

Birth Interval Linked to Autism Risk

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The risk for autism spectrum disorder (ASD) appears to be higher in children born after short or long interpregnancy intervals (IPIs), according to findings from the case-control Study to Explore Early Development (SEED).

Specifically, ASD was more common among second- and later-born children who were conceived less than 18 months or at least 60 months after the mother's previous delivery. The correlation appeared to strengthen after a 60-month interval. IPI was not associated with other developmental disorders.

Lead author Laura A. Schieve, PhD, an epidemiologist from the National Center on Birth Defects and Developmental Disabilities at the Centers for Disease Control and Prevention in Atlanta, Georgia, and colleagues [published](#) results from the SEED cohort online November 22 in *Autism Research*. SEED was established in 2007 at six sites across the United States to study the effect of preconception and prenatal factors on ASD risk.

After adjusting for sociodemographic factors, the adjusted odds ratio for ASD among term births was 1.5 (95% confidence interval [CI], 1.1 - 2.2) for those with a shorter than 18-month interval and 1.5 (95% CI, 0.99 - 2.4) for those with an interval of 60 months or more.

Both short- and long-interval correlations were more pronounced in ASD cases with high severity scores, with adjusted odds ratios jumping to 2.0 (95% CI, 1.3 - 3.3) for a short IPI and 1.8 (95% CI, 0.99 - 3.2) for a long IPI. Children conceived very soon after their previous sibling was born were twice as likely to be severely autistic than those born within the time frame of 18 to 60 months.

The SEED researchers studied three groups (children with ASD; those with other, non-ASD developmental disorders; and children from the general population), all born in second or later births. Mothers' reproductive histories were ascertained by computer-assisted telephone interviews. There were 356 children in the ASD cohort, 627 in the developmental disorders cohort, and 524 in the general population cohort. By sex, boys accounted for 81.7%, 64.9%, and 53.6% of these cohorts, respectively. More than 50% of the participants were white, with more than 70% being white in the control group.

Among children in the ASD cohort, 41.1% had higher disease severity scores. Both children with ASD and those with other developmental disorders were more likely than children in the control cohort to be born prematurely, and their mothers were less likely to be non-Hispanic white or to have completed college, and more likely to have had hypertension or diabetes during pregnancy. Mothers in the ASD cohort were also more likely than mothers in the control cohort to have had an infertility diagnosis and less likely to report actively trying to conceive.

The authors note that whereas previous studies have reported an association between ASD and short or long IPIs, they believe this is the first study to examine IPI associations in both ASD and non-ASD developmental disorders in the same population.

Among explanations offered for associations between ASD and a short IPI are nutrient depletion from the previous pregnancy, particularly of folic acid, which is crucial for neuronal development and DNA methylation. Other possible factors are persistent maternal inflammation from the previous pregnancy, increased maternal stress, and the greater risk for maternal complications in the context of short IPIs. Another possibility is unintended pregnancy leading to delays in beneficial behavior modification, such as smoking cessation.

Furthermore, the current trend among western women to older age at childbearing has also been [associated](#) with shorter IPIs.

"[This] phenomenon might represent an intentional desire for short pregnancy spacing and it might also occur among women who have difficulty conceiving their first birth due to an infertility disorder," the authors write.

At the long end of the interval spectrum, the correlation with ASD may be linked to underlying subfertility, and also with unintended pregnancy, Dr Schieve and associates authors note.

The authors say the differences between the ASD and developmental disorder groups and between the high- and lower-severity ASD groups suggest the mechanism associated with birth spacing might uniquely affect autism, rather than neurodevelopment in general.

"Despite unanswered questions, these findings in concert with those from other studies can inform public health and clinical guidelines about optimal pregnancy spacing," Dr Schieve and coauthors write. "Since pregnancy spacing is potentially modifiable, it is particularly important to more fully understand the underlying explanation for the ASD–IPI associations such that women can be fully informed of the potential risks associated with short and long IPIs."

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