The mathematics of a heart beat could save lives

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(Medical Xpress) -- What we perceive as the beating of our heart is actually the co-ordinated action of more than a billion muscle cells. Most of the time, only the muscle cells from the larger heart chambers contract and relax. But when the heart needs to work harder it relies on back-up from the atrial muscle cells deep within the smaller chambers (atria) of the heart.

The health of these 'high-performance' atrial cells relies on specific concentrations of cellular calcium. Now, for the first time, scientists at The University of Nottingham have produced a mathematical model of calcium activity within the atrial heart cell which will significantly improve our chances of treating heart disease and stroke.

This break-through, which takes scientists into a world of cell activity currently beyond the scope of imaging technology, has just been published in the journal *Proceedings of the National Academy of Sciences* (*PNAS*).

Dr Rüdiger Thul, a lecturer in applied mathematics in the School of Mathematical Sciences, said: “This new model provides clinically relevant insights into the initiation and propagation of sub-cellular calcium signals. Thus, for the first time we can manipulate cellular properties throughout a whole atrial muscle cell in order to deduce which conditions give rise to abnormalities. This has the potential to point to new treatments for heart disease and irregular heart beat such as atrial fibrillation, which can lead to thrombosis and stroke.”

The importance of the atrial kick

A human heart will beat more than one billion times during our lifetime. The main function of the heart is to pump blood. To generate the necessary force to propel blood through all the blood vessels, the heart beats with every contraction of its cells.

Most of these muscle cells surround the larger chambers of the heart, the ventricles. Under resting conditions, the ventricles are mainly responsible for contracting the heart. When blood needs to be pumped more quickly — for instance during exercise — the smaller chambers of the heart contribute to the contraction. This is known as the atrial kick.

As we age or when something is wrong with our heart — such as atrial fibrillation — the atrial muscle cells start to deteriorate. As a result we lose the support of the atrial kick. Atrial fibrillation constitutes the most common form of cardiac arrhythmia — irregular heart beat.

The role of calcium in keeping our heart fit

Several experimental studies have revealed that to trigger contraction in atrial muscle cells the calcium concentration follows an elaborate choreography which shows different concentration values in different

parts of the cell. This is in contrast to ventricular cells where the calcium concentration is almost entirely uniform throughout the cell.

In order to fully understand atrial calcium dynamics we need to be able to monitor the atrial cell in its entirety. Unfortunately this is currently beyond even the best state-of-the-art experimental technology. Moreover, experimental manipulations of cells usually interfere with more than one cellular control mechanism making it harder to tease apart the contributions of different pathways. Therefore, developing cutting edge models of atrial cellular behaviour is crucial to our understanding.

New mathematical model could save lives

Dr Thul said: “The strength of our model is that we can study the intracellular calcium concentration throughout the whole volume of the atrial muscle cell at the same time. This allows for a detailed exploration of the spatio-temporal calcium patterns associated with both healthy and pathological conditions.

“Moreover, we can selectively activate, deactivate, over or under express cellular properties and see how they shape the calcium patterns. Hence, we can deduce which conditions give rise to abnormalities and might lead to diseases such as atrial fibrillation. It is important to remember that whatever pharmaceutical treatment is administered, it acts at the single cell level. The response of an organ always results from the interaction of its cellular components. Looking ahead to treatments of atrial fibrillation and other cardiac pathologies, a fully three-dimensional model of an atrial cell offers an ideal testing ground for new drugs.”

More information: www.pnas.org/content/early/201 … /1115855109.full.pdf

Provided by University of Nottingham