

Inflammation may be common thread behind nervous and heart rhythm problems in cirrhosis

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Liver cirrhosis is the seventh leading cause of death in the United States, taking 25,000 lives per year. It is often the result of alcohol over-consumption or exposure to hepatitis C, either of which can damage the liver and prevent it from filtering toxins. These toxins then accumulate in the blood stream and eventually reach the brain where they disrupt neurological and mental performance, a condition known as hepatic encephalopathy.

Individuals with cirrhosis are also susceptible to a change in heart rhythm (decreased heart rate variability). Since cirrhosis, hepatic encephalopathy and heart rate variability are known to be associated with inflammation, researchers have examined what role cytokines (inflammatory molecules) play.

A new study from The American Physiological Society suggests that these cytokines can lead to both the neurological and cognitive abnormalities and changes in heart rhythm in patients with cirrhosis. The results of the study may also apply to other conditions where heart rate variability is also decreased, such as bipolar disorder and post-menopausal depression.

The study, "Decreased heart rate variability in patients with cirrhosis relates to the presence and severity of hepatic encephalopathy," was carried out by Ali R. Mani, Sara Montagnese, Clive D. Jackson,

Christopher W. Jenkins, Ian M. Head, Robert C. Stephens, Kevin P. Moore and Dr. Morgan. All are affiliated with the University College London Medical School, with the exception of Mr. Jackson, who is with the Royal Free Hospital, London. The study appears in *The American Journal of Physiology-Gastrointestinal and Liver Physiology*.

Three measurements

The study involved 80 patients suffering cirrhosis of the liver. Sixty-five (81%) of the patients had cirrhosis because of chronic alcohol abuse, although none had abused alcohol within three months of the study. Of the remaining 15 participants, seven had developed cirrhosis from chronic hepatitis while the remaining eight had developed the disease in various other ways. The participants were compared to a control group of 11 healthy people.

First, the researchers tested for the presence of hepatic encephalopathy by examining the patient's mental state. They conducted various cognitive tests and obtained an electroencephalogram (EEG). After examination, the study participants were classified as having either overt hepatic encephalopathy, minimal hepatic encephalopathy or no encephalopathy.

Second, they measured heart rate variability using an electrocardiogram. A healthy heart varies the rate at which it beats depending upon a variety of factors. For example, the heartbeat accelerates when inhaling and decelerates when exhaling. Reduced heart rate variability -- that is, a more regular heartbeat -- has been associated with systemic inflammation and with various neuropsychiatric conditions, such as bipolar disorder.

Third, in a subgroup of 18 patients, the researchers also measured for cytokines, which circulate in the blood as part of the inflammation.

Among these cytokines was interleukin-6, a substance that plays a role in cell signaling as part of the body's response to inflammation.

Connected to inflammation

When the researchers began the study, they knew that cirrhosis of the liver leads to hepatic encephalopathy, systemic inflammation and reduced heart rate variability. It was not known whether and how they were related.

Their first major finding was that reduced heart rate variability and the presence of hepatic encephalopathy were very strongly connected. The second major finding was that blood levels of the inflammatory cytokines (including interleukin-6 levels) closely paralleled both the degree of neuropsychiatric impairment and reduced heart rate variability. This suggests that inflammatory response plays a role in these impairments.

Additional Findings

The researchers also found that:

- In patients with cirrhosis, there were significant concentrations of cytokines. By contrast, concentrations were below the level of detection among healthy volunteers.
- There was no significant differences in heart rate variability between patients with alcohol-related cirrhosis and patients with cirrhosis due to other reasons, such as chronic viral hepatitis.
- The risk of death increased as heart rate variability decreased.

The authors concluded that inflammation plays a role in both the reduction in heart rate variability and the development of hepatic

encephalopathy in patients with cirrhosis. In subsequent, yet unpublished research, they have found that treatment for hepatic encephalopathy not only improves mental function but also improves heart rate variability. This treatment also reduces blood levels of cytokines providing further evidence of a link between systemic inflammation, mental and cardiac function in this patient group.

Source: American Physiological Society

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