

Researchers link Gulf War Illness to physical changes in brain fibers that process pain

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Researchers at Georgetown University Medical Center (GUMC) have found what they say is evidence that veterans who suffer from "Gulf War Illness" have physical changes in their brains not seen in unaffected individuals. Brain scans of 31 veterans with the illness, compared to 20 control subjects, revealed anomalies in the bundles of nerve fibers that connect brain areas involved in the processing and perception of pain and fatigue.

The discovery, published online March 20 in *PLOS ONE*, could provide insight into the mysterious medical symptoms reported by more than one-fourth of the 697,000 veterans deployed to the 1990-1991 Persian Gulf War, the researchers say. These symptoms, termed Gulf War Illness, range from mild to debilitating and can include widespread pain, fatigue, and headache, as well as cognitive and gastrointestinal dysfunctions.

Although these veterans were exposed to [nerve agents](#), pesticides and herbicides, among other [toxic chemicals](#), no one has definitively linked any single exposure or underlying mechanism to Gulf War Illness according to the scientists.

This is the first study to show veterans, compared to unaffected subjects, have significant axonal damage. Bundles of [axons](#), which form the brain [white matter](#), are akin to telephone wires that carry [nerve impulses](#) between different parts of the gray matter in the brain. The researchers found that damage to the right inferior fronto-occipital fasciculus was significantly correlated with the severity of pain, fatigue, and tenderness.

"This tract of axons links cortical gray matter regions involved in fatigue, pain, emotional and reward processing. This bundle also supports activity in the ventral attention network, which searches for unexpected signals in the surrounding

environment that may be inappropriately interpreted as causing pain or being dangerous. Altered function in this tract may explain the increased vigilance and distractibility observed in veterans." says lead author Rakib Rayhan, a researcher in the lab of the study's senior investigator, James Baraniuk, MD, a professor of medicine at GUMC.

In this Department of Defense-funded study, the research team used a form of functional magnetic resonance imaging (fMRI) called diffusion tensor imaging. This imaging method examines patterns of water diffusion in the brain to look for changes in the integrity of white matter, which is not seen on regular MRI scans. "This provides a completely new perspective on Gulf War Illness," says Baraniuk. "While we can't exactly tell how this tract is affected at the molecular level—the scans tell us these axons are not working in a normal fashion."

Although preliminary, "the changes appear distinct from multiple sclerosis, major depression, Alzheimer's disease and other neurodegenerative diseases," says Rayhan. "These novel findings are really exciting because they provide validation for many veterans who have long said that no one believes them."

The results must be replicated, say its authors, but for the first time a potential biomarker for Gulf War Illness may be on the horizon as well as a possible target for therapy aimed at regenerating these neurons.

"Pain and fatigue are perceptions, just like other sensory input, and Gulf War Illness could be due to extensive damage to the structures that facilitate them," says Rayhan. "Some of the veterans we studied feel pain when doing something as simple as putting on a shirt. Now we have something to tell them about why their lives have been so greatly

affected."

More information:

[dx.plos.org/10.1371/journal.pone.0058493](https://doi.org/10.1371/journal.pone.0058493)

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