Chronic stress induces fatal organ dysfunctions via a new neural circuit

Hokkaido University researchers revealed that fatal gut failure in a multiple sclerosis (MS) mouse model under chronic stress is caused by a newly discovered nerve pathway. The findings could provide a new therapeutic strategy for the intractable disease, particularly progressive MS, which has no therapeutic strategy at present.

MS affects an estimated 2.5 million people worldwide and causes motor dysfunction, impaired vision and gastrointestinal failures. It is an autoimmune condition of the central nervous system (CNS) mediated by immune cells called autoreactive CD4+ T cells. In EAE mouse models, these pathogenic CD4+ T cells can cause an MS-like when transfused intravenously to healthy mice.

In previous studies using EAE mouse models, Professor Masaaki Murakami of Hokkaido University and his colleagues revealed autoreactive CD4+ T cells cross the blood-brain barrier at specific sites and cause inflammation in the CNS, including the brain and spinal cord. The emergence of a “gateway” for autoreactive CD4+ T cells to cross the barrier was caused by regional neural activation at those sites, which is triggered by specific sensory-sympathetic interactions. They termed these phenomena as gateway reflexes and have now published on at least three: the gravity-, electric-, and pain-gateway reflexes.

In the present study, the team and their collaborators in Japan [https://www.dotemirates.com/en/posts/tag/2333534] and Germany [https://www.dotemirates.com/en/posts/tag/2333497] investigated the possible relations between the micro-inflammation in the brain, and stress-related organ failures. They put healthy mice under stress by disturbing their sleep or by rearing them on wet bedding. The transfer of pathogenic CD4+ T cells under the stress caused severe symptoms such as gastrointestinal failures and even sudden death. Cell transfer alone did not cause these symptoms. Subsequent investigations revealed a complex nerve-related mechanism behind this process.

The injected pathogenic CD4+ T accumulated around blood vessels in two specific sites at the center of the brains of the stressed mice. Micro-inflammation developed around specific blood vessels, and the inflamed sites then released a small molecule called ATP that switched on a nerve pathway that is normally turned off. This switch led to gut dysfunctions, bleeding and death. Also, the bleeding led to increased levels of potassium in the blood, one of factors leading to heart failure.

The team was able to prevent gut failure by suppressing inflammation in the brain or blocking nerve pathways from the brain to the gut. The results suggest that tiny areas of inflammation around some specific vessels in the brain, which are known to happen in various brain diseases including multiple sclerosis, are a risk factor for organ dysfunctions including severe gut and heart failure.

"These results demonstrate a direct link between brain micro-inflammation and fatal gastrointestinal diseases via the establishment of a new neural pathway under certain conditions," says Masaaki Murakami. "Micro-inflammation in the brain is also seen in Alzheimer’s disease and Parkinson’s disease. So it’s of particular interest to investigate possible connections between brain micro-inflammations and organ dysfunctions, including those within the brain, in those patients."

The study was published in the journal eLife.

Booze glorified in YouTube videos viewed by millions: Study

YouTube videos featuring alcohol nearly always promote the "fun" side of drinking and are viewed by millions of users which may include teenagers and children, scientists say.

Researchers from the University of Pittsburgh in the US looked at 137 YouTube videos that featured alcohol brands popular with underage drinkers - from beer to vodka to cognac. Together, the videos had been viewed nearly 97 million times.

Most often - 40 per cent of the time - the videos were traditional advertisements.

Others were "guides," in which a host showcased a particular alcohol, discussing its merits and offering serving suggestions.

About 10 per cent featured men showing off their "chugging" prowess, according to the study published in the Journal of Studies on Alcohol and Drugs.

There is no way of knowing how many of those millions of viewers were underage kids, according to lead researcher Brian Primack, from the University of Pittsburgh.

"Our aim is not to say we should be censoring this. However, knowing about this content should help us develop appropriate educational programmes," said Primack.

The alcohol ads were usually uploaded by ordinary YouTube users, rather than manufacturers. However, the industry is never completely out of the picture, he said.

Companies create their ads to be funny or otherwise engaging, and that may be partly with the hope that people will share them on social media.
Instead, he suggested that parents help their kids be more savvy about alcohol advertising. They could point out how companies can try to manipulate people—by, for instance, portraying alcohol as a key ingredient to socialising and having fun.

"Parents can be important purveyors of media literacy. They can help their kids become more critical thinkers about what they see in ads," Primack said.