ICARE: Interagency Collaborative to Advance Research in Epilepsy
2015 Member Reports

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National Institute of Neurological Disorders and Stroke (NINDS)

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

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

- Basic mechanisms: NINDS supports studies on causes of the epilepsies, including genetics, infection, injury, metabolism, and structural defects. Basic mechanisms of epileptogenesis and ictogenesis are also major areas of study. Additional projects are focused on better understanding causes of co-occurring conditions and their relationship to epilepsy and seizures.
- Translational efforts: NINDS supports several exploratory R21 awards to develop or better characterize new models of epilepsy for therapeutic development, optimize candidate therapeutics, or otherwise prepare for a translational development U01 award. Several U01 awards related to epilepsy have also been funded in recent years, including device and biologics development efforts. In August of 2014, The NINDS Office of Translational Research (OTR) issued revised funding programs for investigators interested in translational research. These include Innovation Grants to Nurture Initial Translational Efforts (IGNITE), which has replaced previous translational R21 awards, and the NINDS Cooperative Research to Enable and Advance Translational Enterprises (CREATE) program for biologics and devices, which has replaced the previous U01 program. Additional information and a decision tree to help guide investigators to the appropriate funding opportunity can be found on the NINDS OTR homepage here http://www.ninds.nih.gov/funding/areas/translational_research/index.htm

  The 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. A review of the ASP was just completed with a final report to be released this spring.

- Clinical studies and trials: NINDS supports a number of observational clinical studies to evaluate the development of epilepsy in those at risk, to better localize the seizure onset zone and evaluate surgical risks and prognosis, to evaluate the effects of AED treatment on pregnant women and on the developing brain, and to assess the outcomes of children and adolescents with epilepsy over the long-term. NINDS is currently supporting a clinical trial to determine the best anticonvulsant for individuals with status epilepticus who have failed first line therapy. In recent years, NINDS has supported clinical trials testing new surgical approaches, best medical treatment of childhood absence epilepsy, best treatment of neurocysticercosis (a parasitic infection of the brain that causes epilepsy), and best treatment of status epilepticus by emergency medical services personnel.

Types of research support:

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

Examples of Recent Activities:

- Epi4K Gene Discovery in Epilepsy Center Without Walls(CWoW) http://www.epgp.org/epi4k/
- Sudden Death in the Young Registry (SDY) - http://www.nih.gov/news/health/oct2013/nhlbi-24.htm
- Center for SUDEP Research (CSR) - http://csr.case.edu/index.php/Main_Page
- Crowdsourced Seizure Detection and Prediction Challenge (in partnership with AES and EF) - http://www.ninds.nih.gov/news_and_events/news_articles/pressrelease_epilepsy_challenge_12162014.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://neuroscienceblueprint.nih.gov/index.htm
- International Epilepsy Electrophysiology Portal https://www.ieeg.org/
- Neurological Emergencies Treatment Trials (NETT) network: http://nett.umich.edu/nett/welcome
- NIH Stroke Trials Network: http://www.ninds.nih.gov/research/clinical_research/NINDS_stroke_trials_network.htm
- NeuroNEXT Phase II/Biomarker network: http://www.ninds.nih.gov/news_and_events/proceedings/20101217-NEXT.htm http://www.neuronext.org/
- Federal Interagency Traumatic Brain Injury Research Informatics System (FITBIR): http://fitbir.nih.gov/
- NINDS Office of Clinical Research website resources: http://www.ninds.nih.gov/research/clinical_research/index.htm
- NINDS Office of Translational Research website resources: http://www.ninds.nih.gov/funding/areas/translational_research/

Priorities and/or Plans for Future:

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

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-excitable 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: NIAAA has no active grants studying epilepsy. However, NIAAA is funding training and research grants investigating mechanisms and management of alcohol use-related (particularly alcohol withdrawal-induced) seizures. These include: Hippocamppal neurotoxicity induced by ethanol withdrawal; Mechanisms of Alcohol Withdrawal; Neurosteroid Modulation of Ethanol Withdrawal Severity; Mechanisms of Alcohol Withdrawal Seizures: Role of

L-type Ca2+ Channels; Alcohol withdrawal and tonic inhibition in the thalamus; An optogenetic investigation of CNS sensitization following alcohol withdrawal.

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.

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 seizures
- Congenital brain malformations and other structural birth defects that impact intellectual function

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.

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. An additional contract was awarded in FY2014 to increase the acquisition of tissues with an emphasis on pediatric developmental disorders, and a data coordination contract was awarded to create a common informatics platform.

Priorities and/or future research activities:

- Intellectual and Developmental Disorders, including common and rare genetic, metabolic, and mitochondrial diseases 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

National Institute of Nursing Research (NINR)

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

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

CDC Epilepsy Program
Centers for Disease Control and Prevention (CDC)
National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)
Arthritis, Epilepsy and Well-Being Branch (AEWB)
Epilepsy Program

Primary Representative: Niu Tian, MD, PhD, Medical Officer
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Mission: CDC works 24/7 to protect America from health, safety and security threats, both foreign and in the U.S. Whether diseases start at home or abroad, are chronic or acute, curable or preventable, human error or deliberate attack, CDC fights disease and supports communities and citizens to do the same. To accomplish our mission, CDC conducts critical science and provides health information that protects our nation against expensive and dangerous health threats, and responds when these arise.

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

- Leads self-management research, program implementation, and dissemination, including:
    - Researching new self-management programs
    - Disseminating our work
- Establishes and expands surveillance and data collection to:
    - Describe the burden of epilepsy

  - Identify risk and protective factors
  - Evaluate prevention efforts
  - Prioritize program development
- Prevents known risk factors for epilepsy by:
  - Developing specific interventions (e.g. to detect cysticercosis infection)
  - Promoting the health promotion and disease prevention efforts of others (e.g. traumatic brain injury, stroke); and
- Develops and promotes programs that create a more supportive environment for people with epilepsy by:
  - Elevating epilepsy as a public health issue to motivate action
  - Complementing activities of key partners such as the Epilepsy Foundation

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

Population and epidemiologic studies of epilepsy include:

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

Prevention Research includes:

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

Epilepsy Stigma research includes:

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

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

Examples of Recent Research Activities:
Public health surveillance:

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

Intramural research underway:

- Analysis of 2010 and 2013 NHIS data to examine access to care for adults with epilepsy
- Analysis of CDC National Violent Death Reporting System data to identify suicide burden in people with epilepsy
- Analysis of NCHS National Vital Statistics Systems Multiple Cause of Death data to identify possible SUDEP cases
- Analysis of Porter Novelli HealthStyles data to examine trends in attitudes toward epilepsy in the U.S. population
- Analysis of 1993-2012 National Inpatient Sample /Healthcare Cost and Utilization Project data to examine trends in hospitalizations in people with epilepsy or seizure diagnosis

Extramural research underway:

- Epidemiologic research:
    - **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 comorbidities in people with epilepsy, and 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 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 barriers to care among children with epilepsy and their families; and to characterize risk factors, outcomes and comorbidities related to prevalent and new-onset pediatric epilepsy. This is a prospective cohort study.

- Prevention research:

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

    - MEW Network Coordinating Center (Dartmouth College and Emory University)

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

- MEW Network Collaborating Centers

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

    - University of Arizona - Evaluation of MINDSET (Management Information Decision Support Epilepsy Tool) for Hispanic-American adults with epilepsy.

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

    - University of Illinois (Chicago) - PAUSE (Personalized Internet Assisted Underserved Self-management of Epilepsy).

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

    - Morehouse School of Medicine - Adapting Evidence-Based Epilepsy Self-Management Programs for Blacks in Georgia.

      Using a Community Advisory Committee, focus groups, and interviews with community stakeholders, this project seeks to promote the adoption and replication of evidence-based MEW Network self-management programs in underserved communities, and to understand the features that facilitate dissemination, replication, and adoption of these programs among African-American adults with epilepsy and their providers.

- New York University - Evaluation of Project UPLIFT (Using Practice and Learning to Increase Favorable Thoughts) for Hispanic adults with epilepsy and depression.

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

- University of Minnesota - Youth, Epilepsy, and Successful Self-Management.

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

- University of Washington - PACES in Epilepsy: Replication, Extension, and Dissemination.

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

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

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

Resources Available:

- The CDC Managing Epilepsy Well Network serves as a community-of-practice facilitating collaboration with external partners interested in studying epilepsy self-management and associated outcomes.

- Opportunities for collaboration on analysis of CDC surveillance system data exists.

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

- Population and Epidemiological studies of epilepsy addressing: (a) incidence; (b) prevalence; (c) risk factors and etiology; (d) comorbidities; (e) access to care; and (f) quality of life;
- Surveillance of mortality (SUDEP, suicide, other causes) in people with epilepsy (all ages);
- Advancing and disseminating self-management research and programs to improve quality of life for people with epilepsy through the Prevention Research Centers' Managing Epilepsy Well (MEW) Network
- 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
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Mission:

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

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

Examples of Recent Activities:

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

- Under the current Cooperative Agreement with the New York State Institute for Basic Research (IBR), the Fragile X Clinical and Research Consortium (FXCRC) has worked on a number of "consensus" documents. These are not guidelines or recommendations, as they didn't go through the processes that would be required, however the work to develop the consensus documents did include a number of clinicians who specialize in the care of individuals with FXS. FXCRC put out a consensus document on seizures in the FXS population, http://fxcrc.org/images/stories/document-library/Seizures_in_Fragile_X_Syndrome.pdf. FXCRC plans to update the consensus document and look at data collected through the Fragile X Online Registry With Accessible Research Database (FORWARD), which contains clinician and parent reported data collected through 25 fragile X specialty clinics across the country. The questions related to seizure are on the Clinician Report Form used in FORWARD, and the relevant questions are included below:

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

o Yes, currently
o Yes, but only in the past
o No (SKIP to 19.)
o Don't know (SKIP to 19.)

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

o Generalized o Partial o Febrile o Unknown

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

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

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

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

Future Activities:

- There is significant potential for collaboration on future research activities when resources permit:

- Expansion of surveillance activities using existing national surveys in order to focus on childhood epilepsy and co-morbidities that affect quality of life and wellbeing:
    - National Survey of Children’s Health (NSCH) can be used to assess the prevalence of epilepsy and seizure disorders, health (functional status and co-occurring mental and behavioral conditions), health insurance, quality of health care, disparities in health care access and ease of care, use of developmental services, time use, school enrolment, and family financial and employment impact of epilepsy.
        - As an example, a manuscript on the prevalence of childhood anxiety and depression was recently submitted that included co-occurrence of a number of conditions, including epilepsy, which was significantly more common among children with anxiety and depression than in those without.
    - Provider-based surveys, such as National Health Care Surveys administered by National Center for Health Statistics can be used to study both ambulatory care and hospital care for epilepsy.
    - Administrative databases, such as MarketScan database or Centers for Medicare & Medicaid Services (CMD) data, can be used to study the prevalence, medical care cost and co-morbidities for persons with epilepsy at a national level.
    - Multiple Cause Mortality Files can provide trend of death rate where epilepsy was recorded as a cause of death. The most frequently recorded other causes of death for those deaths associated with epilepsy can also be evaluated.
- NCBDDD could conduct surveillance of epilepsy as an independent condition in 8-year-old children in four Autism and Developmental Disability Monitoring (ADDM) Network sites. Based on the average number of 8-year old children in an ADDM site, and an estimated prevalence of epilepsy in 8 year olds of 6-10 per 1000, the expected number of 8-year-old children identified with epilepsy would be 210-350 per ADDM site (total among 4 sites of 840-1400). In addition to records already reviewed for ASD, CP and ID (autism spectrum disorder, cerebral palsy, and intellectual disability) surveillance, these ADDM sites would review records from neuroimaging, neurophysiology, and neurology sources, including descriptions of epilepsy or seizures, results from diagnostic testing, age of onset, etiology, medications, and other pertinent medical conditions. The abstracted information would then be reviewed and coded at each site by a pediatric neurologist to determine case status using the International League Against Epilepsy (ILAE) standard case definition and classification of epilepsy. The information that would potentially result from the data collected through this study would include:
    - Prevalence of epilepsy among 8-year-olds in the study population
    - Prevalence of epilepsy in the study population, by race, sex and type of epilepsy, including epilepsy syndromes (ILEA classification), and characterization of difference between groups.
    - Linkage to birth certificates for additional birth variables: e.g., birth weight, maternal age, maternal education
    - Linkage to birth defects data in sites that conduct birth defects surveillance (e.g., the Metropolitan Atlanta Congenital Defects Program conducts surveillance in the same region covered by the GA ADDM site (i.e., the Metropolitan Atlanta Developmental Disabilities Surveillance program)).
    - Mean age of diagnosis of epilepsy and factors that affect age of diagnosis

        - Prevalence of specific co-occurring conditions (e.g., autism, cerebral palsy, intellectual disability, hearing loss, visual impairment, etc.)
        - School placement
        - Medical services use

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

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

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

Primary Representative: Anthony Pacifico, Ph.D.
Email: Anthony.M.Pacifico.civ@mail.mil

Mission: The CDMRP finds and funds the best research through a competitive, two-tier application review process to:

- Target innovative research approaches
- Encourage high-impact research
- Integrate consumer participation at each level
- Support unique goals of each program

Activities and Topics of Interest: Post-Traumatic Epilepsy due to Traumatic Brain Injury.

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

Primary Representative: Paul Rutecki, MD, Acting Director VA ECoE
Email: Rutecki@neurology.wisc.edu

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

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

Major Topics of Interest:

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

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 Association
- Infrastructure: The VA Epilepsy Centers of Excellence are clinically funded by VA Central Office and include 16 centers within four administrative regions. The ECoE has workgroups that focus on both basic science research and clinical research, allowing for collaboration and

information sharing among the ECoE sites. These workgroups help to organize national efforts and provide guidance on potential collaborative studies.

Examples of VA ECoE recent or current epilepsy research activities:

Topics of recent research 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
- Basic mechanisms 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
- Longitudinal case-controlled cohort of OEF-OIF Veterans to comprehensively evaluate for the late effects of combat-related mTBI including evidence of neurodegeneration

Resources Available:

- Basic Science Research Workgroup and Clinical Research Workgroup (monthly calls and open to others that want to collaborate, may inquire through Paul Rutecki, Rutecki@neurology.wisc.edu)
- 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:

- Build collaborative research projects amongst ECoE basic scientists
- 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 use of EMU database and explore potential research opportunities
- Explore potential to collaborate with Integrated Neurology Project for quality/ efficacy research
- Expand PNES Tele-mental health initiative to other ECoE's and the Integrated Neurology Project
- Explore genomic partnerships between ECoE and the Million Veteran Program (MVP)
- Expand collaboration between the ECoE's and the National Polytrauma Centers
- Explore the effect of TBI on sleep patterns
- Determine whether the mTBI case group differs from the non-TBI control group and the effects of single versus multiple mTBIs

- Measure ERPs (specifically multimodal working memory, long-term memory access, & auditory cortical potentials) to: seek additional physiologic evidence of neurodegeneration, clarify functional significance of changes in neurobiological variables through real-time measure of neural coordination, characterize the neurocognitive mechanisms of impairments shown on cognitive performance tests.
- Epilepsy epidemiology & surveillance project
- Preparation of Career Development Award 2 to examine social network of physicians on care provided to Veterans with PNES/ epilepsy
- Synaptic integration in neocortical neurons
- Identify targets for interventions to improve care based on findings from ongoing RECORD Quality project
- Basic mechanisms of epilepsy

American Epilepsy Society (AES)

Primary Representative: Amy Brooks-Kayal, M.D., AES Board President, 2015
Email: Amy.Brooks-Kayal@childrenscolorado.org

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

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

Types of research support:

- The AES supports research through scientific meetings, pre- and post-doctoral and clinical fellowships, young investigator 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.
- Epilepsy Currents – the bi-monthly review journal of the American Epilepsy Society
- Specific Initiatives include:
    - Pre-doctoral and Post-doctoral fellowships
    - Clinical Research Fellowship
    - Junior Investigator Grants
    - Travel grants
    - Mentoring activities
    - Seed grants
    - Support of Workshops and research conferences
    - Q-Pulse clinical practice surveys and commentary

Examples of Recent Activities:

- 2014 Research Funding – AES has increased its commitment to providing support for young investigators, especially those in training, to enter or stay in the field of epilepsy research. In this fiscal year AES is funding seven postdoctoral, four pre-doctoral and one clinical fellowship, three junior investigator grants and one Susan Spencer Clinical Fellowship (with EF and AAN).
- Seed Grants –This program is intended to foster collaborations between two or more established investigators and enable information exchange/technology transfer, including travel of postdoctoral fellows between laboratories and modest supplies for the project. These small awards are designed to provide seed monies for collection of preliminary data and enable investigators to be more competitive for larger awards. Two grants were awarded in 2014.
- Research & Training Workshops – AES provides funding for targeted workshops intended for broad-based, clinical or scientific audiences on topics in neurology and neuroscience that are novel and creative. Two to three are supported each year.
- AES Epilepsy Benchmark Committee – AES continues to collaborate with NINDS on the implementation of the Research Benchmarks. The AES Epilepsy Benchmark Committee facilitates broader participation by AES members and supports the Stewards

in initiating and taking ownership of a wider range of activities. The Stewards are currently preparing a publication on epilepsy advances, to be published in spring of 2016 in Epilepsy Currents.
- Epilepsy Research Connection (ERC) – an initiative of the Epilepsy Leadership Council (formerly Vision 20-20) the ERC is a website (http://www.epilepsyresearchconnection.org/home.php) funded by AES, that provides a single place for investigators to search for epilepsy research funding activities. Launched at the beginning of April, this resource contains funding opportunities from governmental and voluntary agencies.
- Q-Pulse Surveys – 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 results of which are published in 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.

Resources Available:

- AES members provide expertise on study sections, Professional Advisory Boards, etc.
- Epilepsy Research Connection (see above)
- AES Annual Meeting, including access to post-meeting online and published content •
- Administrative support and coordination of Epilepsy Leadership Council (formerly Vision 20-20) activities
- Coordination of IOM Report activities 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
- Robust open access web resources on epilepsy topics
- Searchable access to hundreds of abstracts and Currents commentaries

Priorities and Plans for Future:

- Work toward identifying opportunities for increased coordination amongst the epilepsy research community to make more effective and strategic use of limited dollars in conjunction with the Epilepsy Leadership Council and other partnerships
- Provide leadership in developing and supporting the next generation of basic, translational and clinical researchers
- Address the issues and gaps raised in the IOM report. Continue to form collaborations with other organizations to accomplish the recommendations
- Continue to support Epilepsy Research Connection

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

Primary Representative: Ray Dingledine (Committee Chair, Emory University)
Email: rdingledine@pharm.emory.edu

Mission: The Mission of the Benchmark Stewards is to assist in setting the national epilepsy research agenda. We approach this mission by highlighting the most impactful recent scientific advances and by identifying promising research directions for future resource allocation.

Major Topics of Interest: The current topic areas for Benchmark focus are:

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

A. Identify new genes and pathways associated with the epilepsies and epilepsy-related conditions.
B. Identify new infectious, immune, age-related, environmental, or other causes and risk factors associated with the epilepsies and epilepsy-related conditions.
C. Determine whether factors related to age, gender, race/ethnicity, socioeconomic status, and other features of specific populations affect risk and mechanisms of epilepsy and epilepsy-related conditions.
D. Determine whether the bi-directional relationships that exist between the epilepsies and several co-occurring conditions (e.g., neuropsychiatric or neurodevelopmental disorders) result from the same underlying causal mechanisms, interacting mechanisms, or are a consequence of the first presenting condition.

II. Prevent epilepsy and its progression.

A. Understand epileptogenic processes involved in epilepsies with neurodevelopmental origins, including those due to genetic or presumed genetic causes.
B. Understand epileptogenic processes involved in the development of epilepsy following traumatic brain injury, stroke, brain tumor, infections, neurodegeneration, or other insults to the brain.
C. Identify biomarkers that will aid in identifying, predicting, and monitoring epileptogenesis and disease progression, including markers early after injury/insult that identify those people at risk for epilepsy.
D. Develop or refine models aligned with the etiologies of human epilepsies to enable improved understanding of epileptogenesis and rigorous preclinical therapy development for epilepsy prevention or disease modification.
E. Identify new targets and develop interventions to prevent or modify epileptogenesis and the progression of epilepsy and epilepsy-related conditions.

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

A. Understand the initiation, propagation, and termination of seizures at the network level in different forms of epilepsy.
B. Identify biomarkers for assessing or predicting treatment response, including markers that may identify specific populations that are likely to have good outcomes or develop adverse responses.
C. Develop or refine models that are aligned with etiologies and clinical features of human epilepsies, especially treatment resistant forms, to enable improved understanding of

ictogenesis and preclinical development to improve seizure control with fewer side effects. Establish the sensitivity and specificity of these models with regard to current therapies.

D. Identify, develop, and improve interventions to detect, predict, prevent, or terminate seizures, including approaches suitable for use in the home and other non-medical settings.
E. Identify, develop, and improve anti-seizure therapies that target (either alone, or in combination) novel or multiple seizure mechanisms.
F. Develop, improve, and implement interventions for effective self-management, including treatment adherence.
G. Develop and validate objective patient-centered outcome metrics for clinical studies.

IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.
A. Understand and limit adverse impacts of seizures on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.
B. Understand and limit adverse impacts of anti-seizure treatments (medical, surgical, or other interventions) on quality of life, including effects on neurodevelopment, mental health, intellectual abilities, and other neurological and non-neurological functions.
C. Understand risk factors and mechanisms involved in non-epileptic seizures (NES). Develop effective approaches for earlier and accurate diagnosis and treatment.
D. Identify causes, risk factors, and potential preventive strategies for sudden unexpected death in epilepsy (SUDEP) and other epilepsy-related mortality (for example, suicide) in people with epilepsy.
E. Identify the impact of pharmacological treatment of the epilepsies on fetal and neonatal development. Develop strategies to control seizures in pregnancy without causing harm to either the mother or child.

Examples of Recent activities:

- Last year the Epilepsy Benchmark Stewards transitioned from being primarily sponsored by NINDS to becoming a committee of the American Epilepsy Society working in partnership with NINDS. This change allows us to use the AES process to recruit future Stewards and perhaps elevates the visibility of the Benchmark Stewards.
- A narrative description of the 2014 Epilepsy Benchmarks can be found at http://www.ninds.nih.gov/research/epilepsyweb/2014benchmarks.htm
- (area II.B,C) In studies using status epilepticus models of chronic epilepsy and a mouse model of fragile X syndrome, interventions that inhibited/interfered with BDNF receptor TrkB signaling, inflammatory, JAK/STAT, RAS-ERK1/2, or renin-angiotensin pathways reduced seizure frequency and/or severity, the most striking effect being observed by interfering with TrkB signaling.
- (area II.D) A mouse model of an epileptic encephalopathy has been created by chronic intracranial infusion of human CSF pooled from NORSE patients.

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 plan to publish a mid-term progress update on the 2014 Benchmarks in the April 2016 issue of Epilepsy Currents, 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: 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, Bernard Chang, Jack Lin
Annapurna Poduri, Andrey Mazarati

II. Prevent epilepsy and its progression.
Co-Chairs: Aristea Galanopoulou and Michael Wong
Devin Binder, Adam Hartman, Elizabeth Powell
Avtar Roopra, Richard Staba, Annamaria Vezzani

III. Improve treatment options for controlling seizures and epilepsy-related conditions without side effects.
Co-Chairs: Dennis Dlugos and Gregory Worrell
Kathryn Davis, Beate Diehl, Patrice Jackson-Ayotunde
Andres Kanner, Tobias Loddenkemper, Michael Rogawski
William Stacey, Sridhar Sunderam, Jerzy Szaflarski

IV. Limit or prevent adverse consequences of seizures and their treatment across the lifespan.
Co-Chairs: W. Curt LaFrance, Jr., and Alica Goldman
Miya Asato, Timothy Benke, Robert Doss
Daniel Drane, Samden Lhatoo, Alison Pack
Tanvir Syed

Citizens United for Research in Epilepsy (CURE)

Primary Representative: Susan Axelrod, Founding Chair; Julie Milder, Associate Research Director
Email: Julie Milder – Julie@cureepilepsy.org

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

Major Topics of Interest:
- SUDEP
- Pediatric Epilepsies, with particular emphasis on infantile spasms
- Acquired Epilepsies
- Epilepsy genetics
- Pharmacoresistant epilepsies

Types of Research Support:
- Research grants for basic, translational, and clinical research
- Young investigator travel awards to Gordon Research Conference
- HHMI/CURE research fellowship for medical students
- Conference and workshop support
- Sponsored seminar series
- Infantile spasms bedside to bench to bedside initiative
- Genetic database to house exomes and clinical data of people with epilepsy (EGI)

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
- Epilepsy Genetics Initiative (EGI): EGI is an initiative created by CURE, in partnership with NINDS, to establish a database to hold the genetic data of people with epilepsy. The specific type of data we are talking about is exome sequence data. The data will be analyzed every 6 months to find the cause of epilepsy and results will be reported back to the treating physician. These data will also be made available for research. http://www.cureepilepsy.org/egi/

- 2015 Conference Support, to date: GRC on Glial Biology (Ventura, CA), EF of LA and Charlie Foundation Summit (Los Angeles, CA), ADD Program Symposium (Park City, UT), Exploring and Treating the Epileptic Brain Symposium at the Mediterranean Neuroscience Society Meeting (Sardinia, Italy), IWSP 7 (Melbourne, Australia), GRC on Inhibition in the CNS (Bates College, ME), and 6th Eilat International Educational Course (Jerusalem, Israel).
- CURE Frontiers in Research Seminar Series – spreading the word about cutting edge epilepsy research at research 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

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

Future Activities:

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

Dravet Syndrome Foundation (DSF)

Primary Representative: Abby Hemani, Board President
Email: abby.h@dravetfoundation.org

Secondary Representative: Mary Anne Meskis, Executive Director
Email: maryanne.m@dravetfoundation.org

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

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

Types of research support:

- DSF offers an annual application cycle for our Research Grant Awards and Postdoctoral Fellowships.
- DSF's Research Roundtable is an annual meeting that is open to clinicians, researchers, and other professionals with a strong interest in Dravet syndrome. It is by invitation only and is held each year on the evening prior to the commencement of the American Epilepsy Society Meeting.
- DSF offers occasional financial support at Dravet-specific professional meetings
- DSF hosts a biennial family and professional conference which allows professionals direct interaction with our patient community.

Examples of Recent Activities:
Our 2014 Research Grant Awards & Postdoctoral Fellowships:

- Elaine C. Wirrell, MD - Dravet Syndrome North American Consensus Project
  The goal of this study is to utilize a modified Delphi consensus method to establish best practice guidelines for timely diagnosis of Dravet syndrome in a cost effective manner; pharmacologic and dietary treatment of Dravet syndrome to maximize seizure control, reduce frequency of status epilepticus and improve long- term developmental outcomes; identification
  and management of co-morbidities associated with Dravet syndrome
- Theodore R. Cummins, PhD - Targeting resurgent sodium currents for treatment of DS
  In many individuals with DS, genetic abnormalities reduce the activity of the Nav1.1 sodium channel. This reduces inhibitory tone, leading to overactive brain networks and seizures. Reducing the activity of Nav1.6 sodium channels could restore the balance between excitation and inhibition, effectively normalizing network activity. The action of several promising compounds, including cannabidiol, on these human brain sodium channels and on brain slices from a mouse DS model will be examined.
- Alfred L. George, Jr., MD - Novel Pharmacological Therapy for Dravet Syndrome

Dr. George and his collaborators will investigate the mechanisms underlying a serendipitous observation that GS967, a novel compound with unique effects on sodium channels, prevents premature death in a mouse model of DS. Specifically, they will determine if GS967 prevents seizures and, if it does, then they will examine how it affects electrical activity in the brain. The investigators hope that their studies will guide further development of this and related chemical compounds as potential treatments for Dravet syndrome.

- MacKenzie Howard, PhD - Neural progenitor cell transplantation for the study and treatment of DS

  Dr. Howard's first research goal is to test the effectiveness of cell transplantation therapy for treating DS in a mouse model. This technique involves transplanting non-DS cells into a brain region called the hippocampus, where they develop into specialized inhibitory neurons. His second goal is to use this technique to transplant DS neurons into the hippocampus of non-DS mice. This will allow him to study how the DS neurons develop, connect, and communicate with other cells in a seizure-free environment and give insight into how various functions of individual neurons are altered.
- Jacy Wagnon, PhD - Brain transcriptomes in SCN1A and SCN8A related epileptic encephalopathies

  The majority of Dravet syndrome cases are caused by mutations in the sodium channel gene SCN1A. Mutations in the related gene SCN8A have recently been discovered in patients with related disorders. Mutations in SCN1A and SCN8A cause severe, early-onset, drug-resistant seizures with a high risk for SUDEP (sudden unexpected death in epilepsy). Mouse models carrying patient mutations in SCN1A and SCN8A exhibit seizures and premature death. Dr. Wagnon will analyze gene expression in these two mouse models to identify common, shared pathological pathways that will provide new targets for treatment and prevention of seizures and SUDEP.

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

Priorities and Plans for Future:

- Our annual Research Grant & Postdoctoral Fellowship application cycle begins on September 2, 2015.
- Our annual Research Roundtable will be held on December 3, 2015 in Philadelphia, Pennsylvania.
- Our next Family & Professional Conference will take place on June 23-26, 2016, in Coral Gables, Florida.

Epilepsy Leadership Council (ELC) – formerly Vision 20-20

Primary Representative: Barbara Kroner, PhD
Email: byk@rti.org

Mission: The ELC serves as a collaborative through which epilepsy voluntary, professional and governmental organizations can work on shared goals and projects that will have a positive impact on the lives of individuals with epilepsy, focusing on those areas where working together produces greater efficiency and impact than working independently.

Topics of Interest: Many of the participating organizations support research programs that reflect the missions and goals of the 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/meeting support
- Targeted and investigator-initiated research
- Registries

Examples of Recent Activities:

- Epilepsy Research Connection http://www.epilepsyresearchconnection.org/home.php -- an initiative of the ELC funded by AES, this is an update of the Resources in Epilepsy Research website and provides a single place for investigators to search for epilepsy research funding activities. Launched at the beginning of April, this resource contains funding opportunities from governmental and voluntary agencies.
- IOM Report Implementation – monthly calls to share activities related to the report, including surveillance, access to care, and comorbid health conditions
- HERO (Human Epilepsy Research Opportunity) Website – aim is to increase patient participation in clinical research studies by explaining the importance of the studies and linking to available trials.
- 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 enables 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) are included.
- NINDS and Non-Profit Research Resources Special Interest Group at the AES Annual Meeting – The purpose of this SIG is to generate a focused two-way discussion between government and non-profit funders and basic and clinical researchers attending the AES annual meeting. The intent is to educate researchers on how government and non-profits set their priorities and fund research and to educate funders on what else they could do to support basic and clinical researchers in the epilepsies.

- Partners Against Mortality in Epilepsy (PAME) Conference, held June 19-22, 2014, in Minneapolis. This was the second PAME conference devoted research on Sudden Unexpected Death In Epilepsy (SUDEP) and other epilepsy-related mortality, where clinical and basic science researchers and patient/family members came together to understand and support each other and discuss the latest findings in research.

Resources Available:

- Epilepsy Research Connection (see above)
- REN (see above)
- Special Interest Group at AES (see above)

Priorities and Plans for Future:

- The ELC is in the process of establishing a new structure to facilitate identifying priorities, developing projects and streamlining decision-making. In addition to expanding the ERC, emphasis this year will be on enhancing opportunities for research collaboration and coordination amongst the ELC 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.

Tuberous Sclerosis Alliance (TS Alliance)

Primary Representative: Kari Luther Rosbeck, President and Chief Executive Officer
Email: krosbeck@tsalliance.org

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

Major topics of interest:

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

Types of Research Support:

- The TS Alliance's research grant program annually awards research grants and postdoctoral research focused on TSC, which may include the study of any aspect of epilepsy in TSC, such as molecular mechanisms, preclinical models, biomarker discovery, etc.
- The TSC Clinical Research Consortium provides infrastructure to conduct clinical studies in TSC, including epilepsy-related studies, at seven or more TSC Clinics around the country.

Examples of Research Activities:

- The TSC Clinical Research Consortium is in the final year of a clinical study to identify biomarkers associated with risk of developing seizures in the first two years of life in infants with TSC.
- TS Alliance and the European Commission co-funded a Research Grant awarded to David Kwiatkowski, MD, PhD at Brigham and Women's Hospital, Boston, MA, for "EPISTOP: clinical and molecular biomarkers of epilepsy in tuberous sclerosis complex." This is a study to identify clinical and molecular biomarkers of epileptogenesis in tuberous sclerosis complex combined with a randomized clinical trial of vigabatrin.
- The TS Alliance participates in the Rare Epilepsies Network led by the Epilepsy Foundation in partnership with RTI, Columbia University, and many other patient advocacy organizations.

Resources Available:

- The TSC Natural History Database is a central repository of de-identified clinical data collected at 17 TSC Clinics which serves to identify cohorts for participation in research studies and to provide data to researchers for further analysis. Currently, more than 1550 individuals are enrolled with a target of 2000 participants enrolled by the end of 2015.

Priorities and Plans for Future:

- Building a TSC Biosample Repository of blood and tissue, including resected brain samples from epilepsy surgeries, to be made available to qualified researchers worldwide.
- More detailed analysis of the natural history and response to treatment of epilepsy throughout the lifespan in TSC.

ICARE: Interagency Collaborative to Advance Research in Epilepsy

April 13, 2015
6001 Executive Blvd, Rockville, MD; Conference Room D

AGENDA

8:45	*Arrival/registration*
9:00 – 9:20	**Welcome** (Walter Koroshetz, Acting Director, NINDS/NIH)
9:20 – 9:45	**Introduce new ICARE members**
9:45 – 10:00	**Update on the Epilepsy Benchmarks** (Ray Dingledine, PhD, NINDS/AES Epilepsy Benchmarks Stewards Committee Chair; invited)
10:00 – 11:00	**Community-wide Epilepsy Research Portfolio Analysis**
10:00 – 10:25	Methodology and Preliminary Results (Miriam Leenders PhD, NINDS/NIH)
10:25 – 10:45	Open Discussion, and future plans for ICARE portfolio analyses (Moderator: Brandy Fureman PhD, NINDS/NIH)
10:45 – 11:00	***Break***
11:00 – 12:00	**Collaborative Activities and Opportunities**
11:00 – 11:15	Demonstration of the new Epilepsy Research Connection site (Rob Moss)
11:15 – 11:30	Measuring Our Progress – What's Next for ICARE? (Brandy Fureman PhD, NINDS/NIH)
11:30 – 12:00	Open Discussion on collaborative opportunities
12:00 – 1:15	***Lunch (on your own/small group meetings)***
1:15 – 3:30	**Scientific & Policy Session: Genetic Testing for the Epilepsies**
1:15 – 1:35	Molecular Diagnosis for Epilepsies: The Impact on Patients and Families (Beth Sheidley, MS, CGC, Boston Children's Hospital)
1:35 – 1:55	The Promise of Exome Sequencing in Epilepsy and the New Epilepsy Genetics Initiative (EGI) (Tracy Dixon-Salazar PhD, CURE)
1:55 – 2:15	State of the science in epilepsy genetics and translation to clinical practice (Dennis Dlugos, MD Children's Hospital of Philadelphia)
2:15 – 2:35	Evidence development for clinical utility (Suzanne Belinson PhD, MPH, Blue Cross Blue Shield Association)
2:35 – 2:55	The Role of Education: Addressing Challenges and Opportunities to Clinical Translation (Michael J. Dougherty, PhD, American Society of Human Genetics)
2:55 – 3:30	Open Discussion (Moderator: Vicky Whittemore PhD, NINDS/NIH)
3:30 – 3:45	**Wrap-up and adjourn main meeting**
Post-meeting	**Opportunities for small group meetings and networking** **Tutorials/demonstrations: Rm 3310** (NIH RePORTER, RCDC, Epilepsy Resource Connection)

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