New insights into deadly heart rhythm disorder

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Every year, 300,000 Americans die suddenly when, out of the blue, a "storm" of electrical activity arises within their heart muscle – so violent and so abrupt that their hearts just stop beating. These tragic and dramatic "sudden cardiac deaths" strike people young and old, often without warning.

But despite this, scientists still don't understand just what causes a heart's electrical system to suddenly go so berserk. They have a name for the rhythm disturbance that causes most sudden cardiac deaths – ventricular fibrillation, or VF – but not a full understanding of what makes one person more vulnerable to it than another.

And although research on VF in animals is yielding important clues, it hasn't been clear if lessons learned from the hearts of laboratory mice can be applied to people.

Now, a new paper by a group of researchers published online in the *Proceedings of the National Academy of Sciences* sheds new light on the origins of VF and the ability of research in animals to be translated into humans. The paper, and other research by the team, may help lead to better ways to identify which people are at risk of sudden cardiac death, and to develop treatments to help them reduce their risk.

The paper, which will be in the December 26 print edition of *PNAS*, is by a group of researchers from the United States, Canada and Spain. Most of them are from a State University of New York Upstate Medical

University group that is in the process of moving its research laboratory to the University of Michigan Medical School.

The research team is led by senior author José Jalife, M.D., who describes the electrical storm of VF as a hurricane or tornado that disrupts the regular rhythm of the heart's electrical activity.

The new paper shows that the turbulence that arises in these electrical waves is organized into spiral vortices, no matter what species of mammal is experiencing the VF. These vortices, also called rotors, keep the heart's pumping chambers from pumping in sync, which is required for normal heart function.

The paper also shows that across animal species – from mice and guinea pigs to sheep and humans – the frequency of the VF activity can be scaled using a universal formula related to body mass. So too can the size of the core of the electrical rotors – the "eyes" of the individual electrical storms.

These findings, made using sophisticated imaging techniques developed by the group, pave the way for better translation of VF research results from animals to humans.

For instance, genetic variations that the research team and others are now finding in mice that are prone to VF may also be explored in humans. And it means that further research on why VF begins, and what might be done to prevent it, can also be studied in animals before being applied to people.

""The discovery that the rate of fibrillation changes according to body size is exciting, not only because it brings new and interesting knowledge from the point of view of evolutionary biology, but most important because it erases previous concerns in science about the relevance of

studies in small animals like mice to understanding the most lethal cardiac arrhythmia in people," says Jalife.

Many questions still remain on VF and sudden cardiac death, and new options for preventive screening and treatment may be years in the making. Jalife and his colleagues will continue their research at U-M, using optical techniques and fluorescent dyes whose movement within the surface membrane of cells can be imaged in real time by special video cameras.

They're also studying the membrane ion channels of the heart cells. These are the proteins in the cell membrane that come together to form special tiny openings that only atoms like sodium or potassium can pass through. Mutations in the genes for some of those proteins may alter the proteins in a small but significant way – allowing too rapid ion travel into and out of the cell, or slowing it too much. And that could predispose an animal or person to VF, especially if they also experience another heart issue such as tissue damage from a heart attack.

In human patients, the team is developing the use of mathematical modeling software that can create maps of electrical activity in the heart muscle, based on input from electrodes that are threaded into the heart chambers via the bloodstream. This could lead to more precise treatment of certain areas of the heart muscle where abnormal rhythms might originate.

Until then, the automated external defibrillators that airports, malls and schools around the country have installed in recent years continue to be the best defense against unexpected VF, so that an electrical shock can be delivered by a bystander to restart a person's stopped heart.

Meanwhile, certain heart patients, including Vice President Dick Cheney, have small defibrillators implanted in their chests, able to

deliver that lifesaving shock automatically. Research on which patients benefit most from these implanted devices is still going on, but they are now a viable option for tens of thousands of patients.

Source: University of Michigan