

ICARE: Interagency Collaborative to Advance Research in Epilepsy

2014 Member Reports

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National Institute of Neurological Disorders and Stroke (NINDS)

Primary Representative: Brandy Fureman, 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 cooperative agreement (U01) award. Several U01 awards related to epilepsy have also been funded in recent years, including device and biologics development efforts. The NINDS Office of Translational Research recently announced changes to the scope and management of the translational programs, which will be detailed in new funding opportunity announcements to be released in FY2015.

The Anticonvulsant Screening Program (ASP) 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 ASP 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. 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.

Types of research support:

NINDS supports investigator-initiated projects in basic, translational and clinical research related to epilepsy, as well as projects supported through Funding Opportunity Announcements (FOAs) issued by NINDS or in collaboration with other NIH Institutes and Centers. 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:

- Curing the Epilepsies 2013: Pathways Forward Conference <https://meetings.ninds.nih.gov/?ID=4069>
- 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>

Resources available:

- NINDS Common Data Elements for Epilepsy Research
<http://www.commondataelements.ninds.nih.gov/#page=Default>
- NINDS Anticonvulsant Screening Program (ASP) <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://www.ninds.nih.gov/research/scientific_resources/index_research.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:

In general, the NINDS looks to the Epilepsy Research Benchmarks for priorities identified by the epilepsy community. Plans for future epilepsy research activities include an intent to support Epilepsy Centers without Walls on SUDEP (in FY14) and on Disease Modification and Prevention (in FY15).

National Heart, Lung, and Blood Institute (NHLBI)

Primary Representative: David A. Lathrop, PhD, Chief, Heart Failure and Arrhythmias Branch

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Mission: The National Heart, Lung, and Blood Institute (NHLBI) provides global leadership for a research, training, and education program to promote the prevention and treatment of heart, lung, and blood diseases and enhance the health of all individuals so that they can live longer and more fulfilling lives.

The NHLBI stimulates basic discoveries about the causes of disease, enables the translation of basic discoveries into clinical practice, fosters training and mentoring of emerging scientists and physicians, and communicates research advances to the public. It creates and supports a robust, collaborative research infrastructure in partnership with private and public organizations, including academic institutions, industry, and other government agencies. The Institute collaborates with patients, families, health care professionals, scientists, professional societies, patient advocacy groups, community organizations, and the media to promote the application of research results and leverage resources to address public health needs. The NHLBI also collaborates with international organizations to help reduce the burden of heart, lung, and blood diseases worldwide.

Major Topics of Interest:

Research topics that clearly overlap and that are important to epilepsy research at NHLBI are largely fostered and managed within the [Heart Failure and Arrhythmias](#) and [Heart Development and Structural Diseases](#) Branches in the [Adult and Pediatric Cardiac Research Program](#) in the [Division of Cardiovascular Sciences](#). Both of these branches conduct and manage integrated basic and clinical research programs to study normal cardiac function and pathogenesis to improve diagnosis, treatment, and prevention of heart failure and arrhythmias, as well as pediatric and adult structural heart disease. This includes normal and abnormal cardiovascular development, study of the molecular and genetic etiology of cardiovascular malformations, and gene-environment interactions in development of congenital heart disease, as well as the study of arrhythmogenesis, the genetic and environmental bases of normal cardiac electrical activity and arrhythmias, etiology of rare and common arrhythmias, and sudden cardiac death.

Types of research support:

NHLBI supports a wide array of research mechanisms described here:

<http://www.nhlbi.nih.gov/funding/resmech.htm>. Similarly, NHLBI supports a number of training and career development programs described here:

<http://www.nhlbi.nih.gov/funding/training/redbook/trgnprog.htm>. All of these research and training support mechanisms are available to epilepsy investigators with interests that overlap and intersect with the NHLBI mission. Descriptions and summaries of research meetings convened by NHLBI are found here: <http://www.nhlbi.nih.gov/resources/docs/index.htm>. Some are likely to be of interest to investigators seeking to better understand the underpinnings of epilepsy and ways to better treat and prevent it.

Examples of Recent Activities:

During 2013, NHLBI continued its support of an NIH [Pathway to Independence Award](#), R00 HL107641, entitled “excitability mechanism of neurocardiac regulation.” This research project was first funded as an NIH K99 award in 2011 and converted to an R00 last year. The project specifically focuses on examining the molecular mechanisms that contribute to neurocardiac dysfunction in mouse models of epilepsy and sudden unexplained death in epilepsy (SUDEP). The investigative team at Louisiana State University

Health Science Center in Shreveport headed by Dr. Albert Glsscock, a promising young investigator, is studying the contribution of parasympathetic neurotransmission to potentially lethal heart arrhythmias in two different epilepsy mouse models of brain-driven heart dysfunction associated with SUDEP. This and similar studies may help to better uncover the genetic bases of excitability disorders, especially epilepsy, and how gene mutations may cause excitability defects in multiple tissues at once, such as the brain and heart. Such work is likely to provide an explanation for the prevalence of disease comorbidities associated with epilepsy, and provide a rationale bases for its treatment and future prevention.

Other recent epilepsy-related research funded by NHLBI includes:

Project/Subproject Number	Title	Investigator	Applicant Organization
5R01HG006753-02	Advancing Transfer RNA Discovery, Research and Resources	Lowe, Todd Michael	University of California, Santa Cruz
2R01HL054171-17A1	Rectification and block of ion channel currents	Nichols, Colin G	Washington University
5R01HL070393-12	Ca ²⁺ -dependent K ⁺ -channels: allosteric gating	Cui, Jianmin	Washington University
1R01HL112918-01A1	Structural studies of NaV1.5 and functional implications	Pitt, Geoffrey S	Duke University
5R01HL050411-18	Structural Basis of the Regulation of Na Channels	Tomaselli, Gordon Frank	Johns Hopkins University
5R01HL080050-09	Structure and function of voltage-gated calcium channels	Minor, Daniel L	University of California, San Francisco
5R01HL093776-04	Insular Autonomic Function in Depression	Royall, Donald R	University of Texas Health Science Center, San Antonio
5R01HL089564-05	KCNQ Channels and Vasoconstrictor Signal Transduction	Byron, Kenneth L	Loyola University, Chicago

Resources available:

An extensive list of research resources supported by NHLBI in conjunction with other NIH Institute, Centers, and Offices may be found at: <http://www.nhlbi.nih.gov/resources/resources.htm>. Many of these are likely to be useful to epilepsy researchers”

Priorities and/or Plans for Future:

The NHLBI is collaborating with the National Institute for Neurologic Disorders and Stroke (NINDS) and the Centers for Disease Control and Prevention (CDC) to develop The Sudden Death in the Young (SDY) Registry, a surveillance system and registry that will track all sudden deaths in youths up to age 24 in as many as 15 states. Child death review teams from each state will conduct death scene investigations, including review of medical records, death certificates, and autopsy results. Autopsy protocols will be standardized, and blood samples will be collected and stored in a central biorepository for future study. Additional evaluation will be performed by cardiologists and neurologists in cases of suspected

sudden cardiac death and Sudden Unexpected Death in Epilepsy (SUDEP). The CDC will subcontract to the data coordinating center, which will oversee the database and coordinate biospecimen collection. The NHLBI and NINDS will work closely with the CDC to implement the registry and provide oversight and subject matter expertise. This Registry phase will result in the first prospective, population-based data set compiled for the comprehensive evaluation of SDY in the United States. It will provide the opportunity to estimate incidence more precisely than any previous study and to establish an infrastructure for future expanded use.

In general, NHLBI is interested in fostering epilepsy research that overlaps and intersects with its mandate. Two such areas are sudden unexplained death in epilepsy (SUDEP) and sudden cardiac death (SCD). Topics areas that overlap and intersect in these two areas include study of ion-channel gating; voltage-gated membrane pore subunits; sodium-channel excitability; ion potassium-channels; NAV1, patch-clamp techniques; as well as the study of molecular pathways; cellular targets; defining genetic, therapeutic, biochemical, biological mechanisms. The [NIH Topics map](#) and [NIH RePORTER](#) may be used to identify other areas of research overlap and funded research projects in these important and interrelated areas of research. Investigator-initiated grant proposals in these areas are highly encouraged.

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

Primary Representative: Qi-Ying Liu, M.D., M.Sci., 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; Coordinating and collaborating with other research institutes and federal programs on alcohol-related issues; Collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work; Translating and disseminating research findings to health care providers, researchers, policymakers, and the public.

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.

Types of 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: In June 2013, NIAAA organized the “Alcohol Consumption, Seizure and Epilepsy: Molecular, Cellular and Neural Circuit Mechanisms” workshop that was held as a satellite meeting of the 2013 Research Society on Alcoholism annual meeting. The purpose of this translational conference was to take advantage of the most recent progress in the research of alcoholism and epilepsy to explore the molecular, cellular, neurocircuit and genetic mechanisms underlying the interactions of alcohol use, alcohol withdrawal seizure and epileptogenic processes for better management of seizures

and epilepsy in alcohol use population. Speakers from within and outside alcohol research area covered the following eight topic areas:

- The Neurobiology of Seizure and Epilepsy (Helen E. Scharfman)
- Synaptic Substrates of Alcohol Use- and Withdrawal-Induced Seizure and Epilepsy (David M. Lovinger)
- Genes & Neural Networks Underlying Seizure Susceptibility and Alcohol Withdrawal Seizure (Kari Buck)
- Prenatal Alcohol Exposure and Seizure/Epilepsy Susceptibility (Daniel D. Savage)
- Ion Channels and Alcohol-Related Seizure and Epileptogenesis (Prosper N'Gouemo)
- Glia in Seizure and Epileptogenesis (Sally McIver)
- GABA_A Receptor Subunit Plasticity in Alcohol Use- and Withdrawal-Induced Seizure/Epilepsy (Richard W. Olsen)
- Molecular Mechanisms of Alcohol Withdrawal-Induced CNS Hyperexcitability: the Role of Neuromodulatory Systems (A. Leslie Morrow)

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.

The National Institute of Biomedical Imaging and Bioengineering (NIBIB)

Primary Representative: Steven Krosnick, MD, Medical Officer for Extramural Science Programs at the National Institute of Biomedical Imaging and Bioengineering

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Mission: The mission of the National Institute of Biomedical Imaging and Bioengineering (NIBIB) is to improve health by leading the development and accelerating the application of biomedical technologies. The Institute is committed to integrating the physical and engineering sciences with the life sciences to advance basic research and medical care. This is achieved through: research and development of new biomedical imaging and bioengineering techniques and devices to fundamentally improve the detection, treatment, and prevention of disease; enhancing existing imaging and bioengineering modalities; supporting related research in the physical and mathematical sciences; encouraging research and development in multidisciplinary areas; supporting studies to assess the effectiveness and outcomes of new biologics, materials, processes, devices, and procedures; developing technologies for early disease detection and assessment of health status; and developing advanced imaging and engineering techniques for conducting biomedical research at multiple scales.

Types of Research Support:

NIBIB participates in many funding mechanisms and funding opportunity announcements available at NIH. These can be found at <http://www.nibib.nih.gov/funding/funding-opportunities>. Some of the funding opportunity announcement topics that may be of interest include biomedical technology resource centers, healthy independent living, bioengineering partnerships, big data science, the BRAIN Initiative, mobile health, regenerative medicine, and training.

Resources Available: Information about NIBIB intramural laboratories can be found at <http://www.nibib.nih.gov/research/labs-at-nibib>

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

Primary Representative: Melissa A. Parisi, M.D., Ph.D., Chief, 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

Types of Research Support: NICHD supports basic, translational, and clinical research and research grants, including training awards, meetings, networks, infrastructure, and other resources.

Examples of Recent or Current Epilepsy Research Activities:

- There are 15 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 IDDRCs at Boston Children's Hospital and University of Alabama-Birmingham have provided support in the form of core infrastructure to some of the Tuberous Sclerosis Complex (TSC)-related projects in particular, and these include studies to identify risk factors and biomarkers for infantile spasms in this disorder.
- NICHD 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. Unfortunately, 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. Although this is not a brand-new finding, our 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 suggest 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. These findings do not support the preferential use of lorazepam for this condition.

Resources Available: NICHD, NIMH, and NINDS have joined together to establish the NIH NeuroBioBank, a new 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. Several additional contracts to increase the number of tissue acquisition sites will be awarded in FY2014. See <https://neurobiobank.nih.gov/>

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 followup data repository. See <https://www.nbstrn.org/>

Jackson Laboratories Cytogenetic Models Resource. This resource maintains and distributes chromosome aberration stocks, which provide primarily mouse models for Down syndrome research. See <http://www.jax.org/cyto/index.html>

Priorities and/or future research 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 on Drug Abuse (NIDA)

Primary Representative: Roger G Sorensen, PhD, MPA, Program Official

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Mission: NIDA's mission is to lead the Nation in bringing the power of science to bear on drug abuse and addiction.

Topics of Interest: NIDA does not directly support research on epilepsy. However, NIDA broadly interprets epilepsy within the realm of brain seizure disorders. In this sense, NIDA currently supports research focused on the neurobiological mechanisms and treatment of brain damage produced by drug-induced excitotoxicity and seizures. NIDA's research interests include:

- the expression of drug withdrawal-induced seizures that result from substance (alcohol, barbiturates, benzodiazepines, GHB) dependence,
- the acute, pro-convulsant actions of certain drugs (cocaine, methamphetamine, MDMA or ecstasy, opiates, marijuana),
- the anti-convulsant actions of opiates and THC (marijuana) as potential treatments.

Types of research:

Support of basic/translational/clinical research grants

Examples of recent or current epilepsy research activities:

- Support of basic research grants to develop new pharmaceutical agents to treat drug dependence and epilepsy
- Support of basic research grants to study the mechanisms of enhanced neuronal excitability caused by drug use

CDC Epilepsy Program

Arthritis, Epilepsy and Well-Being Branch (AEWB)

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

Centers for Disease Control and Prevention (CDC)

Primary Representative: Rosemarie Kobau, MPH, MAPP; Epilepsy Program Team Lead

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Mission: CDC's Mission is to collaborate to create the expertise, information, and tools that people and communities need to protect their health – through health promotion, prevention of disease, injury and disability, and preparedness for new health threats.

The [National Center for Chronic Disease Prevention and Health Promotion](#) (NCCDPHP) leads the nation's efforts to create expertise, information, and tools to support people and communities in preventing chronic diseases and promoting health for all. The Center leads partnerships and collaborates fully with state and local health and education agencies, community groups, voluntary associations, private organizations, and other federal agencies. To achieve optimal health for all, NCCDPHP's work on the social determinants of health extends beyond the scope of traditional public health practice to include collaboration in education, housing, transportation, justice, labor, and other sectors. To support Americans with equitable opportunities to take charge of their health, NCCDPHP's work targets [four key action areas](#):

- Epidemiology and Surveillance to provide states and communities with the necessary expertise to collect data and information and to develop and deploy effective interventions, identify and address gaps in program delivery, and monitor and evaluate progress in achieving program goals.
- Environmental Approaches that promote health and support and reinforce healthful behaviors in schools, worksites, and communities. NCCDPHP works to expand access to and availability of healthy foods and beverages; promote increased physical activity; reduce tobacco use, prevent youth initiation, and eliminate exposure to secondhand smoke; and increase the proportion of the U.S. population served by community water systems with optimally fluoridated water.
- Health System Interventions to improve the effective delivery and use of clinical and other preventive services to prevent disease, detect diseases early, and reduce or eliminate risk factors and mitigate or manage complications.
- Strategies to improve Community-Clinical Linkages so that communities support and clinics refer patients to programs that improve management of chronic conditions. Such interventions ensure those with or at high risk for chronic diseases have access to quality community resources to best manage their conditions or risk factors.

The [CDC Epilepsy Program](#) within NCCDPHP seeks to effectively address public health issues related to epilepsy to improve the health of people living with epilepsy, especially those at greater risk for health disparities; improve their quality of life; and decrease the stigma associated with this condition.

Major Topics of Interest:

Epidemiologic studies and surveillance:

- Population surveys of epilepsy burden (prevalence, comorbidities, quality of life impairment; gaps in access to care, and related factors)
- Academic research on epilepsy prevalence and incidence, risk factors, outcomes, healthcare needs, and health disparities;
- Population-based epilepsy mortality surveillance, including sudden unexpected death in epilepsy (SUDEP)

- Population studies on stigma associated with epilepsy

Prevention Research:

- In collaboration with CDC's Center for Global Health, research is underway to develop and validate 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 immigrant populations.
- The [CDC Epilepsy Program](#) and the [Prevention Research Centers Program](#) support the [Managing Epilepsy Well \(MEW\) Network](#), an association of six universities and epilepsy stakeholders. The purpose of the network is to advance the science on epilepsy self-management by conducting research in collaboration with community stakeholders including people with epilepsy, to implement activities, and to broadly disseminate research findings.

Public Awareness/Communication:

- The CDC Epilepsy Program supports studies to test new communication methods to combat stigma associated with epilepsy

Research Support:

The CDC Epilepsy Program conducts epidemiologic/surveillance research and epilepsy self-management research through:

- Data collection and analysis using CDC surveillance systems and staff
- Grants and contracts to academic investigators;
- Cooperative Agreements with investigators affiliated with the CDC Prevention Research Centers (PRC) Program. The PRC Program directs a national network of academic research centers, each affiliated with either a school of public health or medical school that has a preventive medicine residency program.
- Collaboration with other CDC programs and US Department of Health and Human Services agencies

Examples of Recent Research Activities:

Intramural research underway:

- Analysis of 2010 NHIS data examining psychosocial health status including HRQOL (with NIH PROMIS HRQOL measures); social participation (with NCHS social participation measures), psychological distress (with Kessler-6) and duration of distress; and cognitive impairment, by epilepsy status
- Analysis of 2010 NHIS data examining select health behaviors, and access to care by epilepsy status
- Analysis of epilepsy-associated deaths in children in select states in collaboration with the National Center for Child Death Review
- Analysis of NCHS National Vital Statistics Systems Multiple Cause of Death files to examine possible SUDEP cases
- Analysis of CDC National Violent Death Reporting System (NVDRS) to identify suicide burden in people with epilepsy
- NCHS-led analysis of 2009-10 National Survey of Children with Special Health Care Needs data to examine characteristics and functional status of children with epilepsy and special health care needs
- Launch of Sudden Death in the Young Registry to examine sudden cardiac deaths and sudden unexpected death in epilepsy (SUDEP) (0-19 years).
- Analysis of Porter Novelli HealthStyles data to examine changes in attitudes toward epilepsy in the U.S. population

Extramural research underway:

Managing Epilepsy Well Network research:

- **Management Information & Decision Support Epilepsy Tool (MINDSET)**
University of Texas Health Sciences Center Houston is developing and testing a clinic-based epilepsy decision support system designed to enhance epilepsy self-management communication between patients and their provider during a regular clinic visit.
- **Home Based Self-management and Cognitive Training Changes Lives (HOBSCOTCH)**
Dartmouth College is developing and testing a telephone-based self-management program combined with use of a gaming device designed to address memory and attention problems among adults with epilepsy.
- **FOCUS on Epilepsy**
The University of Michigan is conducting a randomized controlled trial of a promising intervention designed to enhance self-management skills among both adults with epilepsy and a primary caregiver.
- **PACES/PACES-R (Rural) (Program for Active Consumer Engagement in Self-Management)**
The University of Washington is developing and testing two programs that are tailored for individuals' specific self-management needs (such as stress, mood, and memory concerns). PACES-R, which includes telephone delivery targeting rural-dwelling adults, is a modification of a program designed for urban adults with epilepsy (PACES).
- **Targeted Self-Management for Epilepsy and Mental Illness (TIME)**
This study, conducted by Case-Western Reserve University, involves development and testing of a self-management intervention for adults with epilepsy and serious, persistent mental illness (SMI) based on the adaptation of an intervention shown to be effective in adults with diabetes and SMI.

*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>

Epidemiologic research studies:

- **Risk Factors of Epilepsy Outcomes: Comorbidities in Populations with Epilepsy**
Medical University of South Carolina
The goal of this study is to examine the prevalence and patterns of common coexisting conditions among people with epilepsy, as well as the relation of these comorbidities with epilepsy outcomes, health care use and cost, and mortality. The study consists of a statewide prevalence study of comorbid conditions among people with epilepsy and a retrospective cohort study of a sample of people with epilepsy compared to a sample with selected other conditions.
- **The Incidence and Prognosis of Epilepsy in Harlem, New York City**
Columbia University
The purpose of this project is to assess early factors that affect outcomes in a 2-year follow-up study of new-onset cases of epilepsy in the population of Harlem and Northern Manhattan. This is a prospective cohort study in which newly diagnosed cases of epilepsy and unprovoked seizures will be ascertained through active surveillance of area hospitals and emergency departments.
- **Epidemiologic Follow-up Study of Newly Diagnosed Epilepsy Among the Elderly**
University of Arizona
This study is analyzing quantitative, administrative and qualitative data to describe the public health burden of epilepsy in people in southeastern Arizona aged 65 years or older with new onset seizures,

and to identify early factors that affect clinical outcomes and health care in this population. The effects of ethnicity and socioeconomic status will also be assessed.

- **Epidemiologic Research and Surveillance in Pediatric Epilepsy**

RTI International, Washington, District of Columbia

The purpose of this study is to describe the incidence and prevalence of epilepsy among children (aged 1 month to 18 years) in a racially and economically diverse population (District of Columbia); to assess use of health care, responsiveness of health systems, and obstacles to care among children with epilepsy and their families; and to characterize risk factors, outcomes and coexisting health conditions (comorbidities) related to prevalent and new-onset pediatric epilepsy. This is a prospective cohort study.

(For additional information, see http://www.cdc.gov/epilepsy/research_projects.htm.)

Resources Available:

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

Plans for the Future:

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

- Epidemiological studies of epilepsy in populations 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);
- Analysis of population data on epilepsy to examine epilepsy burden.
- 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 Name: 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 Focus Areas:
 1. Saving babies through birth defects prevention and research
 2. Understanding autism to help children live to the fullest
 3. Protecting people and preventing complications of blood disorders
 4. Improving the health of people with disabilities

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 disorders, 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:

- Missouri Autism and Developmental Disabilities Monitoring Network (MO ADDM) site project: The scope of the activity was to determine the prevalence of co-morbid epilepsy among 8 year old children identified with autism spectrum disorder (ASD) or cerebral palsy (CP). MO ADDM established collaborative relationships with all EEG laboratories that served the study area in 2002 and 2006. Abstractors were trained to abstract data from records with information about possible seizures/epilepsy, using a standard case definition for epilepsy. Information collected included demographics, EEG/MRI information, specific information about seizure type (including epilepsy syndromes), age at onset, etiology, medication history, and additional medical information. Clinical review by a pediatric neurologist determined case status. Results: For surveillance year 2002, 9.3% of children with ASD were confirmed to have epilepsy; for surveillance year 2006, 8.7% of children with ASD were confirmed to have epilepsy and 32.9% of children with CP cases were confirmed to have epilepsy. Conclusion: Identification of children with ASD and/or CP who have co-occurring epilepsy using ADDM methodology is feasible. The existing ADDM infrastructure can be used to routinely include epilepsy as a co-occurring condition in children with ASD and/or CP.
- Project to Learn about ADHD in Youth (PLAY): PLAY 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 is including 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.

- 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.
- NCBDDD/Division of Human Development and Disability collaborated with the National Center for Chronic Disease Prevention and Health Promotion in the evaluation of national survey data to describe unmet healthcare needs among children with neurological disorders, including epilepsy. These findings have been published.

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.
 - 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, 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.
- Health services research to improve services for those persons and families affected by epilepsy through collaboration with the University of South Carolina and the state of South Carolina; this study evaluates the health, well-being, and social participation of adolescents and young adults (aged 15-24 years) through linked datasets on social, economic, housing, education and employment services use. This robust data system could answer important questions on co-occurring conditions, ambulatory care, hospitalizations, and emergency department use during both childhood and adult years among persons with epilepsy. For example, NCBDDD has used this data system to show that despite the knowledge that a high prevalence of seizures/epilepsy occurs among persons with fragile X syndrome, care is not sufficient in the outpatient/primary care setting to prevent the higher cost and greater intensity of care associated with hospitalizations and emergency room visits due to epilepsy/seizures.
- Characterize risk factors for epilepsy co-occurring with autism spectrum disorders (ASD) by adding neuroimaging, EEG, and neurology evaluation results to data collection from selected study sites for the CDC-sponsored study, Study to Explore Early Development (SEED). SEED methods combine maternal interview for prenatal risk factors for ASD and other developmental disorders, neurocognitive examination of participants (aged 3-6 years), physical examination, and collection of blood samples for genetic and other biomarker testing, to evaluate genetic and environmental risk

factors for ASD. Collection of specific diagnostic testing results for epilepsy could expand the dimensions of risk factor analyses for epilepsy co-occurring with ASD.

- 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]).

Office of the Assistant Secretary for Health, U.S. Department of Health and Human Services OASH/HHS

Primary Representative: Wanda K. Jones, Dr.P.H., Principal Deputy Assistant Secretary for Health

Email: wanda.jones@hhs.gov

Mission: The Office of the Assistant Secretary for Health (OASH) strives to mobilize leadership in science and prevention for a healthier nation, by (1) creating better systems of prevention; (2) eliminating health disparities and promoting health equity; and (3) making *Healthy People* come alive for all Americans. OASH comprises 12 core public health offices — including the Office of the Surgeon General and the U.S. Public Health Service Commissioned Corps — as well as 10 regional health offices across the nation and 10 Presidential and Secretarial advisory committees.

HHS Working Group on the Epilepsies: In response to several queries to HHS early in the first term of the Obama Administration, Dr. Howard Koh, Assistant Secretary for Health, established a working group to provide a forum in which information about activities across the Department could be shared. The working group meets at least quarterly in person, and at other times as needed by phone. Group members also participate in monthly calls hosted by the Vision 20/20 group and the IOM, to follow up the IOM report.

HHS components participating in the group include the Administration for Community Living (ACL), the Centers for Disease Control and Prevention (CDC), the Centers for Medicare & Medicaid Services (CMS), the Food and Drug Administration (FDA), the Health Resources and Services Administration (HRSA), and the National Institutes of Health (NIH). In addition, several Staff Divisions in the Office of the Secretary participate—the offices of the Assistant Secretary for Health, the Assistant Secretary for Planning and Evaluation, and the Assistant Secretary for Public Affairs.

Activities and Topics of Interest: The HHS Working Group on the Epilepsies does not itself conduct research, and it comprises some HHS components whose mission is not research. (HHS' research agencies are represented on ICARE, so their activities are not presented here.) Three items are worth noting for this update:

- The Working Group is developing a paper that presents progress and early results from two years of renewed emphasis stimulated by the recommendations of the IOM report. We hope to submit it for publication this spring.
- CMS is exploring ways to use their demonstration authority, working with CDC (and perhaps HRSA and ACL) to explore various models of care that would improve quality and outcomes, and reduce cost. This would directly support one of the IOM recommendations that CMS and other partners “fund demonstration projects for epilepsy case ascertainment, health care and community services use and costs, and measures of quality of life for use in different data collection systems and for different specific objectives.” In addition, recent provisions supported by the Affordable Care Act, promising collaborative care programs, telehealth programs, and existing state authority allowing licensed practitioners to deliver care in non-clinical settings, all offer possibilities for involvement in a demonstration project to reduce the burden associated with epilepsy. Ideally, collaborative groups of epilepsy stakeholder organizations, healthcare providers, universities, and other interested parties would form around statewide demonstration projects that could be applied to epilepsy to improve health and decrease epilepsy burden.
- The Administration on Intellectual and Developmental Disabilities (AIDD) within the ACL funds University Centers of Excellence for Developmental Disabilities (UCEDDs);

<http://www.acl.gov/Programs/AIDD/Programs/UCEDD>), a nationwide network of centers and a national resource for addressing issues, finding solutions, and advancing research related to the needs of individuals with developmental disabilities and their families. UCEDDs serve as liaisons between universities and communities, working with people with disabilities, members of their families, state and local government agencies, and community providers in projects that provide training, technical assistance, service, research, and information sharing, with a focus on building the capacity of communities to sustain all their citizens. To implement their core functions, UCEDDs leverage organizational funding from AIDD to partner with other federal, state, and local resources. Among the 68 UCEDDs nationwide, many address epilepsy because of its co-occurrence with many causes of developmental disabilities.

The UCEDDs are members of the Association of University Centers on Disabilities (AUCD; <http://aucd.org>), a membership organization that also includes 43 Leadership Education in Neurodevelopmental Disabilities (LEND) Programs receiving core funding from the Maternal and Child Health Bureau (MCHB/HRSA) and 15 Intellectual and Developmental Disability Research Centers (IDDRC), receiving core funding from the Eunice Kennedy Shriver National Institute for Child Health and Development (NICHD/NIH). ACL hopes to have a representative at this ICARE meeting, and to participate in future meetings. They are a new, but critical partner, to the Department's efforts to address the impediments to quality and timely care.

For both the CMS and ACL efforts, engagement with ICARE should provide substantive opportunities to leverage existing assets and to apply research findings more quickly to improve care. These efforts might also present research opportunities with data and with the structural or systems changes they generate. ICARE updates are provided at HHS Working Group meetings, and it would appear that agencies are working much more collaboratively as a result of both of our coordinating groups.

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

Note: This report reflects information from the VA Epilepsy Centers of Excellence system of care. It was reviewed by Dr. Robert L. Ruff. It has not been reviewed by VA Leadership and should not be taken as representing or reflecting official opinion or policy of the Department of Veterans Affairs.

Primary Representative: Robert L. Ruff, MD, PhD, National Director, Neurology

Email: Robert.Ruff1@va.gov

Mission: The Veterans Health Administration (VHA) is to honor America's Veterans by providing exceptional health care that improves their health and well-being.

The VA Epilepsy Centers of Excellence 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 OEF-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

Types of Research Support or Other Research-Related Activities:

- 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 Foundation

- 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 VA ECoE recent or current epilepsy research activities:

The IOM report from the Committee on Gulf War and Health released a report on February 13, 2014 on Long-Term Effects of Blast Exposures. The report concluded that in other brain-injury mechanisms (nonblast TBI), there is sufficient evidence of an association between severe or moderate TBI and permanent neurologic disability including unprovoked seizures and that is plausible that severe or moderate blast TBI is similarly associated with permanent neurologic disability even though studies that specifically addressed blast TBI are lacking. The ECoE have been part of the VA group responding to the report and have written a draft concurring with these findings.

In press is a publication on the prevalence of epilepsy and its association with traumatic brain injury-including mild TBI- performed by Mary Jo Pugh. It is a population-based study of Veterans of the wars in Afghanistan and Iraq (OEF/OIF/OND) who receive VA care provide evidence for a possible link between blast associated *mild* TBI associated with epilepsy. The study found that the likelihood of epilepsy among those with severe, moderate and mild TBI were more likely to be diagnosed with epilepsy than those without documented TBI, with odds ranging from 4 for severe TBI to 1.3 for mild TBI. It also showed similar results from prior Veteran studies where Veterans with penetrating TBI were more likely by a factor of 19 to have epilepsy than similar Veterans without any TBI history.

- Pugh MJ, Orman JA, Jaramillo CA, Salinsky MC, Eapen BC, Towne AR, Amuan ME, Roman GC, McNamee SD, Kent TA, McMillan KK, Hamid H, Grafman JH. The prevalence of epilepsy and association with traumatic brain injury in Veterans of the Afghanistan and Iraq Wars. J Head Trauma Rehabil. In Press.

Topics of other recent activities:

- Pre- and Postsynaptic Consequences of Traumatic CNS Injury
- MRI studies to identify white matter tract lesions in patients with temporal lobe epilepsy, in comparison to normal volunteers, using T1 and diffusion tensor imaging
- Chronic Effects of Neurotrauma Consortium
- Neurochemistry of Epilepsy
- Epileptogenesis after traumatic brain injury
- Psychogenic Seizures in US Veterans
- Rapid anti-epileptic medication prior to arrival trial
- Restructuring Epilepsy Care: Organizational Dynamics and Quality: RECORD Quality
- The POEM study: Policy for Optimized Epilepsy Management
- Mechanisms of synaptic integration in central neurons
- Neurocircuitry of Depression in Temporal Lobe Epilepsy
- Longitudinal case-controlled cohort of OEF-OIF Veterans to comprehensively evaluate for the late effects of combat-related mTBI including evidence of neurodegeneration

Additional citations include, but are not limited to:

- Hamid H, Blackmon K, Cong X, Dziura J, Atlas LY, Vickrey BG, Berg AT, Bazil CW, Langfitt JT, Walczak TS, Sperling MR, Shinnar S, Devinsky O. Mood, anxiety, and incomplete seizure control affect quality of life after epilepsy surgery. *Neurology*. 2014 Jan 31. [Epub ahead of print]
- Hamid H, Fodeh SJ, Lizama HG, Czlupinski R, Pugh MJ, LaFrance Jr. WC, Brandt CA. Validating a natural language processing tool to exclude psychogenic nonepileptic seizures in electronic medical record-based epilepsy research. *Epilepsy & Behavior*. 2013 Dec;29(3):578-580.
- LaFrance WC Jr, Deluca M, Machan JT, Fava JL. Traumatic brain injury and psychogenic nonepileptic seizures yield worse outcomes. *Epilepsia*. 2013 Apr;54(4):718-25. doi: 10.1111/epi.12053.
- LaFrance WC Jr, Reuber M, Goldstein LH. Management of psychogenic nonepileptic seizures. *Epilepsia*. 2013 Mar;54 Suppl 1:53-67. doi: 10.1111/epi.12106.
- Pugh MJ, Finley EP, Copeland LA, Wang CP, Noel PH, Amuan ME, Parsons HM, Wells MA, Elizondo B, Pugh JA. Complex Comorbidity Clusters in OEF/OIF Veterans: The Polytrauma Clinical Triad and Beyond. *Med Care*. 2014 Feb;52(2):172-81. PMID: 24374417.
- Pugh MJ, Hesdorffer D, Wang CP, Amuan ME, Tabares JV, Finley EP, Cramer JA, Kanner AM, Bryan CJ. Temporal trends in new exposure to antiepileptic drug monotherapy and suicide-related behavior. *Neurology* 2013 Nov;81(22):1900-1906. PMID: 24174583.
- Ransom CB, Tao W, Wu Y, Richerson GB: Rapid regulation of tonic GABA currents in cultured hippocampal neurons. *Journal of Neurophysiology*, 109:803-812, 2013.
- Salinsky M, Evrard C, Storzbach D, Pugh MJ. Psychiatric comorbidity in veterans with psychogenic seizures. *Epilepsy Behav*. 2012; 25(3):345-349. PMID:23103308
- Tao W, Higgs M, Spain WJ, Ransom CB: Postsynaptic GABA_B receptors enhance GABA_A receptor function in dentate gyrus granule cells. *Journal of Neuroscience*, 33:3738-3743, 2013.

Resources Available:

- Basic Science Research Workgroup and Clinical Research Workgroup
- 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

Plans for Future Activities:

- Develop Patient Centered Outcomes Research Institute (PCORI) proposal from ECoE sites
- 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 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
- Investigate voltage-gated potassium channels in neocortical neurons
- Explore synaptic integration in neocortical neurons
- Identify targets for interventions to improve care based on findings from ongoing RECORD Quality project
- Determine whether mTBI case group differs from the non-TBI control group and the effects of single versus multiple mTBIs
- Measure ERPs in military TBI cases (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, characterize the neurocognitive mechanisms of impairments shown on cognitive performance tests.

- Epilepsy epidemiology & surveillance project
- Build collaborative research projects amongst ECoE basic scientists
- Funded Career Development Award 2 to investigate GAT1 function in epilepsy
- Expand use of EMU database and explore potential research opportunities
- Explore potential to collaborate with Integrated Neurology Project for quality/ efficacy research
- Preparation of Career Development Award 2 to examine social network of physicians on care provided to Veterans with PNES/ epilepsy

American Epilepsy Society (AES)

Primary Representative: Elson So, M.D., President

Email: eso@mayo.edu

Secondary Representative: Eileen M. Murray, MM, CAE, Executive Director

Email: emurray@aesnet.org

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

Topics of Interest: Topics represent the diversity of the AES membership and cover all aspects of epilepsy research: basic; translational (pharmacology, treatment development); clinical (neuropsychology, neurosurgery, nursing, psychiatric, clinical studies and clinical trials).

Types of research support: The AES supports research through scientific meetings, training grants, initiation grants, and dissemination of research findings.

- The AES Annual Meeting serves as the premiere venue for presentation of important findings through symposia, Investigator Workshops, Special Interest Groups, platform presentations and posters.
- Pre-doctoral and Post-doctoral fellowships
- Clinical Research Fellowship
- Travel grants
- Research Training
- Mentoring activities
- Infrastructure grants
- Seed grants
- Support of Workshops and research conferences
- *Epilepsy Currents* – the Journal of the American Epilepsy Society

Examples of Recent Activities:

A. Increased 2012 and 2013 Research Funding – AES substantially increased its share of joint research funding with Epilepsy Foundation. This increased commitment by AES aims to continue providing young investigators, especially those in training, with the opportunity to enter or stay in the field of epilepsy research. AES funded 7 postdoctoral and 6 pre-doctoral and one clinical training fellowship in the last fiscal year. In this fiscal year AES is funding 7 postdoctoral and four pre-doctoral basic research fellowships along with two clinical training fellowships and two basic research grants.

B. New Seed Grants – Seed grants will promote collaboration between laboratories of established investigators, when the collaboration has great potential for new findings or enhanced methodologies in epilepsy research and funding for the collaboration is otherwise unavailable. Two grants have already been given.

C. Q-Pulse Survey – AES has developed a survey tool that is designed to facilitate quick data collection from a representative sampling of epilepsy specialists on current clinical practice. The first results, designed to identify perceptions of epilepsy case mix, and specifically cases of mesial temporal lobe epilepsy, were published in the most recent issue of *Epilepsy Currents*. The survey tool can also be used in the preparation of a research project, such as in identifying the number of

potential research subjects at different geographical locations, or the availability of certain equipment or technology for basic science research.

D. Translational Research Initiatives – AES holds a number of symposia and workshops on translational research in epilepsy, and incorporate translation perspectives in many educational activities. AES also participated in the development of the recently published international guidelines on translational research. A Translational Research Symposium was held at the 2013 AES Annual Meeting as an Epilepsy Benchmark session.

E. AES Epilepsy Benchmark Committee –was newly formed within the AES to more formally integrate the Benchmark Stewards into AES. The intent was to enable broader participation by AES members and enable the Stewards to initiate and take ownership of a wider range of activities. This should also facilitate the use of the Benchmarks more generally, such as by other non-governmental partners. AES will continue to collaborate with NINDS on monitoring research progress and participate in the next Epilepsy Research Conference.

F. Infrastructure Funding – AES co-funds an infrastructure grant with the Epilepsy Foundation. These support establishment of national or international networks to do collaborative research in epilepsy.

G. Research Initiative Funding –AES provides initial funding for innovative, collaborative research in all disciplines (clinical, social, basic science, etc.) associated with the epilepsy field.

H. Research & Training Workshops – AES provides funding for targeted workshops intended for broad-based, national clinical or scientific audiences and on specific collaborative consensus or review topics in neuroscience that are novel and creative

Resources Available:

- AES members for study sessions, Professional Advisory Boards, etc.
- Resources in Epilepsy Research website
- AES Annual Meeting, including access to post-meeting online and published content
- Partner with the Epilepsy Foundation and American Academy of Neurology
- Coordination of Vision 20-20 activities
- A sponsor of the IOM Report on Epilepsy
- Organizer for jointly developed Partners in Mortality in Epilepsy Conference- post-conference materials available on our website.
- Self-Assessment Exam and study guide for neurologists taking recertification exams.

Priorities and Plans for Future:

- Work toward identifying opportunities for increased coordination amongst the epilepsy research community to make more effective use of limited dollars
- Encourage young basic and clinical science researchers to enter and remain in the field of epilepsy
- Address the issues and gaps raised in the IOM report. Continue to form collaborations with other organizations to accomplish the recommendations.

The NINDS/AES Benchmark Stewards Committee (a.k.a. the Benchmark Stewards)

Primary Representative: Ray Dingleline (Committee Vice-Chair, Emory University) and alternate Dan Lowenstein (Committee Co-Chair, UCSF)

Email: rdingle@emory.edu

Mission: The NINDS/AES Benchmark Stewards Committee is comprised of individuals nominated from the membership of the American Epilepsy Society (AES) who agree to assist the community by regularly reporting on progress made in the Epilepsy Research Benchmarks. The Benchmarks are priorities for research toward clinically meaningful advances in understanding and treating the epilepsies. The Benchmark Stewards are also charged with providing input into periodic revisions of the Benchmarks made in conjunction with Curing the Epilepsies Conferences, held approximately every six years. The latest Conference was held in April 2013 and resulted in the current 2014 Benchmarks (see below, and appended). The Stewards became an official NINDS/AES Committee in December 2013, and will now follow the established committee procedures of the AES.

- The 2014 Epilepsy Research Benchmarks are found at <http://www.ninds.nih.gov/research/epilepsyweb/2014benchmarks.htm>

The main topic areas of the Benchmarks are:

- Understand the causes of the epilepsies and epilepsy-related neurologic, psychiatric, and somatic conditions.
- Prevent epilepsy and its progression.
- Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.
- Limit or prevent adverse consequences of seizures and their treatment across the lifespan.

Examples of Recent activities:

The Benchmark Stewards prepared a progress update on the advances made in the 2007 Benchmark areas in Fall 2012 (found here: http://www.ninds.nih.gov/research/epilepsyweb/benchmarks_2007-2012progress.pdf). The Stewards also provided key input into the topic areas that became the main sessions at the Curing the Epilepsies Conference in April 2013. Several Stewards also played important roles in the conduct of the Conference itself, serving as discussion moderators for sessions and capturing input that was incorporated into the capstone session on new directions for the 2014 Benchmarks. The Stewards also reviewed the final set of 2014 Benchmarks.

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 research activities:

The Benchmark Stewards group plans to publish a mid-term progress update on the 2014 Benchmarks in the mid-2016 timeframe, and will compile another progress update in late 2018 in preparation for the next Curing the Epilepsies Conference in 2019.

2014 AES/NINDS Epilepsy Research Benchmarks Stewards

Chair: Dan Lowenstein Vice-Chair: Ray Dingledine

NINDS Co-Chair: Brandy Fureman

AES staff: Margaret Jacobs

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

Co-Chairs: Heather Mefford and Rochelle Caplan

Madison Berl	Annapurna Poduri
Bernard Chang	Andrey Mazarati
Jack Lin	

II. Prevent epilepsy and its progression.

Co-Chairs: Aristeia Galanopoulou and Michael Wong

Devin Binder	Avtar Roopra
Adam Hartman	Richard Staba
Elizabeth Powell	

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

Co-Chairs: Dennis Dlugos and Gregory Worrell

Chad Carlson	Tobias Loddenkemper
Kathryn Davis	Michael Rogawski
Jacqueline French	William Stacey
Patrice Jackson-	Sridhar Sunderam
Ayotunde	Jerzy Szaflarski
Andres Kanner	

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

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 is a nonprofit organization dedicated to finding a cure for epilepsy by raising funds for research and by increasing awareness of the prevalence and devastation of this disease.

Major Topics of Interest:

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

Types of Research Support:

- Research grants for basic, translational, and clinical research
- Young investigator travel awards to Gordon Research Conference
- Conference and workshop support
- Sponsored seminar series

Examples of Recent Activities:

- Current grant mechanisms: Challenge Award, SUDEP Award, Prevention of Acquired Epilepsies Award, Pediatric Epilepsies 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>
- 2014 Conference Support: When Epilepsy is Catastrophic: Molecular Causes and Their Consequences (symposium at Baylor, April 2014), Gordon Research Conference (August 2014), PAME: Partners Against Mortality in Epilepsy Conference (June 2014), 1st Biennial Parent and Professional Symposium on Dravet Syndrome and Related Epilepsies (June 2014), San Servolo Epilepsy Summer Course (July 2014)
- CURE Frontiers in Research Seminar Series – spreading the word about cutting edge epilepsy research at institutions throughout the US and Canada:
<http://www.cureepilepsy.org/seminarseries/>
- HHMI Medical Fellows partner – support medical students to take a year away from their studies to pursue epilepsy research

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 Board

Epilepsy Foundation (EF)

Primary Representative: Janice M. Buelow, RN, PHD, FAAN, Vice President, Programs and Research
Email: jbuelow@efa.org

Mission: The mission of the Epilepsy Foundation is to stop seizures and SUDEP, find a cure and overcome the challenges created by epilepsy through efforts including education, advocacy and research to accelerate ideas into therapies.

Major Topics of Interest:

- Training grants and fellowships in basic, clinical and behavioral science.
- Targeted research initiatives such as morbidity and mortality, veterans with non-epileptic seizures, and development of focal seizures in the elderly.
- Development of new therapies for epilepsy, accelerating the advancement of research from the laboratory to the patient.

Types of Research Support:

The Foundation dedicates its research efforts toward 1) bringing new clinicians into the field; 2) funding new therapies that will bring change in treatment and management for people with epilepsy in a timeframe that matters; 3) encouraging exploration of key issues such as self-management, cognitive issues and researching the impact of public awareness; 4) and bringing attention to exciting ideas and therapies through our Seal of Innovation award.

- **Research and Training Fellowships:** The Epilepsy Foundation offers a series of training grants and fellowships in basic, clinical and behavioral science to scientists at the start of their careers.
- **Targeted Research Initiatives:** areas that are underfunded or of growing importance.
- **Infrastructure Grants:** co-funded with AES, these support establishment of national or international networks to do collaborative research in epilepsy.
- **Epilepsy Foundation - New Therapy Commercialization Grants Program** is to drive the development of new therapies for epilepsy, accelerating the advancement of research from the laboratory to the patient. The Foundation funds innovative senior level research projects led by the nation's leading scientists with the potential to discover new treatment options and ultimately a cure.
- **The Epilepsy Innovation Seal of Excellence awards** are, like the New Therapy Commercialization Grants (NTCG) program above, designed to accelerate the advancement of research from the laboratory to the patient. SEALS are provided to academic and commercial groups worldwide. The program seeks to advance the development of new therapies including but not limited to medicines, biologics or devices.
- **Advocacy work** to support federal funding for epilepsy research.

Examples of Recent Activities:

- **The Rare Epilepsy Network (REN)** -- funded as part of a PCORI grant to establish a Patient-Powered Research Network to facilitate research on the rare epilepsies. The REN will enable collection of specific information related to each of the rare epilepsies, as well as common data across all of these disorders. Data from electronic medical records (EMR) will be included.

From PCORnet website (<http://pcornet.org/patient-powered-research-networks/pprn17-epilepsy-foundation/>): *The Rare Epilepsy Network (REN) PPRN is an initiative created by and for patients with catastrophic rare epilepsies. The REN's goal for this proposal is to build a patient-centered and -*

driven database designed to provide the patients and their families an opportunity to participate in research that will improve lives and quality of care for people with rare epilepsies. Our PPRN is led by the Epilepsy Foundation (EF), a patient advocacy organization dedicated to the welfare of the almost 3 million people with epilepsy living in the United States. EF will lead this grant through our Principal Investigator, Dr. Janice M. Buelow. Dr. Buelow is director for all programs and research at EF and interfaces with all EF affiliates in the United States and with each of the patient advocacy organizations that compose the REN. Network organization: Each of seven partnering organizations is represented by a caregiver who has a loved one with the disorder. They are joined by two co-investigators/epidemiologists, Drs. Hesdorffer (Columbia University) and Kroner. Partnering Patient Organizations: Aicardi Syndrome, Dravet Syndrome Foundation, Dup15q Alliance, Epilepsy Foundation, Hypothalamic Hamartoma, Lennox-Gastaut Syndrome Foundation, Phelan-McDermid Syndrome Foundation, Tuberous Sclerosis Alliance

- Supporter of Partners Against Mortality in Epilepsy (PAME) Conference – June 19-22, 2014, Minneapolis. This is the second PAME conference devoted predominantly to Sudden Unexpected Death In Epilepsy (SUDEP), where clinical and basic science researchers and patient/family members will come together to understand and support each other.
- Organizer of the 2014 Epilepsy Pipeline Conference – June 5 -7, 2014 in San Francisco. <http://www.epilepsy.com/accelerating-new-therapies/2014-epilepsy-pipeline-conference-program>. Showcasing the most promising epilepsy therapies from healthcare companies dedicated to pioneering and advancing drugs, biologics, technologies and devices for epilepsy and seizures.
- 2014 Shark Tank Competition <http://www.epilepsy.com/make-difference/get-involved/special-events/2014-epilepsy-pipeline-conference/shark-tank-competition>

Resources Available:

- Epilepsy.com website
- Business Advisory Board, Scientific Advisory Board, Professional Advisory Board
- Annual “Walk” for Epilepsy
- Partner with American Epilepsy Society
- Epilepsy Resource Center: Ask the Epilepsy Resource Center and J Kiffin Penry Patient Travel Assistance Fund
- Epilepsy and Seizures 24/7 helpline
- eCommunities
- Studio E: The Epilepsy Art Therapy Program
- Epilepsy Legal Defense Fund
- 47 Affiliate’s; 1 Chapter
- Epilepsy Therapy Project/Epilepsy Foundation

Priorities and Plans for the Future:

- Continue to evaluate research portfolio and goals for unmet needs and to improve quality and amount of researchers in the field of epilepsy
- Continue efforts toward increased federal research funding
- Protection of people in clinical trials
- Access to all clinical trials and research outcomes funded by federal government
- Continue coordinating research agenda with Vision 20/20 organizations and maximizing research dollars
- Furthering NINDS Epilepsy Benchmarks
- Incorporating IOM Report recommendations

The Epilepsy Study Consortium (TESC)

Primary Representative: Jacqueline French, MD, Professor of Neurology, NYU School of Medicine, President, TESC

Email: Jacqueline.french@nyumc.org

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

Topics of Interest: Clinical trials, Clinical trial methodology, Protocol development, Novel Therapeutics

Types of Research Support:

We have 25 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.

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

Examples of recent activities:

- A. ASERT Study "Suicidal ideation and behavior screening in intractable focal epilepsy eligible for drug trials"

Three suicidal ideation and suicidal behavior instruments were used to assess the prevalence of lifetime and recent suicidal ideation and suicidal behavior in patients with frequent treatment-resistant focal seizures who would be eligible for randomized clinical trials. This was done to determine which instrument was optimal for use in epilepsy.

- B. 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

C. Photosensitivity Study – “Effects of Marketed AEDs and placebo in the Human Photosensitivity Screening Protocol”

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.

Resources Available: Additional information can be found on the TESC website:

www.epilepsyconsortium.org

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

Patient-Centered Outcomes Research Institute (PCORI)

Primary Representative: Sarita Wahba

Email: swahba@pcori.org

Mission: The Patient-Centered Outcomes Research Institute (PCORI) helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader healthcare community.

Major topics of interest in epilepsy research:

PCORI funds research proposals that score well against the 5 PCORI merit review criteria:

- Impact of the condition on the health of individuals and populations
- Potential for the study to improve healthcare and outcomes
- Technical merit
- Patient-centeredness
- Patient and stakeholder engagement

Types of research support or other research-related activities:

- Patient-centered comparative effectiveness research
- Building networks to improve the efficiency with which CER is conducted

Examples of Recent Activities:

Rare Epilepsy Network PPRN, PI Jan Buelow, Epilepsy Foundation

The Rare Epilepsy Network (REN) PPRN is an initiative created by and for patients with catastrophic rare epilepsies. The REN's goal for this proposal is to build a patient-centered and -driven database designed to provide the patients and their families an opportunity to participate in research that will improve lives and quality of care for people with rare epilepsies. Our PPRN is led by the Epilepsy Foundation (EF), a patient advocacy organization dedicated to the welfare of the almost 3 million people with epilepsy living in the United States. EF will lead this grant through our Principal Investigator, Dr. Janice M. Buelow. Dr. Buelow is director for all programs and research at EF and interfaces with all EF affiliates in the United States and with each of the patient advocacy organizations that compose the REN. Network organization: Each of seven partnering organizations is represented by a caregiver who has a loved one with the disorder. They are joined by two co-investigators/epidemiologists, Drs. Hesdorffer (Columbia University) and Kroner. Partnering Patient Organizations: Aicardi Syndrome, Dravet Syndrome Foundation, Dup15q Alliance, Epilepsy Foundation, Hypothalamic Hamartoma, Lennox-Gastaut Syndrome Foundation, Phelan-McDermid Syndrome Foundation, Tuberous Sclerosis Alliance

Cognitive AED Outcomes in Pediatric Localization Related Epilepsy (COPE), PI David Loring, Emory

Goal: Determine changes in attention and other cognitive abilities associated with the three medications often used to treat the most common form of pediatric epilepsy and communicate the results to help parents and clinicians select the most appropriate therapy

Resources available:

- Broad PCORI Funding Announcements
- Pragmatic Clinical Trials

Future plans: PCORI has 4 funding cycles per year. We invite epilepsy researchers to apply for PCORI funding during any of our funding cycles. For more information about the application process, visit us at pcori.org/apply.

Tuberous Sclerosis Alliance (TS Alliance)

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

Steven L. Roberds, PhD, Chief Scientific Officer

Email: krosbeck@tsalliance.org; sroberds@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: The TS Alliance's major topics of interest in epilepsy include understanding mechanisms of epileptogenesis in TSC, preventing infantile spasms, biomarkers to help optimize and personalize drug treatment for epilepsies in TSC.

Types of Research Support:

- 1) The TS Alliance Research Grants Program supports basic research by postdoctoral scientists and studies that accelerate the translation of basic research findings into improvements in quality of life for those affected by TSC in such areas as:
 - Development of biomarkers to enable more robust and efficient clinical studies,
 - Methods of eliminating tumors rather than only shrinking or stabilizing tumor growth, or
 - Neurological, cognitive, or behavioral manifestations of TSC.
- 2) Six research webinars on various topics such as "New Recommendations from the TSC Clinical Conference/Update on Diagnostic Criteria for TSC", "Vigabatrin-associated visual field loss" and "Sudden, unexpected death from epilepsy" have been presented in the past year.

Examples of Research Activities:

The TS Alliance is one of ten organizations representing rare disorders that frequently involve epilepsy to receive funding from the Epilepsy Foundation through a contract from Patient-Centered Outcomes Research Institute (PCORI). The Epilepsy Foundation-led team will use the PCORI funds to create a Rare Epilepsy Network (REN) Registry to increase patient/caregiver engagement in research and health care decisions.

The TSC Clinical Research Network is conducting two clinical studies at five TSC Clinics to find biomarkers or signals that identify which newly diagnosed infants with TSC are at highest risk of developing infantile spasms by age two or signs of autism by age three.

Resources Available:

- TS Alliance's October 15, 2013 Research Webinar, "The Promise of Research on Seizures in TSC," https://www.youtube.com/watch?v=2x_B981M69c
- TS Alliance's January 27, 2014 Research Webinar entitled "Vigabatrin Associated Visual Field Loss (VAVFL): What You Need to Know," presented by Darcy Krueger, MD, PhD, Cincinnati Children's Hospital Medical Center. <https://www.youtube.com/watch?v=V4JmWdhVqGs>
- TS Alliance's White Paper, *Vigabatrin Associated Visual Field Loss: What You Need to Know*
- <http://tsalliance.org/documents/Vigabatrin%20Associated%20Visual%20Field%20Loss%20White%20Paper.pdf>

Priorities and Plans for Future: Interventional clinical trial in children with TSC, utilizing biomarkers that predict future development of epilepsy, with an effective and safe mTOR inhibitor dosing regimen or with vigabatrin.

Vision 20/20 (see attached list for members)

Primary Representative: Joan Austin, PhD, RN, Interim Chair, Vision 20-20

Email: joausti@iu.edu

Mission: The overall mission of Vision 20-20 is to improve the lives of patients with epilepsy and their families. Vision 20-20 provides a forum for epilepsy voluntary, professional and governmental organizations to come together to explore ways of identifying and pursuing common goals. Through coordination and collaboration resources can be used more effectively and projects can be accomplished more efficiently than if the groups functioned separately and autonomously. There are currently 35 organizations that are members in Vision 20-20.

Topics of Interest: Many of the participating organizations support research programs that reflect the missions and goals of their individual organizations. Topics include SUDEP, genetics, infantile spasms, TBI, stroke, therapeutic development, channelopathies, infection, comorbidities, and epidemiology.

Types of research support:

- Basic, clinical and translational research
- Incidence and prevalence
- Pre-doc, Post-doc and clinical fellowships
- Travel awards
- Seed/pilot grants
- Infrastructure awards
- Workshops
- Targeted and investigator-initiated research
- Registries

Examples of Recent Activities:

- A. Resources in Epilepsy Research <http://epilepsyresearchresource.org> -- site is maintained by AES and designed to help match researchers with the proper funding opportunities. This online database is a comprehensive listing of initiatives, application instructions and an inventory of currently-funded research from participating Vision 20-20 organizations (currently being revised and updated).
- B. IOM Report Implementation – monthly calls to share activities related to the report, including surveillance, access to care
- C. HERO (Human Epilepsy Research Opportunity) Website – aim is to Increase patient participation in clinical research studies by explaining importance of the studies and linking to available trials.
- D. The Rare Epilepsy Network (REN) -- funded as part of a PCORI grant to establish a Patient-Powered Research Network to facilitate research on the rare epilepsies. The REN will enable collection of specific information related to each of the rare epilepsies, as well as common data across all of these disorders. Data from electronic medical records (EMR) will be included.
- E. Vision 20-20 Special Interest Group – “Non-Profit Resources for Epilepsy Research: What We Don’t Know That We Don’t Know About the Availability of Epilepsy Research Resources”. The purpose of this SIG is to generate focused two-way discussion between non-profit affiliates of AES and basic and clinical researchers attending the AES annual meeting. The intent is to educate researchers on how non-profits set their priorities and fund research or make other resources available and to educate non-profit leaders on what else they could do to support basic and clinical researchers in the epilepsies.

- F. Partners Against Mortality in Epilepsy (PAME) Conference – June 19-22, 2014, Minneapolis. This is the second PAME conference devoted predominantly to Sudden Unexpected Death In Epilepsy (SUDEP), where clinical and basic science researchers and patient/family members will come together to understand and support each other.

Resources Available: Resources in Epilepsy Research (see above), Vision 20-20 SIG (see above)

Priorities and Plans for Future:

- In addition to updating the RER emphasis this year will be on enhancing opportunities for research collaboration and coordination amongst the Vision 20-20 organizations. This will include exploring avenues for co-funding, common applications, and joint review committees.
- Continuing to implement recommendations of the IOM report, with an emphasis on surveillance, data integration and prevention.

Vision 20-20 Participant Organizations

March 1, 2014

Non-profit/Voluntary:

Aicardi Syndrome Foundation	www.aicardisyndrome.org
Anita Kaufman Foundation	www.akfus.org
Brain Recovery Project	www.brainrecoveryproject.org
Charlie Foundation	www.charliefoundation.org
Citizens United for Research in Epilepsy (CURE)	www.cureepilepsy.org
Danny Did Foundation	www.dannydid.org
Dravet.org	www.dravet.org
Dravet Syndrome Foundation	www.dravetfoundation.org
Dup 15q Alliance	www.dup15q.org
Epilepsy Foundation (EF)	www.epilepsyfoundation.org
Epilepsy Therapy Project (ETP)	
Epilepsy.com:	
Finding A Cure Against Epilepsy and Seizures (FACES)	www.faces.med.nyu.edu
Hemispherectomy Foundation	www.hemifoundation.org
HHV-6 Foundation	www.hhv-6foundation.org
Hope for Harper	www.hope4harper.com
Hope for Hypothalamic Hamartomas (HH)	www.hopeforhh.org
International Foundation for CDKL5 Research	www.CDKL5.com
Intractable Childhood Epilepsy (ICE) Alliance	www.ice-epilepsy.org
Lennox-Gastaut Syndrome (LGS) Foundation	www.lgsfoundation.org
My Epilepsy Story	www.myepilepsystory.org
PCDH19 Alliance	www.pcdh19info.org
Phelen-McDermid Syndrome Foundation (PMSF)	www.22q13.org
Physician-Parent-Caregivers (PPC)	www.physicianparent.org
Polymicrogyria (PMG) Awareness Organization, Inc.	www.pmgawareness.org
Preventing Teen Tragedy (PTT)	www.preventingteentragedy.org
RE Children's Project	www.rechildrens.org
Ring14 USA Outreach, Inc.	www.ring14usa.org
SUDEP Aware	www.sudepaware.org
Tuberous Sclerosis Alliance	www.tsalliance.org

Professional:

American Clinical Neurophysiology Society (ACNS)	www.acns.org
American Epilepsy Society (AES):	www.aesnet.org
International League Against Epilepsy (ILAE)	www.ilae.org
National Association of Epilepsy Centers (NAEC)	www.naec-epilepsy.org

Governmental:

Center for Disease Control and Prevention (CDC):	www.cdc.gov
Health Resources & Services Administration (HRSA)	www.hrsa.gov
National Institute of Neurological Disorders and Stroke (NINDS)	www.ninds.nih.gov
Veterans Administration (VA)	
Epilepsy Centers of Excellence	www.epilepsy.va.gov

For profit:

Seizure Tracker	www.seizuretracker.com
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2014 NINDS Benchmarks for Epilepsy Research

On April 17-19, 2013, NINDS hosted *Curing the Epilepsies 2013: Pathways Forward*, the third in a series of *Curing the Epilepsies* conferences held in partnership with epilepsy advocacy and professional organizations to assess progress in epilepsy research and help set an agenda for future years. As an important outcome, these conferences have led to the development of *Benchmarks for Epilepsy Research*, which reflect priorities for research toward clinically meaningful advances in understanding and treating the epilepsies. Following this tradition, and with input received during and prior to the April 2013 conference, NINDS has developed 2014 Benchmarks for Epilepsy Research as a framework for focusing research and benchmarking progress over the next five to ten years. Responsibility for achieving goals highlighted by the Benchmarks is shared by all members of the broad epilepsy community. For example, NINDS looks to them to inform plans for research investments; investigators may pursue questions aligned with the Benchmarks; and other governmental and nongovernmental organizations may also identify opportunities to contribute. Since their initial development in 2000, the Benchmarks have helped to galvanize the research community around important goals, such as preventing epileptogenesis, addressing aspects of epilepsy beyond seizures, and confronting the challenge of SUDEP – all of which are now vibrant areas of investigation. NINDS looks forward to working with the community to achieve further success in the coming years.

Preamble

The 2014 Benchmarks for Epilepsy Research are organized into key research goals in four areas in which significant progress should be likely over the next five to ten years. While advances may arise from many different research directions and may not be predictable, these broad goals are intended to serve as a shared framework for focusing the community's efforts and benchmarking important advances in the field as they are achieved.

Several themes emerged during discussions to develop the 2014 Benchmarks. First, the epilepsies are a spectrum of rare and more common disorders that vary in cause and disease course, and this heterogeneity represents both opportunities and challenges for epilepsy research. Distinct forms of epilepsy may ultimately require unique approaches to treatment and prevention. It is also possible, however, that individual epilepsy syndromes with known causes or other well-defined features will serve as gateways for understanding mechanisms with broader relevance to other epilepsies. Either way, the broad range of both causes and clinical features associated with the epilepsies suggests that knowledge and expertise in medical disciplines outside the traditional boundaries of neurology, such as psychiatry, immunology, cancer biology, cardiology, and others, will be critical. As a second theme, there is growing appreciation of a spectrum of conditions beyond seizures that reduce quality of life for people with epilepsy, including cognitive impairment, neurodevelopmental, and intellectual disabilities; psychiatric and behavioral disorders; stigma and other psychosocial issues; and effects on sleep, bones, and endocrine, reproductive, and other body systems. These conditions, often called comorbidities of epilepsy, have complex relationships with the underlying causes of epilepsy, ongoing seizures and other pathological network activity, and the effects of seizure treatments. To better reflect this complexity, the 2014 Benchmarks refer instead to epilepsy-related conditions and consequences, within a revised organization that encourages the integration of these topics into research on the epilepsies as a whole. In addition, the 2014 Benchmarks also reflect recognition of a range of factors specific to certain populations that should be considered in understanding the development and treatment of epilepsy and related conditions and consequences, including issues relevant to children, women, the elderly, and other groups.

Across all areas of the Benchmarks, progress will depend on continued advances in research tools and methods and their application to epilepsy research, particularly as new and emerging research technologies provide unprecedented capabilities in brain imaging, electrophysiology, and genomics and other systems biology approaches. Like other biomedical fields, epilepsy research is accumulating vast amounts of data, and opportunities for capturing clinical data at the point of care are also increasing. Embracing a culture of data sharing, collaboration, and integration across scales and approaches may best enable the epilepsy community to capitalize on these resources. Efforts to develop, validate, and disseminate novel approaches to analyzing large datasets, including genomic data and high-density brain activity monitoring, will also be essential. In addition, although many useful animal models exist for epilepsy research, important opportunities exist for further development of model systems that more closely reflect the etiologies and clinical features of human epilepsies. Translational experiments in preclinical models that are [rigorously designed and conducted, and transparently reported to the community](#), will help to accelerate the pace of therapy development. Independent replication to determine the robustness of preclinical findings is likely to aid the successful translation of interventions to prevent epileptogenesis, modify disease, control seizures, or address epilepsy-related conditions and consequences beyond seizures.

As a final note, while the scope of the Benchmarks broadly encompasses many areas of biomedical research on the epilepsies, NINDS recognizes that important advances may also come from areas not explicitly highlighted. Moreover, focusing on the Benchmarks and biomedical research alone will not be sufficient to ensure better outcomes and improved quality of life for people with epilepsy. A [report from the Institute of Medicine](#) recently established recommendations and priorities that address public health aspects of the epilepsies beyond biomedical research, including issues related to surveillance and population research, measures for and access to high-quality care, patient and health care provider education, and public awareness. Together, the Benchmarks and the IOM report serve as complementary guides for the efforts of diverse stakeholders.

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.