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GI neuroimmune disruption contributes to Gulf War Illness

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Many Persian Gulf War veterans experience Gulf War Illness (GWI), a chronic condition with symptoms ranging from gastrointestinal to neurological. While exposure to the anti-nerve gas pyridostigmine bromide (PB) is linked to the development of GWI, the exact cause and mechanisms of the illness remain unclear. Recently, an animal study published in *The FASEB Journal* tested the hypothesis that exposure to PB contributes to the development of GWI by disrupting the neural and immune systems of the intestine.

A team of researchers led by Brian D. Gulbransen, Ph.D., a Michigan State University (MSU) Foundation Professor working in the university's neuroscience program, conducted the experiment. The team used male and female mice that had been exposed to either normal drinking water or water containing one of two concentrations of PB for seven days.

They assessed the effects of the drug on the gut in vivo every three days and recorded body weight throughout the experiment. At days 7 and 30, they harvested colonic and brain tissue to analyze the drug's acute and chronic effects on gut functions, immune responses in the gut and brain, and the structure and function of the enteric nervous system, which directs the function of the gastrointestinal tract.

The study's key results showed that exposing mice to PB in a way that mirrored Gulf War veterans' exposure caused them to develop long-lasting gastrointestinal issues and immune system changes in the gut and brain. Overall, the work demonstrates that exposure to PB alone is

sufficient to cause broad alterations in brain-gut communication that could contribute to the development of GWI. Interestingly, the study also found that PB affects male and female animals differently, a finding that could indicate distinct mechanisms underlying the development of the syndrome in men and women.

"Even though our male and female animals were treated the same, we found exciting sex-dependent differences that can give us a better idea of how to address treatment in patients," Gulbransen stated. "Understanding the sex-specific mechanisms underlying this disorder may yield important insights that lead to specific and novel therapies."

"These findings provide an entirely plausible foundation for this condition and thus are a sentinel for future monitoring and perhaps improved treatments, and even neutralizing agents for battlefield deployment," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*.

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