NIH initiates “Centers Without Walls” to study sudden unexpected death in epilepsy

Projects build a virtual center for research on death associated with epilepsy

Nine groups of scientists will receive funding totaling $5.9 million in 2014 to work together on increasing the understanding of sudden unexpected death in epilepsy (SUDEP), the leading cause of death from epilepsy. The consortium becomes the second Center Without Walls, an initiative to speed the pace of research on difficult problems in epilepsy by promoting collaborative research. The National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health, funds this initiative.

“We hope that by encouraging scientists with expertise in a variety of areas to join forces in the Centers Without Walls initiative for SUDEP research, we may learn how to prevent the tragic death of as many as 3000 children and adults each year in the United States,” said Walter Koroshetz, M.D., acting director of NINDS.

NINDS established the Centers Without Walls program in 2010 to address challenges and gaps in epilepsy research. The program encourages collaborations, including sharing of data and resources, between researchers from a variety of disciplines and institutions.

Seizures are common, affecting almost 1 in 20 people. Each year, SUDEP occurs in 1 out of 1000 people with epilepsy, often in people between 20 to 40 years old. SUDEP refers to deaths with no known causes in individuals with epilepsy; there are no strategies for preventing it.

The grants announced today form the Center for SUDEP Research, which is made up of related projects with the common goal of quickly taking SUDEP lab results into the clinic.

“These projects represent a wide range of strategies for figuring out what causes SUDEP and identifying risk factors that may help prevent it. The design of the program, which combines fundamental laboratory research with translational and clinical findings, will provide us with...
answers to many of the questions we have about SUDEP,” said Vicky Whittemore, Ph.D., NINDS program director who will be part of the leadership of the Center.

The projects are:

Center for SUDEP Research: Autonomic and Imaging Biomarkers of SUDEP
Principal Investigator: Samden Lhatoo, M.D.; Case Western Reserve University, Cleveland; NS090407
Dr. Lhatoo’s team will examine ways in which changes in brain structure are linked to abnormal physiological responses and altered breathing patterns that occur during seizures. Using various imaging technologies, they will identify risk factors for SUDEP that may eventually be therapeutic targets.

Center for SUDEP Research: The Neuropathology of SUDEP
Principal Investigators: Maria Thom, M.D.; University College London; Orrin Devinsky, M.D.; New York University, New York City; NS090415
Combining the world’s largest collection of brains from individuals who have died from SUDEP with tissue collected from individuals undergoing epilepsy surgery, Dr. Thom and her colleagues will use a variety of techniques to examine the role of two chemicals, adenosine and serotonin, in unexpected death associated with epilepsy.

Center for SUDEP Research: Morphometric Core
Principal Investigator: Alica M. Goldman, M.D., Ph.D.; Baylor College of Medicine, Houston, Texas; NS090406
Dr. Goldman’s group will focus on changes in the size and structure of the brain and brainstem from individuals who have died due to SUDEP.

Center for SUDEP Research: Molecular Diagnostics Core
Principal Investigators: John William Belmont, M.D., Ph.D., and Alica Goldman, M.D., Ph.D., Baylor College of Medicine; NS090362
Dr. Belmont’s team will conduct DNA genetic analyses on samples obtained from individuals who have died or are at high risk of developing SUDEP. The tissue will be collected from institutions that are part of the Center for SUDEP Research. The goals of this project are to identify the genes that cause SUDEP and allow researchers to develop tools to predict who is at risk for it.

Center for SUDEP Research: Respiratory and Arousal Mechanisms
Principal Investigator: George B. Richerson, M.D., Ph.D.; University of Iowa, Iowa City; NS090414
Research from Dr. Richerson’s lab suggests that dysfunction in brainstem pathways involved in controlling breathing may be involved in SUDEP. With the help of individuals with epilepsy as
well as mouse models, Dr. Richerson and his colleagues will investigate these pathways and look for biomarkers that may be used to screen individuals most at risk of developing SUDEP.

Center for SUDEP Research: Induced Pluripotent Stem Cells and Mouse Neurocardiac Models
Principal Investigators: Jack M. Parent, M.D. and Lori Isom, Ph.D.; University of Michigan, Ann Arbor; NS090364
Drs. Parent and Isom will examine changes in neuronal function and heart rhythm that may contribute to SUDEP in individuals with Dravet syndrome, a severe form of pediatric epilepsy with higher risk of sudden death. Using stem cells derived from individuals with Dravet syndrome, data obtained from these individuals before, during and after seizures, and mouse models, they will look for biomarkers to identify risk.

Center for SUDEP Research: Cardiac Gene and Circuit Mechanisms
Principal Investigator: Jeffrey Noebels, M.D., Ph.D.; Baylor College of Medicine; NS090340
Dr. Noebels and his colleagues will investigate how changes in genes can increase the risk of SUDEP by causing abnormalities in heart rate and breathing patterns. They will identify genes that contribute to SUDEP and test candidate drugs that may reduce the risk of unexpected death.

Center for SUDEP Research: Informatics & Data Analysis Core
Principal Investigator: Guo-Qiang Zhang, Ph.D.; Case Western Reserve University; NS090408
The main goal of the Informatics and Data Analysis Core (IDAC) is to make it easier for researchers to share data and resources across all of the institutions in this Center Without Walls. IDAC will also provide support for the SUDEP projects by assisting with data collection, analysis and study design.

Center for SUDEP Research: Administrative Core
Principal Investigators: Samden Lhatoo, M.D.; Case Western Reserve University; Jeffrey Noebels, M.D., PhD.; Baylor College of Medicine; NS090405
The Administrative Core will serve as a virtual hub for the SUDEP projects. Drs. Lhatoo and Noebels will oversee, facilitate and prioritize the research that results from the Center for SUDEP Research projects.

For more information about epilepsy, please visit: http://www.ninds.nih.gov/disorders/epilepsy/epilepsy.htm

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NINDS (http://www.ninds.nih.gov) is the nation’s leading funder of research on the brain and nervous system. 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.
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