Study finds genetic basis for re-experiencing symptoms in PTSD

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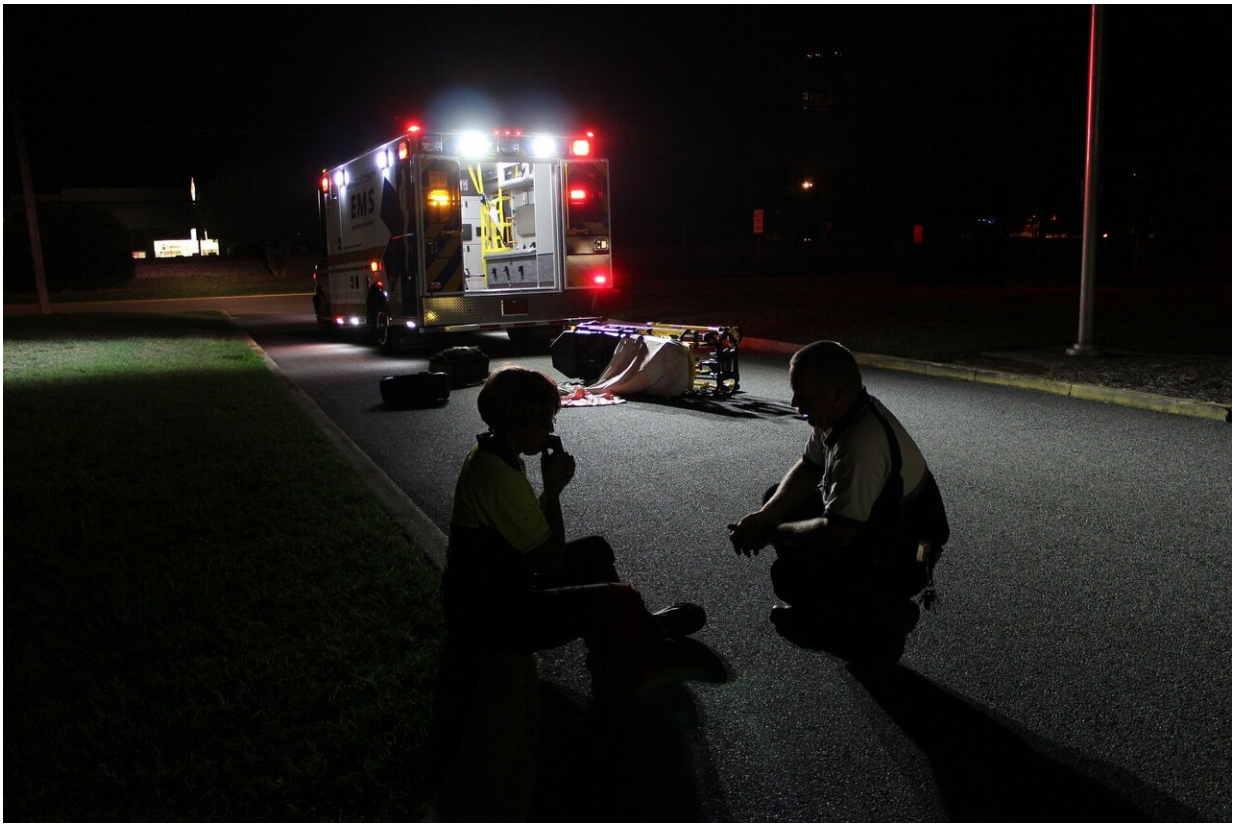

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A study based on the Million Veteran Program of the U.S. Department of Veterans Affairs has identified multiple locations in the human genome related to the risk of re-experiencing traumatic memories, the

most distinctive symptom of posttraumatic stress disorder.

Researchers from the VA Connecticut Healthcare System, Yale University School of Medicine, the VA San Diego Healthcare System, and the University of California San Diego collaborated with colleagues on this large genome-wide association study of more than 165,000 veterans.

In addition to providing valuable information on genetic factors that may put people at risk for PTSD, the study also demonstrates "the immediate utility of the MVP sample for disorders prevalent in U.S. veterans," say the researchers.

The results appear online July 29, 2019, in the journal *Nature Neuroscience*.

PTSD is usually considered to have three main clusters of symptoms: re-experiencing, avoidance, and hyperarousal. Avoidance and hyperarousal are common to other anxiety conditions as well, but re-experiencing is largely unique to PTSD. Re-experiencing refers to intrusive thoughts, nightmares, and flashbacks of the traumatic event.

Using the vast genetic and health record data available through MVP, the research team set out to identify gene variants that increase the likelihood of PTSD re-experiencing. This study was considerably more powerful than previous PTSD genome-wide association studies (studies that look at the genomes of a large group of people for connections between shared gene variations and medical conditions or other traits) because of a larger sample size.

The researchers compared the genomes of 146,660 white veterans and 19,983 black veterans who had volunteered for MVP.

The study revealed eight separate regions in the genome associated with re-experiencing symptoms among the white veterans. It did not show any significant regions for black veterans, considered separately as a group, because there were far fewer black study participants available, making it harder to draw conclusions. The association between PTSD re-experiencing and common variants in three of these genome regions were highly significant: gene CAMKV, a region near genes KANSL1 and CRHR1, and gene TCF4.

Key results were replicated using the UK Biobank sample, which has about 500,000 participants.

The results also showed genetic overlap between PTSD and many other psychiatric, behavioral, and medical conditions. Two genes previously associated with schizophrenia and bipolar disorder were found to be linked to re-experiencing in PTSD. This could mean that the hallucinations experienced in schizophrenia may share common biochemical pathways with the nightmares and flashbacks of people with PTSD, say the researchers.

The study also revealed that re-experiencing shares genetic risk factors with hypertension. Previous studies found that PTSD and hypertension often occur together. This result suggests that the link could be at the genetic level. The researchers explain that the finding could lead to new drug treatments based on patients' genes. It is possible that hypertension drugs that affect these same genes could be effective for treating PTSD.

The study also adds evidence to a theory of how PTSD develops. A variant located at the gene CRHR1 was linked to PTSD re-experiencing. This gene is involved with the body's stress response. In past studies, biological evidence has linked processes involving CRHR1 to PTSD. The new results provide additional strong evidence in support of the theory that CRHR1 and other genes related to the body's steroid-

hormone stress response are linked to PTSD risk.

All together, the results "provide new insights into the biology of PTSD," say the researchers. They have implications for understanding PTSD risk factors, as well as identifying new drug targets.

More information: Genetics of post-traumatic stress disorder in US veterans, *Nature Neuroscience* (2019). DOI: 10.1038/s41593-019-0447-7

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