Epigenetics may help explain link between prenatal smoking and adolescent substance use

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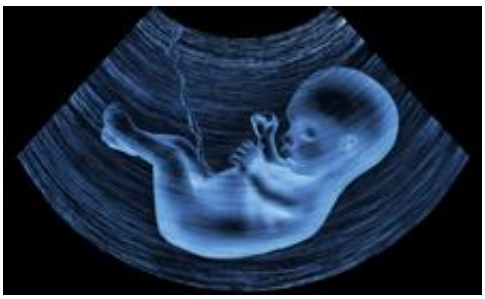

Credit: King's College London

New research from King's College London and the University of Bristol has found that smoking during pregnancy is associated with substance use in adolescence, and that this link may be partially explained by epigenetic changes evident at birth.

Substance abuse is one of the leading preventable causes of death worldwide. Some people are more vulnerable to substance abuse than others, and these differences seem to result from both genetic and environmental factors.

Recent research has focused on how exposure to risk factors in pregnancy, such as tobacco smoking, may affect foetal development in a way that increases risk for later substance use in the offspring.

One possible explanation for this is changes in DNA methylation, an epigenetic process that regulates how genes are 'switched on and off'. While growing evidence points to a link between DNA methylation and substance use, previous studies are based on adults who have already used substances. As a result, it has been difficult to tease apart whether it is the changes in DNA methylation that increase risk for substance use, or whether using substances leads to changes in DNA methylation.

Published today in *Translational Psychiatry*, this study is the first to address this challenge by using longitudinal data on prenatal risks, DNA methylation and adolescent substance use, based on 244 young people from the Bristol-based 'Children of the 90s' cohort, who have been followed from pregnancy to early adulthood.

The researchers found that prenatal smoking was associated with DNA methylation changes at birth, which in turn was linked to higher substance use (and an earlier age of onset) in adolescence. Smoking exposure in the womb not only increased risk for adolescent tobacco smoking, but also alcohol and cannabis use, potentially implying a broader vulnerability to substance use. In addition to prenatal smoking, genetic factors were also found to be important, consistent with previous data showing that risk of substance use is partly inherited.

DNA methylation changes at birth were located in a number of genes important for brain development, including PACSIN1, which is involved in how neurons branch out and communicate with one another, and is active in regions of the brain previously implicated in drug-seeking behaviour and risk for addiction.

Dr Charlotte Cecil from the Institute of Psychiatry, Psychology & Neuroscience (IoPPN) at King's College London, said: 'Together, our findings add to existing knowledge about the adverse effects of prenatal smoking on child health. The study also lends new insights into the

biological mechanisms through which tobacco smoking during pregnancy may increase risk for future substance use.

Dr Edward Barker, also from the IoPPN at King's, said: 'Substance abuse and addiction are very complex psychiatric problems caused by a multitude of factors. As such, our findings are only part of a bigger picture that still needs to be fully mapped out. For example, although we know that maternal smoking is a key risk factor for many adverse child outcomes, it is likely to work alongside a host of other risks.

'While we found a link between prenatal smoking, DNA methylation and adolescent substance use, it is also important to note that these findings do not prove causation, and will need to be replicated in larger studies.'

More information: Cecil, C., Walton, et al. (2016). DNA methylation and substance use risk: A prospective, genome-wide study spanning gestation to adolescence. *Translational Psychiatry*.

Provided by King's College London