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Applied physics helps decipher the causes of sudden death

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Sudden cardiac death accounts for approximately 10% of natural deaths, most of which are due to ventricular fibrillation. Each year, it causes 300,000 deaths in the United States and 20,000 in Spain. Researchers have demonstrated for the first time that the transition to calcium alternans, an arrhythmia associated with increased risk of sudden death, has common features with the magnetic ordering of metals. This new finding improves our understanding of the physical causes of sudden death and will advance the design of drugs to prevent it. The article, titled "Calcium Alternans is Due to an Order-Disorder Phase Transition in Cardiac Cells," was published in the scientific journal *Physical Review Letters*.

Today, heart diseases are a major cause of death in developed countries. Sudden cardiac death, which involves a sudden loss of heart function, is particularly important. In normal situations, the heart acts as a pump in which the order to contract and pump blood is caused by small changes in the electrical properties of the myocardial cells. Many cases of sudden death are due to problems in the synchronization of this electrical order, resulting in an uncoordinated contraction of the heart known as ventricular fibrillation. In this state, the heart is unable to pump blood and death occurs within minutes unless a defibrillator shock is administered.

One possible trigger of ventricular fibrillation is a cardiac arrhythmia known as alternans, in which the contraction is coordinated on each beat but there is a beat-to-beat alternation in the strength of contraction. To

understand the origin of this arrhythmia, it is necessary to study how the contraction occurs within the cell, where hundreds of small subunits composed of groups of channels release calcium ions when they receive the electrical trigger. This is what marks the strength of contraction: if they release more calcium, the contraction is strong; if they release little, the contraction is weak.

Scientists Enrique Álvarez Lacalle Blas Echebarria of the UPC's Department of Applied Physics and researchers from California State University have demonstrated through simulation models that the alternation is due to a type of transition that has intrigued physicists for decades: an order-disorder transition originally studied to understand the loss of magnetic characteristics when the temperature rises above a threshold value.

A breakthrough for designing new drugs

A ferromagnetic material is formed by small magnets that can focus in one direction or another. If each of these magnets points in a different direction, that is, if the system is disordered, its magnetic effect is cancelled. However, below a certain temperature, all the magnets begin to focus in the same direction and the system is ordered. This makes the whole material behave like a large magnet.

In the case of the heart, each subunit within the cell responsible for releasing calcium may decide whether or not to do so. When this happens in a disordered way, the number of cells releasing and not releasing is the same and the total calcium release is always the same. However, in some situations there is a transition to an ordered state, as in ferromagnetic materials. In this state, all the cells decide to release or not release calcium at the same time, resulting in a sequence of strong and weak contractions and ultimately a transition to ventricular fibrillation. The conclusion seems to be that order can kill in some cases.

According to the scientists, understanding the transition that causes sudden death can help design drugs to prevent it. The results of the research pave the way for the study of possible applications.

On the next step of the research, Blas Echebarria says "we are currently studying whether the same effect is observed in atrial cells. This would advance our understanding of atrial fibrillation, which does not cause sudden death as ventricular fibrillation does, but it involves a high risk of stroke and has a very high prevalence, especially in people over 60 years, reducing their quality of life". In the new stage the researchers are working with scientists at the Catalan Institute of Cardiovascular Sciences (ICCC-CSIC), whose experiments they are attempting to model.

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