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In-utero methadone or subutex exposure could alter gene expression, cause severe neonatal abstinence syndrome

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Some infants born with neonatal abstinence syndrome (NAS) secondary to in-utero opioid exposure have a more difficult time going through withdrawal than others, but the underlying reasons are not well understood. While genetic and epigenetic (when genes are turned on or off) changes have recently been identified as potential factors, researchers at Boston University School of Medicine (BUSM) and Boston Medical Center (BMC) conducted a first of its kind study to identify some of these epigenetic changes that may influence symptom severity.

The researchers focused on how exposure to opioids such as methadone or subutex may alter expression of the mu-opioid receptor (OPRM1) gene, which is known as a primary site of action for narcotics in the nervous system and plays an important role in opioid dependent adults.

Looking at data from 86 infants whose mothers took either methadone or subutex during pregnancy, the results showed that infants with higher levels of the DNA modification called DNA methylation had more severe NAS symptoms. This meant that they required more medication(s) over a longer period of time to get through withdrawal. The researchers hypothesize that this may be due to a decrease in number of opioid receptors due to the silencing of the OPRM1 gene.

Future research in this area will focus on comparing methylation levels

of mothers and infants to evaluate if the epigenetic changes are passed on from mother to child. The implications are that this very early in-utero and neonatal exposure to opioids may lead to lasting epigenetic changes that may alter one's future sensitivity to opioid and other addictive medications.

"What makes these results so intriguing is that these epigenetic changes could be passed on from mother to child, resulting in these children potentially having future issues and sensitivities around opioid and other addictive substances," said Elisha Wachman, MD, a staff neonatologist at BMC and assistant professor of pediatrics at BUSM.

This study is published in the *Journal of Pediatrics*.

More information: *Journal of Pediatrics*, www.ncbi.nlm.nih.gov/pubmed/24996986

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