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Study finds PTSD interacts with klotho gene, may cause premature aging in the brain

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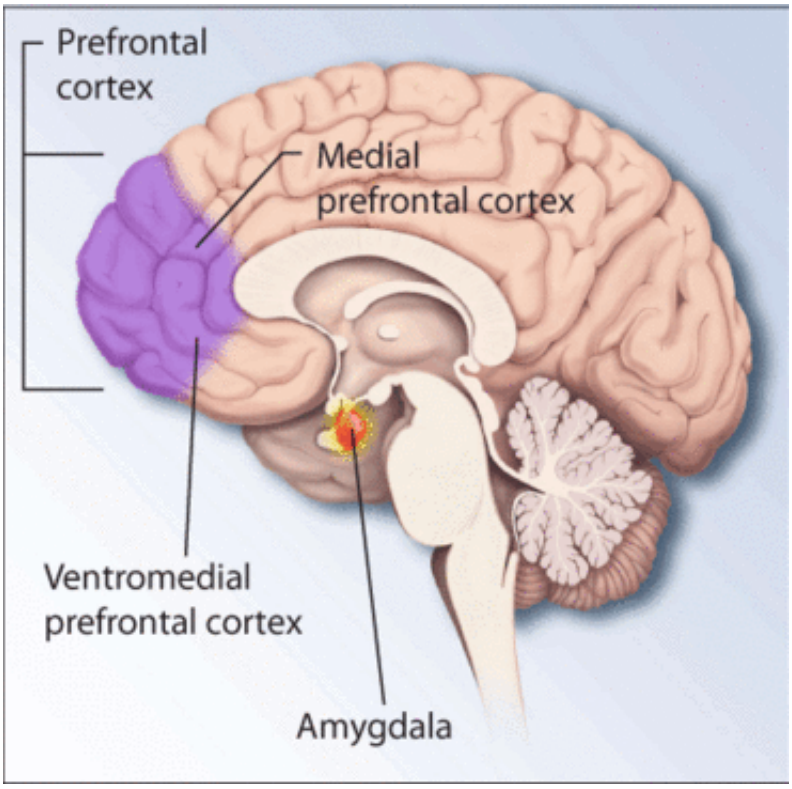

Regions of the brain associated with stress and posttraumatic stress disorder. Credit: National Institutes of Health

Genetics and the environment (including psychiatric stress) may contribute to the pace of cellular aging, causing some individuals to have a biological age that exceeds their chronological age.

Researchers from the National Center for PTSD at VA Boston Healthcare System and Boston University School of Medicine (BUSM) now have found that a variant in the klotho gene, a gene previously associated with longevity, interacts with post-traumatic stress disorder (PTSD) to predict accelerated aging in brain tissue. These same researchers had previously shown this effect in living subjects when epigenetic age (biological age) was measured in blood, but this is the first time it has been studied in brain tissue.

Using data from individuals who donated their brains to the VA National PTSD Brain Bank, the researchers were able to examine how genetic variation and PTSD status interacted with each other to predict biological age and gene expression. They found that older adults with PTSD showed evidence of accelerated epigenetic aging in brain tissue if they had the 'at risk' (variant) at a particular location in the klotho gene. Follow-up molecular experiments led by BUSM co-authors Cidi Chen, Ph.D., research associate professor and Carmela Abraham, Ph.D., professor of biochemistry, showed that this variant regulated the transcription of the klotho gene, suggesting functional consequences of the genetic variant.

Both PTSD and klotho impact inflammation, cardiometabolic conditions and neurodegeneration, including Alzheimer's disease. According to the researchers, better understanding how klotho and PTSD interact and the mechanisms linking both genes and traumatic stress to age-related health conditions is important for the development of novel therapeutics.

"This work allows us to better pinpoint who is at risk for accelerated cellular aging, and possibly, premature disease onset (such as neurodegeneration). This can help to identify the populations at greatest risk so that targeted treatments can be matched to the individuals who need it most. As well, the results point to potential therapeutic targets (klotho) in the development of pharmacological approaches to slow the

pace of cellular aging," adds lead author Erika Wolf, Ph.D., clinical research psychologist for the National Center for PTSD at VA Boston Healthcare System and associate professor of psychiatry at BUSM.

These findings appear online in the journal *Neuropsychopharmacology*.

More information: undefined undefined et al. Klotho, PTSD, and advanced epigenetic age in cortical tissue, *Neuropsychopharmacology* (2020). DOI: 10.1038/s41386-020-00884-5

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