Two studies of veterans link PTSD to accelerated aging

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Mark Miller (left) and Erika Wolf, authors of two studies that show premature

aging in veterans with PTSD. Photo by Jackie Ricciardi

We've all heard of people "aging overnight" after a traumatic event. Scientists actually have a word for this phenomenon: "Marie Antoinette Syndrome," named for the French queen. When she was captured after fleeing Paris and sentenced to death by guillotine, observers claimed her hair turned white from shock.

While accounts of the queen's hair may just be legend, scientists have long suspected that chronic psychological stress—triggered by events like war, abuse, or imprisonment—may accelerate aging, leading to early onset of age-related disease or even premature death. Now, two studies from researchers at the Boston University School of Medicine (MED), jointly funded by the US Department of Veterans Affairs (VA) and the National Institute of Mental Health, report significant links between post-traumatic stress disorder (PTSD) in veterans and accelerated aging. Many vets with PTSD are aging too fast, at a surprisingly young age.

"We're seeing evidence, on multiple levels, of accelerated aging among very young veterans—people in their early 30s," says Erika Wolf, a MED assistant professor of psychiatry and clinical research psychologist at the US Department of Veteran Affairs' National Center for PTSD, who is lead author on the two studies. "These could snowball into major health problems down the road."

"The idea that traumatic events can have a physical effect on people has been around for a long time," says Mark Miller, associate professor of psychiatry at MED and senior author on the two studies. "Observations suggest that traumatic stress starts a cascade of biological consequences that can produce visible signs of aging. More recent research shows how this is happening on a cellular level, and for the first time we have the

methods to actually see it in a person's DNA."

The first study, published online on September 30, 2015, in the journal Psychoneuroendocrinology, used new tools for examining DNA for signs of aging and comparing it to a person's actual age. The tools, developed in 2013 by scientists at the University of California, Los Angeles, and the University of California, San Diego, look at specific areas of a person's genome and note how they are methylated—tagged with a tiny molecule of one carbon and three hydrogen atoms, known as a methyl group. Methylation is one of the primary ways that the body switches genes on and off, and certain patterns of DNA methylation correlate to a person's chronological age.

For the Psychoneuroendocrinology study, Wolf, who is also funded by the VA Clinical Science Research & Development Career Development Award, examined data from 281 veterans, studied at the VA's Translational Center for TBI and Stress Disorders (TRACTS) database. TRACTS has collected health information—including brain scans, blood tests, and the results of comprehensive psychological exams—from 450 veterans who have been exposed to trauma. She found small but significant evidence that veterans with PTSD had accelerated aging of their DNA.

"As we age, what we see in the DNA is a lot of 'flip-flopping'—regions that are methylated become unmethylated, and vice versa," says Wolf. This pattern appears across genes involved with cell death, cardiac function, neurogeneration, and other cellular processes. "There's a lot of variability, but it makes sense that they are involved with aging."

The second study, published online in January 2016 in the journal Biological Psychiatry, examined broader, age-related health consequences of PTSD. Specifically, Wolf looked at metabolic syndrome—a constellation of symptoms including obesity, high blood

pressure, abnormal blood lipids, and high blood sugar that can contribute to Type 2 diabetes, coronary artery disease, and even neurodegenerative diseases like Alzheimer's. Metabolic syndrome is elevated among veterans, says Wolf, with an estimated 25 percent affected. That number may be as high as 40 percent among people with PTSD.

Wolf wondered exactly how PTSD correlated to metabolic syndrome, and whether the two together led to reduced cortical thickness—a shrinking of specific brain areas responsible for things like emotional regulation and memory. Again using data from TRACTS, Wolf examined health information from 346 military veterans who had deployed to Iraq or Afghanistan. She found that PTSD was directly associated with metabolic syndrome, and that metabolic syndrome was strongly associated with reduced cortical thickness.

Wolf hopes to continue the research looking at longitudinal data, so she can see how this accelerated aging proceeds over a decade or more. She also wants to expand the research to include Vietnam veterans, who could provide an even longer-term view.

The findings are significant, says Wolf, because they highlight a problem—metabolic syndrome—that is not usually considered in treating PTSD and is "ripe for intervention." Furthermore, says Miller, they suggest that clinicians may need to expand their repertoire of treatments for PTSD to target sleep, diet, and exercise.

"A lot of research is looking at the causes and risk factors of PTSD," says Miller. "Our research is looking at the other side of the PTSD puzzle—what are the consequences for the body?"

"Traditionally, treatment for PTSD involves psychotherapy that focuses on the memory of traumatic events," adds Miller. "That's an undeniably relevant and important part of treatment. But these studies are suggesting

that the clinical picture of PTSD is much bigger than a problem with somebody's memory. The profound biological changes that accompany it affect not just the mind and memory, but the whole body."

More information: Erika J. Wolf et al. Accelerated DNA methylation age: Associations with PTSD and neural integrity, *Psychoneuroendocrinology* (2016). DOI: 10.1016/j.psyneuen.2015.09.020

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