Common medications taken during pregnancy are not associated with risk for autism

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Babies exposed in the womb to the majority of medications that target neurotransmitter systems, including typical targets of antidepressants and

antipsychotic drugs, are not any more likely to develop autism than non-exposed babies, according to research conducted at The Seaver Autism Center for Research and Treatment at the Icahn School of Medicine at Mount Sinai and published October 31 in *JAMA Psychiatry*.

However, the rates of autism were higher among children of mothers with worse general health before pregnancy, suggesting that the mother's health plays a more critical role in a child's development than the medications she takes.

While previous research has suggested that children of women who use certain drugs during pregnancy are more likely to be diagnosed with autism those studies only looked at the autism risk in relation to a very small number of drugs. Additionally, the designs of previous studies inherently involved a tight link between offspring exposure and maternal disorder and, therefore, could not fully distinguish between the results of the drug itself and those related to the maternal disorder for which the drug was prescribed.

To overcome such limitations, a multidisciplinary team of researchers at the Icahn School of Medicine at Mount Sinai developed a new method that enabled them to systematically evaluate the effects of a wide range of drugs on the fetus in a sample of nearly 100,000 children born between 1997 and 2007 and followed up for autism until January 2016.

"When we assessed the effects of prenatal exposure to medications that affect major neurotransmitter systems, we found that the most of the associations are substantially modified when accounting for maternal characteristics," said Magdalena Janecka, Ph.D., a postdoctoral fellow at The Seaver Center and first author of the paper. "What this suggests is that higher estimates of autism risk among offspring of mothers who take certain medications during pregnancy are most likely not due to pharmacological effects of those drugs."

Specifically, the study team performed a case-cohort study using data from a large health maintenance organization in Israel. Researchers grouped medications prescribed to pregnant women based on the biological target on which those drugs act, rather than the condition the drug was prescribed to treat. The rationale behind this approach was that if certain types of pharmaceuticals affect the risk of the disorder by interfering with some facet of neurodevelopment, they will exert their effects regardless of maternal indication or of the internal system upon which they were designed to act. This new method allowed the study team to systematically evaluate the actions of more than 180 drugs, sorting them into 55 groups within which the medications were similar in terms of their function but were prescribed for different conditions.

The exposure interval in this study was defined as the pregnancy period (280 days before the child's birth), and women in the study were considered exposed to a given medication regardless of the number of prescriptions or their redemption rate. Children were classified as exposed to a given group if their mother received a prescription for any medication from that group during pregnancy. Drugs could be classified into multiple groups, reflecting their diverse actions on maternal and fetal systems. Maternal number of diagnoses was defined as the total number of medical/reported health issues between one year prior to pregnancy and the child's birth.

"After adjusting for the child's year of birth, and a number of maternal factors—including her age at the child's birth, history of psychiatric and neurological disorders, and number of medical diagnoses around pregnancy—our data indicate that the majority of medications known to affect neurotransmitters, and taken by women during pregnancy, may not themselves influence the estimates of offspring autism risk," says Dr. Janecka. "In actuality, maternal number of diagnoses can confound associations between prenatal exposures and autism, and therefore should be accounted for in future studies."

The biology-first method used in this study, in which the shared biological properties of medications are explicitly acknowledged in the analytical procedures, aims to understand the causal mechanisms that underlie the effects of prenatal exposure to medications and, therefore, could be pertinent to studies of other conditions that originate in utero. Researchers at The Seaver Center are currently investigating further how maternal health could affect a child's risk of autism.

More information: *JAMA Psychiatry* (2018). jamanetwork.com/journals/jamap … psychiatry.2018.2728

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