

Brain inflammation in veterans with Gulf War illness

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In a new discovery, researchers at Massachusetts General Hospital (MGH) have detected widespread inflammation in the brains of veterans diagnosed with Gulf War Illness (GWI). These findings, published online in the journal *Brain, Behavior, and Immunity* on February 3, could serve as a guidepost for identifying and developing new therapies for people with GWI, as well as many other chronic conditions that have



recently been linked to inflamed brain tissue, or neuroinflammation.

About 30 percent of soldiers who fought in the 1991 Gulf War suffer from GWI. Veterans with GWI display a range of symptoms, including fatigue, chronic pain and cognitive problems such as memory loss. The cause of GWI is unknown, but several potential culprits are suspected. They include exposure to nerve gas, as well as medicine given to protect against this neurotoxin; exposure to pesticides; and the stress of extreme temperature changes, <u>sleep deprivation</u> and <u>physical exertion</u> during deployment

Many of the symptoms of GWI overlap with those of another condition, fibromyalgia, notes the senior author of the study, Marco Loggia, Ph.D., whose laboratory at MGH's Athinoula A. Martinos Center for Biomedical Imaging focuses on understanding the brain mechanisms of pain and neuroinflammation in humans. Last year, Loggia and his colleagues showed in another study that fibromyalgia patients have extensive neuroinflammation. "So, we asked, Do veterans who have Gulf War Illness demonstrate evidence of neuroinflammation, too?"

To find out, Loggia and his team collaborated with the Gulf War Illness Consortium at Boston University, which helped them to recruit Gulf War veterans. The study included 23 veterans, of whom 15 had GWI, as well as 25 healthy civilian subjects. All study participants' brains were scanned using positron-emission tomography (PET) imaging, which measured levels of a molecule called translocator protein that rises in the presence of neuroinflammation. The scans detected little evidence of neuroinflammation in the healthy controls and veterans who were free of GWI. By contrast, the study found extensive inflammation in the brains of veterans with GWI, "particularly in the cortical regions, which are involved in 'higher-order' functions, such as memory, concentration and reasoning," says Zeynab Alshelh, Ph.D., one of two research fellows in Loggia's lab who co-led the study. "The neuroinflammation looked very



similar to the widespread cortical inflammation we detected in fibromyalgia patients," says Alshelh.

What might cause neuroinflammation? The <u>central nervous system</u> has legions of immune cells that protect the brain by detecting bacteria, viruses, and other potentially harmful agents, then producing inflammatory molecules to destroy the invaders, explains Loggia. However, while this response can be beneficial in the short term, it may become exaggerated, says Loggia, "and when that happens, inflammation becomes pathological—it becomes the problem."

Research by Loggia's lab and other investigators has also implicated neuroinflammation in a number of additional conditions, including <u>chronic pain</u>, depression, anxiety, autism, <u>amyotrophic lateral sclerosis</u> (ALS), multiple sclerosis (MS), Huntington's disease and migraine. The findings of the GWI study, says Loggia, "could help motivate a more aggressive evaluation of neuroinflammation as a potential therapeutic target."

More information: Zeynab Alshelh et al, In-vivo imaging of neuroinflammation in veterans with Gulf War illness, *Brain, Behavior, and Immunity* (2020). DOI: 10.1016/j.bbi.2020.01.020

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