Chronic stress induces fatal organ dysfunctions via a new neural circuit

Date: August 21, 2017
Source: Hokkaido University
Summary: New research reveals the mechanisms behind the effects of chronic stress and tiny inflammations in the brain on fatal gut failure.

Share:

FULL STORY

Micro inflammation developed at specific sites in the brain (top panel). Pathological analysis of the stomach showed damage to tissues in the stomach (bottom right) compared to mice not under stressful conditions (bottom left).


New research reveals the mechanisms behind the effects of chronic stress and tiny inflammations in the brain on fatal gut failure.

Hokkaido University researchers revealed that fatal gut failure in a multiple sclerosis (MS) mouse model, EAE, 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 a MS-like disease 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 sensor-
Chronic stress induces fatal organ dysfunctions via a new neural circuit — ScienceDaily

ry-sympathetic interactions. They termed these phenomena as gateway reflexes and have published on at least three, the gravity-, electric-, and pain-gateway reflexes.

In the present study, the team and their collaborators in Japan and Germany investigated the possible relations between chronic stress, 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 or stress alone did not cause these symptoms. Subsequent investigations revealed a complex nerve-related mechanism behind this process.

The injected pathogenic CD4+ T cells 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 failure. Also, the bleeding led to increased levels of potassium in the blood, which was 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 stress,” 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 itself, in those patients.”

The study was published in the journal eLife.

Story Source:
Materials provided by Hokkaido University. Note: Content may be edited for style and length.

Journal Reference:

Cite This Page: MLA APA Chicago


RELATED STORIES

Muted Stress Response Linked to Long-Term Cannabis Use
July 31, 2017 — A new study reveals a dampened physiological response to stress in chronic cannabis users. This is the first study to examine the effects of acute stress on salivary cortisol levels in chronic ... read more

Research Examines Role of Early-Life Stress in Adult Illness
Oct. 24, 2016 — Chronic exposure to psychosocial stress early in life can lead to an increased vulnerability later in life to diseases linked to immune dysfunction and chronic inflammation, including arthritis, ... read more

https://www.sciencedaily.com/releases/2017/08/170821102733.htm
Link Between Intestinal Bacteria, Depression Found

July 28, 2015 — The complex mechanisms of interaction and dynamics between the gut microbiota and its host have been illuminated by recent research. Data show that relatively minor changes in microbiota profiles or ...
read more »

Acute Stress Primes Brain for Better Cognitive and Mental Performance

Apr. 16, 2013 — Chronic stress is known to cause major health problems, yet acute stress can be good for you. A new study shows why. Stress generates new nerve cells in the brain that, two weeks later, help you ...
read more »

FROM AROUND THE WEB

Friendly Gut Bacteria May Trigger MS
Catharine Paddock PhD, Medical News Today, 2011

Meningeal inflammation and multiple sclerosis
Li-Ping Liu, Neuroimmunology and Neuroinflammation, 2016

Dietary fatty acids may influence flare-ups in MS, autoimmune disease
Catharine Paddock PhD, Medical News Today, 2015

What Is My Life Expectancy If I Have Lupus?
Hannah Nichols, Medical News Today

Hypoxia Inducible Factor-1α in Astrocytes and/or Myeloid Cells Is Not Required for the Development of Autoimmune Demyelinating Disease
Natacha Le Moan et al., eNeuro, 2015

Electrical Stimulation: A Panacea for Disease?
IEEE Pulse, 2016

What is the vagus nerve?
Medical News Today

Untargeted Plasma Metabolomics Identifies Endogenous Metabolite with Drug-like Properties in Chronic Animal Model of Multiple Sclerosis
Laila M. Poisson et al., Journal of Biological Chemistry, 2015