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Broken heart syndrome markers could help identify those at risk

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Scientists have identified two key molecules which play a role in the development of Takotsubo syndrome, known as broken heart syndrome.

Researchers from Imperial College London found that increased levels of two small molecules that regulate how genes are decoded, called microRNAs, increase the chance of suffering from Takotsubo syndrome.

The two microRNAs, named -16 and -26a, have previously been detected in the blood of patients with Takotsubo syndrome, but it was not known until now if they were involved in development of the disease.

But the latest research, funded by the British Heart Foundation and published in the journal *Cardiovascular Research*, may help scientists to better understand the disease as well as potentially leading to new ways to identify and treat those at risk.

Professor Sian Harding, Professor of Cardiac Pharmacology at Imperial's National heart & Lung Institute, said: "Takotsubo syndrome is a serious condition, but until now the way it occurs has remained a mystery. We don't understand why some people respond in this way to a sudden emotional shock while many do not.

"This study confirms that prior stress, and the microRNAs associated with it, can predispose a person to developing takotsubo syndrome in situations of future stress. Stress comes in many forms and we need further research to understand these chronic stress processes."

Mysterious condition

Takotsubo syndrome is a sudden form of acute heart failure which is estimated to affect around 2,500 people in the UK each year and is mainly seen in post-menopausal women. It can cause the same symptoms as a heart attack, and although the coronary arteries are not blocked, the risk of complications is similar to those of an actual heart attack.

It's not yet fully understood what causes Takotsubo syndrome, but it is usually brought on by emotional or physical stress such as the loss of a loved one, leading to it's common name of 'broken heart syndrome." Sharp rises in adrenaline caused by an acute stress like bereavement are known to be the trigger for a loss of movement in part of the heart wall, which then causes the acute heart failure. There are currently no treatments to prevent a repeat attack, which can occur in these patients.

In the study, researchers looked at both human and rat heart cells, measuring how they respond to adrenaline after exposure to the two molecules. When they looked at heart cells that had been treated with the microRNAs, they saw the cells were more sensitive to adrenaline and more likely then to develop loss of contraction. Takotsubo-like changes were therefore seen at lower levels of adrenaline.

MicroRNAs -16 and -26a are linked to depression, anxiety and increased stress levels. These new findings could provide a link between long term stress and the dramatic Takotsubo response to a sudden shock.

Identify those at risk

The team explains that in future, a blood test measuring levels of these molecules could be developed for use in identifying those at risk of an episode of Takotsubo syndrome. The microRNAs could also be used as a potential drug target.

Professor Metin Avkiran, Associate Medical Director at British Heart Foundation said: "Takotsubo syndrome is a sudden and potentially catastrophic heart problem but our knowledge about what causes it remains limited. As such, it is vital that we learn more about this neglected condition and develop new ways of preventing and treating it.

"This research is not only a crucial step towards better understanding of

this mysterious disease but also could provide new ways to identify and treat those at risk of Takotsubo. We now need further research determine if drugs that block these microRNAs could be the key to avoiding broken hearts."

More information: E L Robinson et al, Dissecting the transcriptome in cardiovascular disease, *Cardiovascular Research* (2021). DOI: 10.1093/cvr/cvab117

Provided by Imperial College London