Zebrafish teach researchers more about atrial fibrillation

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Researchers from the Faculty of Health and Medical Sciences have shown a possible link between a genetic variation and the widespread type of cardiac arrhythmia, atrial fibrillation.

The scientists conducted the study in zebrafish, which is a recognised scientific animal model within cardiac research.

Here, researchers from the University of Copenhagen in Denmark and the Max Planck Institute in Germany put special focus on the gene pitx2c. The result came as a surprise to them, says Assistant Professor

Pia Lundegaard from the Department of Biomedical Sciences.

"It seems that we may also have to think of atrial fibrillation as an atrial cardiomyopathy—that is, a challenged heart—rather than as a purely electrical disorder," she says.

Defects in muscle fibres and mitochondria

Contrary to expectations, the researchers did not find any disturbances in the ion channels that spread electrical signals between the heart's muscle cells.

Instead, they found defects in the structure of the heart muscle itself and in the mitochondria that normally function as the cell's power plant. The defects already occurred in the foetal stage of the fish and deteriorated exponentially with age.

"Usually the structure of a cross-section of the sarcomeres—the muscle fibres—shows a very fine grid structure. But in these fish, it is clear that the structure is disorganised from a very early stage," explains Pia Lundegaard, adding:

"At the same time, we can see in our pictures that there are too many mitochondria. So, it seems that the heart is trying to compensate for the defective muscle fibres. This indicates that there is a structural defect in the heart which over time will cause a rhythm defect."

Antioxidant prevents defects

According to the research study, the increased number of mitochondria appears to aggravate the negative spiral, the reason being that also the mitochondria are defective and gradually increase the level of so-called

oxidative stress.

In other words, they create an unhealthy environment in the cell where different proteins are broken down.

At the same time, however, the researchers found that early and ongoing treatment with the antioxidant NAC seemed to counteract the defect and in the long term prevent atrial fibrillation in the fish.

However, Pia Lundegaard from the Department of Biomedical Sciences emphasises that heart patients should not stockpile antioxidants such as NAC for that reason.

She points out that the studied gene is just one of many possible factors behind atrial fibrillation, which is also greatly influenced by the individual's lifestyle.

In addition, to better demonstrate the effect of the studied gene, the gene defect has been designed to be stronger in the test fish than commonly seen in humans.

Better control procedures

The improved understanding of the disease nevertheless provides greater insight into the reason why some atrial fibrillation medications may not always work as well as one might wish.

Therefore, Pia Lundegaard hopes that the result of the new research will be that more practitioners reconsider the possible causes behind rhythm disorders.

"The rhythm disorder may be secondary to what is actually the problem. We hope that in the future, we can develop better control procedures

that will prevent some people's hearts from being worn down for a long time and eventually fail," she says.

The next step for the research group is to investigate other genes associated with atrial fibrillation. Likewise, the group will investigate whether antioxidants other than NAC can prevent the disorder.

More information: Michelle M. Collins et al, Early sarcomere and metabolic defects in a zebrafish pitx2c cardiac arrhythmia model, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1913905116

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