

Cardiac Mechanisms Underlying Sudden Unexpected Death

Three studies highlighted at the American Epilepsy Society's (AES) Annual Meeting

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SEATTLE, December 6, 2014 – Sudden death is more than 20 times more common in patients with epilepsy than in the general population. Defects in cardiac and respiratory function are assumed to play a role in this phenomenon, but few studies have explored the underlying mechanisms and risk factors in human patients. Groundbreaking findings describing the link between cardiac abnormalities and sudden unexpected death in epilepsy (SUDEP) will be presented at the American Epilepsy Society's (AES) 68th Annual Meeting.

In the first of three studies (Platform Session C.02) to be presented in full at the Annual Meeting, researchers from the University of Michigan Medical School examine how alterations in the cardiac excitability of patients with Dravet Syndrome—a severe and intractable form of pediatric epilepsy—may increase the risk of SUDEP.

“Given how unpredictable SUDEP is in patients, this study will hopefully shed light on the potential mechanisms that alter cardiac excitability and make DS patients susceptible,” says lead author Chad Frasier, PhD, a postdoctoral researcher in the Isom Laboratory at the University of Michigan Medical School.

Researchers have long suspected that cardiac arrhythmia precedes SUDEP in patients with Dravet Syndrome, but the specific nature of this relationship has remained unclear. Frasier and colleagues compared beating rate, beat period, field potential duration, and sodium current (I_{Na}) density in cardiac cells from one healthy participant and two patients with Dravet Syndrome who had distinct mutations in the *SCN1A* gene. Their findings reveal that increased I_{Na} density may underlie cardiac arrhythmia in patients with Dravet Syndrome, potentially triggering SUDEP.

“These findings are exciting in that they corroborate what we’ve seen in animal models. But they go a step further by allowing us to investigate cells directly from patients with varying genetic backgrounds. We’re hoping this will improve not only our understanding of SUDEP, but also provide a good model to test patient susceptibility in the future,” Frasier says.

An additional study (Poster 2.261) by researchers at the University of Florida College of Medicine identifies a defect in cardiac repolarization that may increase the risk of SUDEP in children with intractable epilepsy. Edgard Andrade and Zhao Liu used video EEG and conventional EKG to monitor cardiac abnormalities during the post-seizure state in 12- and 17-year-old males with drug-resistant epilepsy. Their findings suggest that abnormalities in cardiac repolarization—the heart’s ability to reach a resting state before electrical stimulation—may dangerously slow the heart rate and induce asystole, or flatline, during the post-seizure state and significantly raise the risk for SUDEP.

“Our preliminary findings are very encouraging, and may identify possible preventive therapies in affected children. Research studies enrolling a large patient population are indicated to better understand this disease process,” says Edgard Andrade, MD, MS, FAAP, a clinical associate professor at UF. The findings will be presented in a poster session.

A third study (Poster 3.036), to be presented in poster form by researchers from the University of Oxford and Bristol University in the UK and Purdue University in the US, investigates the effects of repeated brief epileptic seizures on cardiac rhythms in freely moving rats with an experimentally induced temporal lobe epilepsy. The authors report that in every epileptic rat seizures were accompanied by dramatic changes in heart activity, including abnormal heart rhythms, dramatically decreased heart rate and asystole, followed by high heart rates which persisted for some time even after seizure activity had subsided.

“The dramatic cardiac changes caused by repeated seizures could build up over time leading to progressive damage to the heart until a final, fatal seizure-induced episode occurs” says Professor John Jefferys, FMedSci, Professor of Neuroscience, Department of Pharmacology at the University of Oxford. “These findings give us an exciting lead into understanding how epilepsy can impact the functioning of the rest of the body, and ultimately towards understanding SUDEP and informing therapeutic development.”

The authors believe that other bodily functions may be also be affected by seizures. “Our collaboration with bioengineers, led by Pedro Irazoqui at Purdue, has produced innovative miniature implantable devices that will help us find out how long-term epilepsy affects functioning of the heart, lungs and other bodily systems. We now are well placed to work out the kinds of change that can contribute to SUDEP and, in time, to predict and prevent it,” Jefferys says.

All three research studies will be provided in full at the American Epilepsy Society Annual Meeting in Seattle, December 5-9. Abstracts referenced above can be found on the American Epilepsy Society’s [Annual Meeting Page](#).

Editor’s Note: Authors of these studies will be available at a press briefing on **December 6, 2014 at 10:45 AM (PT)/ 1:45 PM (ET)**, in the onsite press room, Room 304, Level 3 of the Washington State Convention Center. The call-in number for off-site journalists is 1-605-475-4000, passcode 521653#.

About the American Epilepsy Society

The American Epilepsy Society (AES) is a non-profit medical and scientific society. Our individual members are professionals engaged in both research and clinical care for people with epilepsy, from private practice, academia and government. For more than 75 years, AES has been unlocking the potential of the clinical and research community by creating a dynamic global forum where professionals can share, learn and grow. AES champions the use of sound science and clinical care through the exchange of knowledge, by providing education and by supporting advances in the specialty.

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