Researchers uncover new biological mechanisms underlying the link between childhood trauma and psychosis

April 17 2023

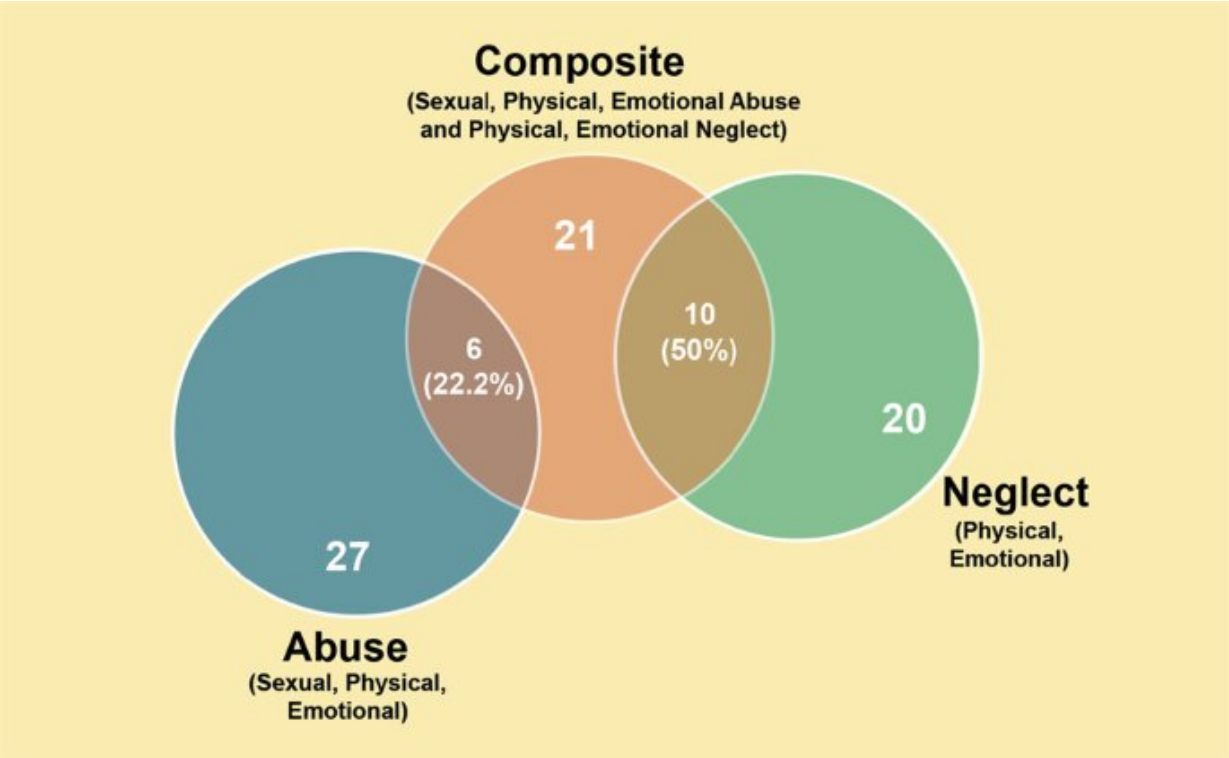

Diagram showing the mediating overlapping genes between composite, abuse and neglect analyses with psychosis. Credit: *Molecular Psychiatry* (2023). DOI: 10.1038/s41380-023-02044-9

New research led by the Institute of Psychiatry, Psychology &

Neuroscience (IoPPN) at King's College London has identified changes on several key genes that may explain why people who experience traumatic events in childhood are at increased risk of psychosis.

Researchers found that people who had experienced childhood trauma such as neglect and/or abuse had differences in their epigenetic marks. "Epi" means "on top of" in Greek. Epigenetics are the chemical markings on DNA that affects its expression. Unlike genetic changes, epigenetic changes do not alter your DNA sequence, but can influence how your body reads a DNA sequence. Epigenetic marks can be influenced by a number of environmental exposures, from everyday experiences to diet and social stress.

Published in *Molecular Psychiatry*, the study is the first to have examined the link between childhood trauma and epigenetic changes in the DNA of people with psychosis. Using samples from the European Network of National Schizophrenia Networks Studying Gene–Environment Interactions (EU-GEI), a multi-center study of genetic and environmental causes of psychotic disorders, researchers examined epigenetic variants across the genome (the entire set of DNA in a human, which in the context of epigenetics refers to the "epigenome") using DNA extracted from blood tissue of 366 patients with first-episode psychosis and 517 healthy controls.

After analyzing 614,719 epigenetic variants, researchers identified a number of epigenetic changes across the epigenome which mediated the association between childhood traumatic events and psychosis. Of particular interest, some of the altered epigenetic marks are found in genes that have not been linked with psychosis and schizophrenia before, whereas others implicated known psychosis- and schizophrenia-related pathways such as the immune system, neural signaling (which are processes involved in the transmission of neurotransmitters from one neuron to another) or histaminergic processes (which are involved in the

beneficial effect of many antipsychotics).

"We conducted the first study which explored the genome to uncover how epigenetic changes mediate the association between early childhood adversity and psychosis. Our findings provide novel evidence that individuals with a diagnosis of psychosis who have experienced childhood traumatic events have altered epigenetic patterns. We identified epigenetic changes at several genes previously implicated in schizophrenia and child abuse, as well as identifying regions on the genome that have not previously been implicated in psychosis and stressful life events," says Dr. Luis Alameda, lead author of the study which is part of his Ph.D. conducted at King's IoPPN.

Researchers also separately explored the epigenome of those who were exposed to childhood abuse and childhood neglect. The findings revealed that the epigenetic profiles are entirely different depending on whether the individual was exposed to abuse or neglect, with no overlap in the genes affected.

"Our study revealed distinct epigenetic marks across the epigenome that were linked with different types of childhood traumatic events and psychosis. We know from previous clinical research that childhood abuse is often linked to psychosis symptoms of hallucinations and delusions, whereas childhood neglect is more often linked to symptoms of social withdrawal or lack of emotion. The findings of this epigenetics study shed light on the potential underlying biological mechanisms of these relationships. It will be interesting for future studies to expand the sample size as well as to other important developmental periods such as adolescence," says Dr. Chloe Wong, Senior Lecturer in Epigenetics at King's IoPPN and senior author of the study.

The research received support from the ESRC Center for Society and Mental Health at King's College London and the National Institute for

Health and Care Research (NIHR) Maudsley Biomedical Research Center, part of the NIHR and hosted by South London and Maudsley NHS Foundation Trust in partnership with King's College London.

Lead author, Dr. Luis Alameda, has recently been awarded the 2022/23 King's Outstanding Thesis Prize for his Ph.D., obtained in June 2022, which explores the epidemiological, clinical and epigenetic mechanism between childhood trauma and psychosis. He will receive the award at the July 2023 graduation ceremony. Dr. Alameda is currently working in Lausanne Switzerland and leads the Treatment and Early Intervention in Psychosis (Tipp) program and is also a visiting clinical research fellow at the IoPPN.

More information: Luis Alameda et al, Exploring the mediation of DNA methylation across the epigenome between childhood adversity and First Episode of Psychosis—findings from the EU-GEI study, *Molecular Psychiatry* (2023). DOI: 10.1038/s41380-023-02044-9

Provided by King's College London