Stress gene dysregulation found in kids after injury from abuse differs from that found after accidents

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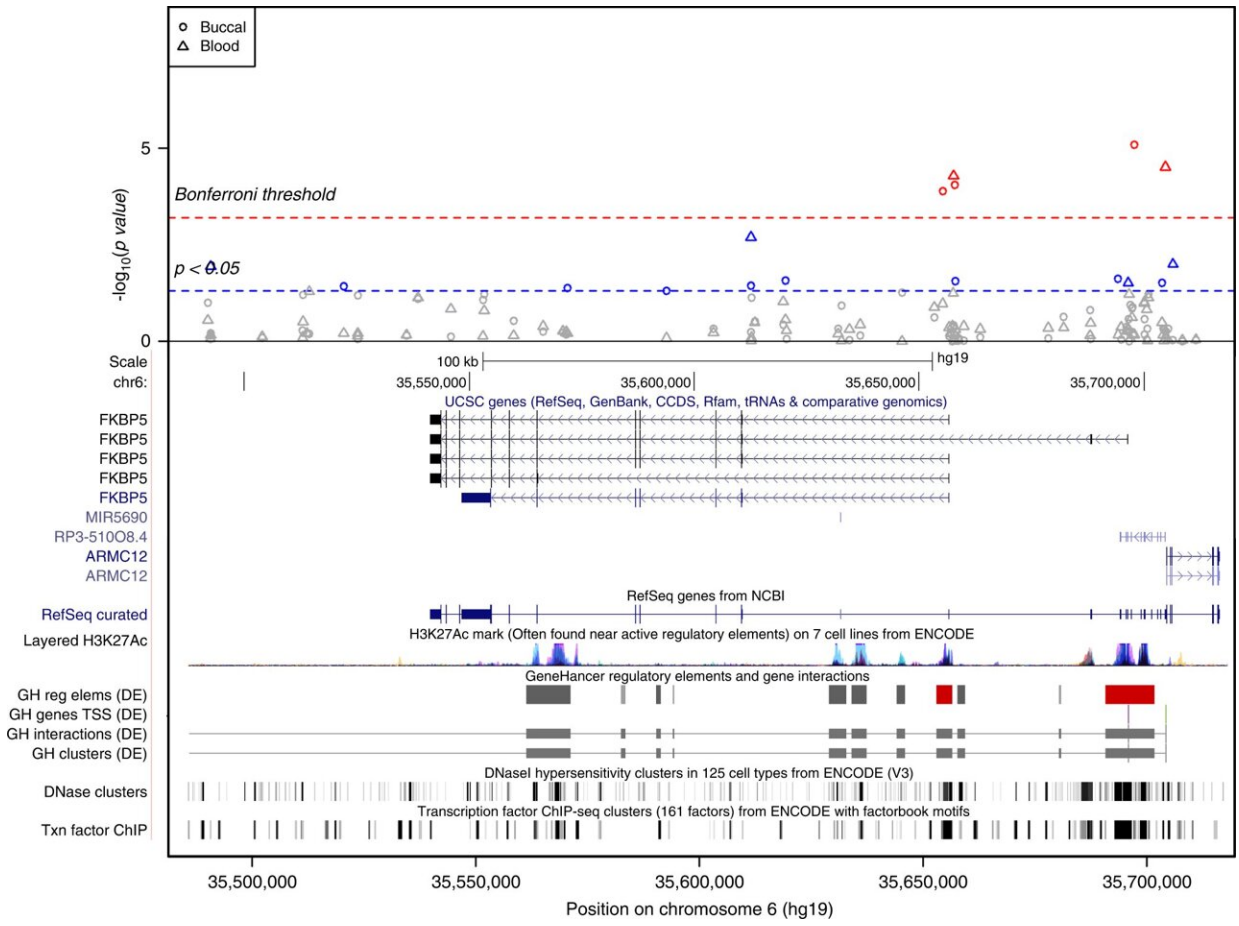

Manhattan-style plot demonstrating the statistical significance (y-axis) and genomic locations (x-axis) of abuse-associated differential DNA methylation at CpGs within the FKBP5 locus (from both buccal and blood cells). Credit: *Pediatric Research* (2023). DOI: 10.1038/s41390-022-02441-w

Epigenetic changes in the regulation of a key gene in the body's stress response system were detected in babies and young children with abusive injuries, as opposed to accidental, according to a pilot study published in the journal *Pediatric Research*.

The epigenome influences levels of gene expression in response to the physical, social and emotional environment, without altering the DNA sequence. Multiple studies in adults have found that traumatic and adverse childhood experiences are associated with epigenetic alterations in the FKBP5 gene, an important regulator of stress response.

This study is the first to find epigenetic changes in the FKBP5 gene at the time of diagnosis in cases of abuse, regardless of injury severity, socioeconomic status, or psychosocial risk factors.

"The epigenetic differences we found in young children who suffered injuries from abuse were striking and may reflect prolonged toxic stress from living in a truly dangerous environment," said senior author Mary Clyde Pierce, MD, Emergency Medicine physician at Ann & Robert H. Lurie Children's Hospital of Chicago and Professor of Pediatrics at Northwestern University Feinberg School of Medicine.

"Unfortunately, the story doesn't end there. Unmitigated stress is linked to adverse health outcomes in adulthood and survivors of childhood abuse experience higher rates of cardiovascular disease, diabetes, cancer, as well as mental health problems."

In the United States, child abuse affects over 650,000 children each year.

The study included 82 acutely injured children younger than 4 years old.

An expert panel classified the injuries as abusive, accidental, or indeterminate. Cheek swabs and blood samples were gathered to measure DNA methylation of the FKBP5 gene (a chemical change that regulates gene activity).

Dr. Pierce and colleagues found that children with abusive injuries had lower methylation of the FKBP5 gene promoter area, which typically correlates with increased gene expression.

"The dysregulation of the stress gene we observed at diagnosis suggests that the biological response to abuse starts very early," said Dr. Pierce. "It is possible, however, that early interventions could reverse the epigenetic alterations in the stress system. More research is needed to confirm our findings and potentially identify an epigenetic signature to see if interventions are working."

More information: Todd M. Everson et al, Epigenetic differences in stress response gene FKBP5 among children with abusive vs accidental injuries, *Pediatric Research* (2023). DOI: 10.1038/s41390-022-02441-w

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