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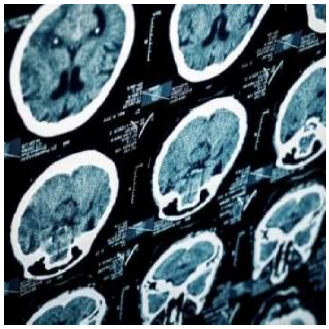
# Cardiac Mechanisms Underlying Sudden Unexpected Death



Three new studies presented at the annual meeting of the American Epilepsy Society (AES 2014) describe the link between cardiac abnormalities and sudden unexpected death in epilepsy (SUDEP).

Sudden death is more than 20 times more common in patients with epilepsy than in the general population. Experts say defects in cardiac and respiratory function may play a role in this phenomenon, but few studies have explored the underlying mechanisms and risk factors in human patients.

Cardiac Arrhythmia in Patients with Dravet Syndrome

In the first of three studies, researchers from the University of Michigan Medical School examined how changes in the cardiac excitability of patients with Dravet Syndrome (DS) — a severe and intractable form of paediatric 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,” said lead author Chad Frasier, PhD, a postdoctoral researcher in the Isom Laboratory at the University of Michigan Medical School.

Although researchers have long suspected that cardiac arrhythmia precedes SUDEP in patients with Dravet Syndrome, the specific nature of such a relationship has remained unclear. For the study, Frasier's team compared beat rate, beat period, field potential duration, and sodium current (INa) density in cardiac cells from one healthy participant and two patients with Dravet Syndrome who had distinct mutations in the SCN1A gene.

Results show that increased INa 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," Frasier explained. "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.”

Defects in Cardiac Repolarisation

An separate study by researchers at the University of Florida College of Medicine identifies a defect in cardiac repolarisation that may increase the risk of SUDEP in children with intractable epilepsy. Edgard Andrade and Zhao Liu used video electroencephalogram (EEG) and conventional electrocardiogram (EKG) to monitor cardiac abnormalities during the post-seizure state in 12- and 17-year-old males with drug-resistant epilepsy.

Based on the study findings, abnormalities in cardiac repolarisation — 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 increase the risk for SUDEP.

"Our preliminary findings are very encouraging, and may identify possible preventive therapies in affected children," said Edgard Andrade, MD, MS, FAAP, a clinical associate professor at UF. "Research studies enrolling a large patient population are indicated to better understand this disease process."

Effects of Repeated Epileptic Seizures on Cardiac Rhythms

A third study examined the effects of repeated brief epileptic seizures on cardiac rhythms in freely moving rats with an experimentally induced temporal lobe epilepsy. Researchers from the University of Oxford and Bristol University in the UK and Purdue University in the US observed that in every epileptic rat, seizures were accompanied by dramatic changes in heart activity. These changes included 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,” said Professor John Jefferys, FMedSci, Professor of Neuroscience, Department of Pharmacology at the University of Oxford.

The results provide an important lead into understanding how epilepsy can impact the functioning of the rest of the body, and ultimately towards

understanding SUDEP and informing therapeutic development. Also, the research team believes 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," Prof. Jeffreys said. "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.”

Source: Newswise
Image Credit: Medical News Today

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