Study uncovers different routes to problem behaviour

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There are two distinct pathways involved in the development of callous unemotional (CU) traits in young teenagers – one primarily linked to environmental risk factors, the other to genetic ones – according to new research led by King's College London.

CU traits in youth are characterised by a lack of guilt, empathy and disregard for others and are associated with early-onset persistent conduct problems, severe antisocial behaviour, and adult psychopathy. The findings, published today in *Molecular Psychiatry*, could help identify the timing, and potential targets for interventions which may prevent the development of CU traits.

Teenagers with CU traits can either have high or low levels of anxiety and/or depression. The study involved 84 13 year olds with CU traits

who all showed severe behavioural problems. Researchers analysed levels of anxiety and depression, pre and post-natal environmental risk factors and epigenetic changes (or DNA methylation) to the oxytocin receptor gene at birth, age 7 and 9.

Dr Charlotte Cecil, lead author of the study, from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London says: "We were particularly interested in studying the oxytocin receptor gene, often referred to as the 'love hormone'. We know from previous studies that higher levels of DNA methylation in this gene relate to lower levels of oxytocin in the body. In turn, Oxytocin, has been shown to promote prosocial behaviour, such as empathy, trust, attachment and bonding, which are typically impaired in youth with CU traits. "

The researchers found that in youth with low levels of anxiety/depression, CU traits at 13 were associated with higher DNA methylation at the oxytocin receptor gene at birth, as well as prenatal risks, such as maternal mental health problems, criminal behaviours or substance abuse. For these youth, higher DNA methylation levels at birth also related to lower levels of victimisation and bullying during childhood.

In contrast, in youth with high levels of anxiety/depression, CU traits at 13 were not associated with DNA methylation at the oxytocin receptor gene, but were associated with different kinds of prenatal environmental risks, including family conflict and domestic violence.

Dr Edward Barker, senior author from the IoP at King's says: "Our study suggests there are two distinct pathways to developing callous unemotional traits. We found that children with low levels of anxiety/depression were in fact born with higher levels of DNA methylation in the oxytocin receptor gene, which may contribute to

callousness, and discourage victimisation by peers. On the other hand, youth who display high levels of anxiety/depression and callousness may do so in response to prenatal social adversity which may independently be linked to callousness.

"Acknowledging these different pathways is important as it could help us develop better interventions to prevent CU traits. For example, addressing the prenatal environment for high-risk mothers may be effective in reducing CU traits in children, either by reduced methylation, or directly by reducing family risks factors, such as maternal depression, anxiety, substance use, that can negatively affect child development both during pregnancy and after birth."

More information: Cecil, C. et al. 'Environmental risk, Oxytocin Receptor Gene (OXTR) methylation and youth callous-unemotional traits: a 13-years longitudinal study' published in *Molecular Psychiatry* (in press)

Provided by King's College London