and rigorous preclinical therapy development for epilepsy prevention or disease modification.
 - E. Identify new targets and develop interventions to prevent or modify epileptogenesis and the progression of epilepsy and epilepsy-related conditions.
- III. Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.
 - A. Understand the initiation, propagation, and termination of seizures at the network level in different forms of epilepsy.
 - B. Identify biomarkers for assessing or predicting treatment response, including markers that may identify specific populations that are likely to have good outcomes or develop adverse responses.

- C. Develop or refine models that are aligned with etiologies and clinical features of human epilepsies, especially treatment resistant forms, to enable improved understanding of ictogenesis and preclinical development to improve seizure control with fewer side effects. Establish the sensitivity and specificity of these models with regard to current therapies.
 - D. Identify, develop, and improve interventions to detect, predict, prevent, or terminate seizures, including approaches suitable for use in the home and other non-medical settings.
 - E. Identify, develop, and improve anti-seizure therapies that target (either alone, or in combination) novel or multiple seizure mechanisms.
 - F. Develop, improve, and implement interventions for effective self-management, including treatment adherence.
 - G. Develop and validate objective patient-centered outcome metrics for clinical studies.
- IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.
- A. Understand and limit adverse impacts of seizures on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.
 - B. Understand and limit adverse impacts of anti-seizure treatments (medical, surgical, or other interventions) on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.
 - C. Understand risk factors and mechanisms involved in non-epileptic seizures (NES). Develop effective approaches for earlier and accurate diagnosis and treatment.
 - D. Identify causes, risk factors, and potential preventive strategies for sudden unexpected death in epilepsy (SUDEP) and other epilepsy-related mortality (for example, suicide) in people with epilepsy.
 - E. Identify the impact of pharmacological treatment of the epilepsies on fetal and neonatal development. Develop strategies to control seizures in pregnancy without causing harm to either the mother or child.

Examples of Recent Activities:

The Benchmarks Stewards have submitted interim progress reviews for each of the areas of the Benchmarks for publication in the May/June 2016 issue of *Epilepsy Currents*.

Opportunities for Collaboration: ICARE members are welcome to contact any of the Benchmark Stewards for collaboration/interaction on topics of shared interest (current roster below).

Priorities and/or Plans for Future Activities:

- The next progress reviews for each of the areas of the Benchmarks will be completed in 2019, in advance of the next Curing the Epilepsies Conference.
- In addition to progress reviews, the Stewards are considering opportunities for activities to promote progress related to the Benchmarks within and beyond AES.

2014 AES/NINDS Epilepsy Research Benchmarks Stewards

Chair: Ray Dingledine

AES staff: Cara Long

I. Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.

Co-Chairs: Heather Mefford and Rochelle Caplan

Madison Berl, Bernard Chang, Jack Lin, Annapurna Poduri, Andrey Mazarati

II. Prevent epilepsy and its progression.

Co-Chairs: Aristeia Galanopoulou and Michael Wong

Devin Binder, Adam Hartman, Elizabeth Powell, Avtar Roopra, Richard Staba, Annamaria Vezzani

III. Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.

Co-Chairs: Dennis Dlugos and Gregory Worrell

Kathryn Davis, Beate Diehl, Patrice Jackson-Ayotunde, Andres Kanner, Tobias Loddenkemper, Michael Rogawski, William Stacey, Sridhar Sunderam, Jerzy Szaflarski

IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.

Co-Chairs: W. Curt LaFrance, Jr., and Alica Goldman

Miya Asato, Timothy Benke, Robert Doss, Daniel Drane, Samden Lhatoo, Alison Pack, Tanvir Syed

Citizens United for Research in Epilepsy (CURE)

Primary Representative: Susan Axelrod, Founding Chair; Julie Milder, Associate Research Director

Email: Julie Milder – Julie@cureepilepsy.org

Mission: CURE's mission is to cure epilepsy, transforming and saving millions of lives. We identify and fund cutting-edge research, challenging scientists worldwide to collaborate and innovate in pursuit of this goal. Our commitment is unrelenting.

Major Topics of Interest:

- SUDEP
- Pediatric Epilepsies, with particular emphasis on infantile spasms
- Acquired Epilepsies
- Epilepsy genetics
- Pharmacoresistant epilepsies

Research Support:

- Research grants for basic, translational, and clinical research
- Young investigator travel awards to Gordon Research Conference
- HHMI/CURE research fellowship for medical students
- Conference and workshop support
- Sponsored seminar series
- Infantile spasms bedside to bench to bedside initiative
- Genetic database to house exomes and clinical data of people with epilepsy (EGI)
- Partnership with Department of Defense to support a team science initiative focused on post-traumatic epilepsy as a result of traumatic brain injury.

Examples of Recent Activities:

- Current grant mechanisms: CURE Epilepsy Award, Innovator Award, Taking Flight Award
- For a description of each mechanism:
<http://www.cureepilepsy.org/research/grant-categories.asp>
- Infantile Spasms Initiative – directed team science:
<http://www.cureepilepsy.org/research/is.asp>
- Epilepsy Genetics Initiative (EGI): EGI is an initiative created by CURE, in partnership with NINDS, to establish a database to hold the genetic data of people with epilepsy. The specific type of data we are talking about is exome sequence data. The data will be analyzed every 6 months to find the cause of epilepsy and results will be reported back to the treating physician. These data will also be made available for research.
<http://www.cureepilepsy.org/egi/>
- Partnership with Department of Defense: 5-year, \$10M initiative to focus on post-traumatic epilepsy with a team science approach. RFA to be released April 2016. Read more here:
<http://www.cureepilepsy.org/news/story.asp?id=149>
- 2016 Conference Support committed, to-date: Partners Against Mortality in Epilepsy (Alexandria, VA), Gordon Research Seminar on Synaptic Transmission (Waterville Valley, NH), Gordon Research Seminar and Gordon Research Conference on Mechanisms of Epilepsy and Neuronal Synchronization (Girona, Spain), Excitatory-Inhibitory Signaling Balance workshop (Montreal, Quebec), Global Symposium on Ketogenic Therapies (Banff, Alberta), Immunity and Inflammation in Epilepsy (Milan, Italy)

- CURE Frontiers in Research Seminar Series – spreading the word about cutting edge epilepsy research at research institutions throughout the world:
<http://www.cureepilepsy.org/seminarseries/>
- HHMI Medical Fellows partner – support medical students to take a year away from their studies to pursue epilepsy research

Resources Available: EGI (www.CUREepilepsy.org/EGI)

Priorities and/or Plans for Future Activities:

- Continuation of existing programs, with ongoing evaluation so CURE is poised to accelerate any program if an opportunity presents
- Assessing impact of the research program through various metrics in order to remain flexible and adjust where deemed necessary, with help from expanded internal research team and 5-member Scientific Advisory Council

Dravet Syndrome Foundation (DSF)

Primary Representative: Abby Hemani, Board President

Email: abby.h@dravetfoundation.org

Mission: The mission of Dravet Syndrome Foundation (DSF) is to aggressively raise research funds for Dravet syndrome and related epilepsies; to increase awareness of these catastrophic conditions; and to provide support to affected individuals and families.

Major Topics of Interest: DSF supports research with an emphasis on Dravet syndrome and related ion channelopathies. Most of our projects are funded through our standard application process, which includes our Research Grant Program and our Postdoctoral Fellowship Program. We have an interest in studies on the causes of Dravet syndrome, genetics, basic mechanisms, co-morbidities and translational efforts.

Research Support:

- **DSF Research Grant Awards** - DSF's Research Grant Program offers funding for research directly related to Dravet syndrome and associated disorders. These grants fund initial research hypotheses that have not been fully explored.
- **DSF Research Postdoctoral Fellowships** - DSF's Postdoctoral Research Fellowship Grant develops academic physicians and scientists committed to research related to Dravet syndrome and associated ion channel epilepsies. The fellowship is intended to support a full-time research effort.
- **DSF Research Roundtable** - This annual meeting brings together researchers, geneticists, neurologists, and other professionals with a strong interest in Dravet syndrome and related epilepsies. The roundtable allows the establishment of a "research roadmap" to guide DSF in funding research projects that address the critical challenges of this syndrome.
- **DSF Biennial Family & Professional Conference** - This 3-day event is unique in that it is designed to unite all groups committed to improving the lives of those with Dravet syndrome - including families, caregivers, clinicians, researchers and professionals in the pharmaceutical industry. There will be speaker presentations on the latest advances in research as well as sessions with up to date information impacting patient care. This event allows the opportunity to foster new relationships and collaborations, both for families and professionals.
- DSF offers occasional financial support at Dravet-specific professional meetings.

Examples of Recent Activities:

- **2015 Awards Alex Nord, PhD - DSF Research Award – \$110,000 (2 year project)**
Regulation of SCN1A expression as pathogenic mechanism in Dravet Syndrome
The majority of individuals with Dravet Syndrome (DS) carry mutations in the SCN1A gene, causing a non-functional Nav1.1 protein to be produced in the brain. However, other genetic factors beyond SCN1A coding mutations likely account for the substantial remaining DS causal burden. The activity of genes, such as SCN1A, is controlled by regulatory DNA elements that turn genes on at the right time and place during development. We hypothesize that mutations in regulatory DNA elements that control SCN1A activity in the brain represent a significant genetic mechanism in DS and SCN1A-associated disorders. The goals of this study are to understand the role of regulatory DNA elements and SCN1A gene expression using mouse models and genomic

technologies. These experiments may reveal novel pathological mechanisms and improve genetic diagnosis in DS by enabling screening of important regulatory DNA not captured by current tests.

- **John C. Oakley, MD, PhD - DSF Research Award – \$160,000 (2 year award)**

Understanding the relationship between gene mutation, seizures, and cognitive impairment in Dravet syndrome

Seizures and co-morbidities in Dravet syndrome (DS) are not well treated with current therapies and no cure exists. In most cases, DS is caused by mutations in the gene SCN1A resulting in reduced expression of a voltage-gated sodium channel Nav1.1 critical to the excitability of neurons. Work by myself and many others shows that inhibitory cells in the nervous system are particularly effected. We hypothesize that the resulting changes in network function are the cause of seizures and co-morbidities such as cognitive disability. As seizure frequency and severity increases prior to difficulties with memory, learning, and other cognitive functions, it is tempting to attribute impairments to seizure-related brain injury which, if involving cell death, may be irreversible. This has led to a focus on improved seizure control as the primary treatment for cognitive disability. However, recent cognitive outcome studies failed to demonstrate a relationship between seizure type and severity and outcomes. In addition, in our own work in mouse models of DS, we have found evidence of cell death. This suggests that the network remains, in principle, intact and that restoring normal SCN1A function, even after seizures have begun, may substantially improve network function, seizure control, and cognition. In the proposed study, we seek to determine in our well-validated mouse model of DS whether a reduction in Scn1a expression beginning in adulthood, in the absence of prior seizures, is sufficient for seizure susceptibility and cognitive impairment. To determine whether, under optimal conditions, restoring Scn1a expression, gene therapy, improves cognition and seizures. These studies will provide insights into the potential outcome of gene therapy under the best conditions in which near total correction of the genetic defect is expected and provide preliminary data to support further, more detailed work into the specific brain regions, cell-types, and degree of restored Scn1a expression required to adequately treat seizures and multiple comorbidities, information critical to the development of potential gene therapy in humans.

- **Samir Das, PhD - DSF Postdoctoral Fellowship – \$50,000 (1 year project)**

Structure and function of the sodium channel Beta 1 subunit: a target for Dravet syndrome mutations

Our neurons can mediate extremely rapid messages through the use of electrical signals. Such signals arise from the movement of tiny charged particles such as sodium ions into the cell. The sodium ions can only enter the cells through a protein, termed ‘sodium channels’. Their opening and closing decide how much sodium can enter the cell which directly affects the brain function. Simple changes in the genetic code can create faulty channels leading to severe epilepsy and Dravet syndrome to infants. Here, we will solve the high resolution structures of the sodium channel both “normal” and “diseased” condition which will shed light on the disease mechanism.

- **Alison Muir, PhD - DSF Postdoctoral Fellowship – \$50,000 (1 year project)**

Dravet Syndrome – Where are the missing mutations?

Making a genetic diagnosis in Dravet syndrome is important for many reasons. First, it gives families and physicians insight into disease management and risks for further complications. It also helps discussion about recurrence risk for future pregnancies and influences medication decisions. Finally, it allows researchers insight into how the disease manifests and provides avenues for drug development. However, for 20% of families with Dravet syndrome, no genetic cause is identified. Certain types of mutations are missed by conventional testing and may be

present in patients without a genetic diagnosis. We propose to use innovative approaches to hunt for two types of these “missing mutations”: 1) “mosaic” mutations of SCN1A found in only a subset of cells and tissues. 2) “regulatory” mutation that cause changes to how much protein is made.

Resources Available: We are open to opportunities for collaboration with other rare epilepsy organizations, as well as clinicians, researchers or private companies with an interest in the Dravet patient community.

Priorities and/or Plans for Future Activities:

- Our annual Research Grant & Postdoctoral Fellowship applications are due on September 2, 2016.
- Our annual Research Roundtable will be held on December 1, 2016 in Houston, Texas.
- Our next Family & Professional Conference will take place on June 23-26, 2016, in Coral Gables, Florida, in collaboration with Niklaus Children’s Hospital.

Patient-Centered Outcomes Research Institute (PCORI)

Primary Representative: Thomas P. Caruso, Ph.D., MBA, PMP. Associate Director, Program Operations – Research Infrastructure
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Mission: PCORI helps healthcare stakeholders make informed health care decisions, and improves health care delivery and outcomes by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers, and the broader health care community.

Major Topics of Interest:

- **The Rare Epilepsy Network (REN)** initiative is created by and for patients with catastrophic rare epilepsies. The goal is to build a patient-centered and driven data base designed to provide patients and their families an opportunity to participate in research that will improve lives and quality of care for people with rare epilepsies. Our Patient-Powered Research Network is led by the Epilepsy Foundation, a patient advocacy organization dedicated to the welfare of the almost 3 million people with epilepsy living in the United States.
- **Cognitive AED Outcomes in Pediatric Localization Related Epilepsy (COPE) Project:** Children with LRE represent a particularly vulnerable population for treatment related cognitive side effects because they are still developing cognitively and socially. Negative treatment effects on cognition can diminish developmental outcomes. If medication differences in the amount of cognitive side effect risk exist, then selecting treatments associated with poorer cognitive outcome needlessly interferes with cognitive development and school performance. Choosing a medication with the least cognitive impairment will maximally preserve cognitive abilities. This study will determine changes in cognitive abilities (eg, attention) associated with three of the most common medications used to treat pediatric LRE. Regardless of the specific findings, results of this study will provide the information needed to help parents and their clinicians choose treatment options that maximize cognitive abilities in children with LRE and provide the data needed for practice guidelines to be established on the basis of cognitive side effect risks.

Research Support:

PCORI has a sizeable and growing portfolio of projects designed to improve patient care and outcomes through patient-centered comparative clinical effectiveness research, or CER. The work under these priorities is managed by our scientific programs, which track and evaluate its effectiveness. PCORI is also charged with developing and improving the science and methods of CER because methods matter when it comes to producing valid, trustworthy, and useful information that will lead to better healthcare decisions and ultimately, to improved patient outcomes. PCORI's strong emphasis on engaging patients and the broader healthcare community in all work is evident in the criteria we have developed for the research funded. PCORI also provides awards to encourage engagement of patients and other stakeholders in CER.

Examples of Recent Activities: Rare Epilepsy Network accomplishments during Phase I include development of governance policies, identification of data elements, survey development, database creation, IRB approval, and population of their database. REN's survey includes 11 modules that address demographics, diagnosis and treatment, medical history and quality of life. Additionally, EEG, MRI, video EEG reports can be uploaded. REN is adding a follow-up survey to collect longitudinal data for the affected person and caregiver.

Resources Available: PCORnet, the National Patient-Centered Clinical Research Network, is an innovative initiative of the Patient-Centered Outcomes Research Institute (PCORI). It is designed to make it faster, easier, and less costly to conduct clinical research than is now possible by harnessing the power of large amounts of health data and patient partnerships. In the process, it is transforming the culture of clinical research from one directed by researchers to one driven by the needs of patients and those who care for them.

Priorities and/or Plans for Future Activities: The goals for Phase II are three-fold. First, we will expand the number of patients/caregivers for participation in our database, adding more rare epilepsies, and work to retain them. Second, we will build capacity for research both within the REN, and externally through PCORnet partners (IAN, PMS, PEDSnet, NYC-CDRN) and other external researchers to maximize research in the REN. They are designing a long-term sustainability plan to assure that the REN remains viable for further research. To sustain the REN, they are developing the Rare Epilepsy Institute (REI) to be housed at the EF as part of its Institute model. The REI will be a resource for awareness, education and funding raising. It will be supported and led by EF in collaboration with the rare epilepsy organizations and the two Co-PIs.

Pediatric Epilepsy Research Foundation (PERF)

Primary Representative: Roy D. Elterman, MD, President

Email: Perf2004@gmail.com

Mission: The mission of the Foundation is to enhance the quality of life of children with epilepsy and other neurologic disorders. To accomplish this mission, the Foundation, in particular, seeks to support: efforts to improve treatment options for infants, children and adolescents with epilepsy; meritorious clinical and basic science research related to epileptic conditions in children; and the encouragement of the recruitment and education of young physicians in the field of child neurology.

Major Topics of Interest: Developing young investigators in pediatric neurology and specifically pediatric epilepsy. We are equally interested in developing networks and infrastructure in pediatric neurology, again with a specific interest in pediatric epilepsy.

Research Support:

The Pediatric Epilepsy Research Foundation provides grant funding to outstanding child neurologists in the US/Canada for meritorious clinical, translational, basic science, comparative-effectiveness, implementation research, etc. related to neurologic conditions in infants, children and adolescents. Epilepsy projects are given preference. PERF offers two grant categories

PERF Career Development Grant

To be eligible for this grant, the applicant should be a child neurologist who has completed training in an ACGME-approved program (no more than seven years prior to the application) and who is a legal resident of the United States or Canada.

Non-child neurology trained physicians (meeting ACGME-approved training criteria) and PhD's developing careers in child neurology may also be considered.

Applicants with current or approved pending NIH funding are not eligible.

PERF Grant for Infrastructure/Registry Research

To be eligible for this grant, the applicant should be a child neurologist at any stage in his or her career and must be a legal resident of the United States or Canada.

Non-child neurologists and PhD's developing infrastructure/registry projects in child neurology may also apply.

Examples of Recent Support and Activities:

"Impact of Seizures in Infants and Children with Ischemic Stroke" 2010

"Tuberous Sclerosis Complex (TSC) Natural History Database" 2011

"Transcriptional mechanisms underlying hypoxia-induced white matter injury during early postnatal development" 2012

"Multi-center Neonatal Seizure Registry" 2013

"Early Onset Epilepsy Consortium" 2013

"Care Management for Pediatric Epilepsy: Predictive Modeling and Evaluation" 2014

"Mechanistic Studies and Therapy Development for Epileptic Encephalopathies" 2015

"Pediatric Status Epilepticus Research Group (pSERG)" 2015

"Seizures in Pediatric Stroke II (SIPS II)" 2015

The Epilepsy Study Consortium (TESC)

Primary Representative: Jacqueline French, MD; Professor of Neurology, NYU School of Medicine; President, TESC and Dennis Dlugos, MD; Professor of Neurology, Children's Hospital of Philadelphia; Vice President – pediatrics, TESC

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Mission: The Epilepsy Study Consortium is a group of scientific investigators from academic medical research centers who are dedicated to accelerating the development of new therapies in epilepsy to improve patient care. The organization's goals include building a partnership between academics, industry and regulatory agencies and optimizing clinical trial methodology in order to responsibly speed new treatments to patients.

Major Topics of Interest:

- Clinical trials
- Clinical trial methodology
- Protocol development
- Novel Therapeutics

Research Support:

We have 29 academic medical centers in the US and 11 in Australia as members of the consortium. These centers have been screened to find the optimal sites for clinical trial research. Each site specializes in epilepsy and has a rather large patient population which enables careful patient selection, and good recruitment.

We have been involved in a number of early trials from industry, as well as trials funded by non-profits.

We have created diagnostic review forms and seizure classification forms that are now widely used in epilepsy studies, to ensure that patients enrolled in trials have been properly selected and classified, in an attempt to reduce noise in studies.

The Consortium has also assisted sponsors with protocol development, CRF and source document design and assembled DSMBs.

We sponsor a biennial research conference focusing on issues related to antiepileptic drug (AED) development from preclinical discoveries through clinical evaluations. This symposium brings together representatives from academia, industry, the NIH, and the FDA to review what has been learned and to discuss strategies to enhance AED development

Website: www.aedtrials.com

Six grants of \$1,500 were awarded to fellows and early career faculty interested in new therapies for epilepsy. The grants were used to cover expenses associated with attending the Antiepileptic Drug & Device Trials XIII Symposium. The registration fee was also waived. In addition to the grants, the Epilepsy Consortium sponsored 'mentoring lunches' which were held throughout the meeting. This enabled the grant recipients to meet with faculty members with interests similar to their own.

Funding of one fellow to attend Epilepsy Foundation Pipeline Conference in February, 2016.

We organized a Coordinator Boot Camp. This was made available to all Consortium Coordinators. There were 26 coordinators representing 15 Consortium sites who attended with a wide variety of experience from 4 months to over 15 years. There are plans to continue this in the future.

Examples of Recent Activities: HEP - The Human Epilepsy Project is a five-year, prospective, observational study whose primary goal is to identify clinical characteristics and biomarkers predictive of disease outcome and progression, and treatment response in participants with new onset or recently diagnosed focal epilepsy. The data to be collected on these participants include high-resolution clinical phenotyping (including comorbidities) and treatment response, neuroimaging, electrophysiology, and genomics and proteomics. A major objective of the project is to create an open data repository of clinical information and biologic samples for future studies

Photosensitivity Studies – The photosensitivity proof of concept model has been used to evaluate potential antiseizure effects of new agents in relatively small groups of patients with photically induced generalized epileptiform responses on their EEG. The Epilepsy Consortium is performing central EEG review and on-site training to all of the sites involved.

Resources Available: Additional information can be found on the TESC website:
www.epilepsyconsortium.org

Priorities and/or Plans for Future Activities: We are available to assist for trials of new diagnostic or therapeutic interventions performed by any non-profit or for-profit entity.

Tuberous Sclerosis Alliance (TS Alliance)

Primary Representative: Kari Luther Rosbeck, President and Chief Executive Officer

Email: krosbeck@tsalliance.org

Mission: The Tuberous Sclerosis Alliance is dedicated to finding a cure for tuberous sclerosis complex (TSC) while improving the lives of those affected.

Major Topics of Interest:

- Identify biomarkers that accurately predict those with TSC at high risk of developing epilepsy
- Develop approaches to prevent development of epilepsy in those with TSC at high risk
- Further investigate the epilepsy-related genotype-phenotype correlations in TSC
- Understand the range of signaling pathways that play a role in the development of epilepsy in TSC
- Understand the relationship of mTOR activity to epilepsy

Research Support:

- The TS Alliance annually awards research grants and postdoctoral fellowship supporting research focused on TSC, which may include the study of any aspect of epilepsy in TSC, such as molecular mechanisms, preclinical models, biomarker discovery, etc.
- The TSC Clinical Research Consortium provides infrastructure to conduct clinical studies in TSC, including epilepsy-related studies, at seven or more TSC Clinics around the country.
- The TSC Preclinical Consortium is establishing the infrastructure and processes in 2016 to test candidate drugs for efficacy in mouse models of TSC using standardized, rigorous protocols.

Examples of Recent Activities:

- The TSC Clinical Research Consortium recently identified an EEG biomarker associated with risk of developing seizures in infants with TSC and is planning to start a clinical trial in the fall of 2016 to test whether treatment of infants with TSC who exhibit the EEG biomarker will prevent the development of clinical seizures.
- The TSC Preclinical Consortium has identified two TSC-relevant mouse models for testing of candidate anti-epileptogenic or anti-seizure drugs and is developing standardized protocols.
- The TS Alliance participates in the Rare Epilepsies Network led by the Epilepsy Foundation in partnership with RTI International, Columbia University, and 22 organizations that represent patients with a rare syndrome or disorder that is associated with epilepsy or seizures.

Resources Available:

- The TSC Natural History Database is a central repository of clinical data collected at 18 TSC Clinics which serves to identify cohorts for participation in research studies and to provide data to researchers for further analysis. Currently, more than 1900 individuals are enrolled.
- Academic and industrial researchers have an opportunity to join the TSC Preclinical Consortium, which will begin testing candidate drugs for epilepsy in TSC in 2017.
- The TSC Biosample Repository has begun collecting blood and tissue, including resected brain samples from epilepsy surgeries that is associated with detailed clinical data in the TSC Natural History Database and will be made available to qualified researchers worldwide.

Priorities and/or Plans for Future Activities:

- Growing the TSC Biosample Repository collection of blood and brain samples.

- Opening the TSC Preclinical Consortium to nomination of candidate drugs to be tested by additional researchers when anti-epileptic experimental protocols have been validated.
- Collecting more in-depth data in the TSC Natural History Database of epilepsy trends and response to treatment throughout the lifespan in TSC.