Medical Xpress

Uncovering links between mental stress and physical health, including cardiovascular disease

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In June 2016, the German national football team was gearing up to face Slovakia in the European championship. With pulses set to race among

thousands of fans in the crunch match in host country France, a group of scientists in Germany was watching with interest.

Their aim? To explore the link between short-term, acute mental stress and physical effects, including heart attacks and strokes. The cardiovascular diseases related to such medical emergencies are the leading cause of death worldwide, claiming 18 million lives annually.

Risk triggers

While advances have been made in treating risk factors like diabetes and obesity, much remains unknown about stress-connected triggers, according to Professor Hendrik Sager, a cardiologist at the Technical University of Munich in Germany.

"This urgent need for action motivated me to explore the contribution of non-classical risk factors such as mental stress," said Sager.

He led a research project exploring how acute mental stress causes severe coronary troubles. Called STRATO, the project wrapped up in January 2024 after six years.

The Germany-Slovakia football match took place a year and a half before the February 2018 start of STRATO. The Germans won 3-0.

The group of scientists, including Sager, arranged for blood samples to be taken from 35 healthy fans before and immediately after the game. The experiment was part of information gathering for STRATO, which analyzed the results.

When the team examined the blood samples, they showed a rapid depletion of white blood cells known as leukocytes.

Plaque attack

Investigating further, the scientists found that the same effect occurred in mice when mental stress was induced in them by restricting their movement. Using cell-tracking methods, the team learned that the lost leukocytes were taken up by tissues, including the heart.

This can cause fatty deposits called plaques in arteries to rupture, possibly leading to a heart attack or other coronary troubles. Contributors to plaque build-up include high-cholesterol diets, smoking, obesity and diabetes.

"Plaque rupture occurred twice as often in stressed over non-stressed mice," said Sager. "We now have an underlying biological mechanism for how acute stress precipitates cardiovascular events."

He believes the redistribution of leukocytes to the heart, lungs and skin may have evolved in humans' ancestors to boost survival chances under threat by providing more oxygen to organs or preparing injured tissues for regeneration.

STRATO also looked into measures for reducing stress-related effects.

The team found that pre-treating mice with certain anti-inflammatory antibodies achieved this by blocking molecules that aid leukocyte movement.

Early influences

At the other end of the scale are longer-term links between early-life stress, or ELS, and conditions in later life.

Another project has been trying to unravel these connections. Called EarlyCause, it is due to end on 30 June 2024 after four and a half years.

EarlyCause researchers have focused on three ELS-linked mental and physical conditions: depression, coronary heart disease and diabetes.

These stresses include maternal depression during pregnancy, child abuse, parental loss and socioeconomic deprivation. More than half of children may experience some form of ELS, according to a 2022 study.

Professor Karim Lekadir, who researches artificial intelligence in medicine at the University of Barcelona in Spain, runs EarlyCause.

He said that knowledge about how stresses lead to later-life conditions is limited, partly because of the difficulty of establishing links to illnesses that may appear decades afterwards.

"It's not necessarily intuitive that suffering from psychological adversity in childhood would lead to cardiovascular disease 50 years later," said Lekadir. "And it's not a trivial thing to study."

Surprise finding

The project's researchers have conducted experiments on mice, rats and cells, analyzed existing human data and employed machine-learning techniques.

The work has uncovered potential biological pathways connecting ELS to later disease. These involve the likes of impaired response to glucose, alterations in metabolism and tissue inflammation, and changes in the make-up of gut bacteria.

One finding is that people who endure ELS appear likelier to develop

multiple conditions rather than just one.

"That's surprising because, intuitively, it would seem easier to have just one disease," said Lekadir. "It also suggests that early-life stress has a strong long-term mental and physical impact."

The finding lends urgency to tracking the effects of ELS. The team has built machine-learning models to help track people at risk.

"Those models were promising," said Lekadir. "They showed that you can integrate all this data and do risk-profiling. We need to look more into prevention through screening, identifying people who are at risk and monitoring them."

The emergence of multiple conditions in people who have faced ELS suggests close connections between causes. That may help with tackling more than one at a time, according to Lekadir.

"In a way, that's good news because you could potentially attack a single mechanism rather than the diseases separately," he said.

More information:

- STRATO
- EarlyCause
- EU health research and innovation

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