

Mom's Antidepressant Use Linked to Autism Risk in Children

Use of selective serotonin reuptake inhibitors (SSRIs) by pregnant women may increase the risk for autism spectrum disorder (ASD) in their offspring, new research suggests.

In a study of more than 1800 children, investigators found an adjusted 2-fold increased risk for ASD among mothers who used an SSRI during the year before delivery and a 3-fold increased risk when SSRIs were ingested during the first trimester.

"The potential association between use of antidepressants during pregnancy and risk of [ASDs] has never been investigated before," lead author Lisa A. Croen, PhD, senior research scientist and director of the Autism Research Program at Kaiser Permanente Northern California (KPNC) in Oakland, told *Medscape Medical News*.



**Dr. Lisa A.
Croen**

However, she noted that the results "should be interpreted with extreme caution" and that further studies are needed to determine if this association represents a causal connection.

"At this point, we do not recommend that women make any changes to their treatment approach for depression and/or anxiety," said Dr. Croen.

Instead, she recommends that those prescribed SSRIs during pregnancy discuss the issue with their doctors.

"We know that there are real risks to the woman and their children if mental health disorders in mom go untreated, and there are real benefits to appropriate treatment. So the potential risk of autism must be balanced with the real benefit of treatment," she said.

The study was [published online](#) July 4 in the *Archives of General Psychiatry*.

Autism Cases Increasing

According to the study, autism cases have increased from 4 to 5 per 10,000 in 1966 to almost 100 per 10,000 today.

"While at least some of this observed increase in prevalence can be attributed to changing diagnostic standards, availability of services, and greater public awareness, there is considerable scientific and public concern about environmental factors that may contribute to autism risk, most likely in interaction with genetic factors," write the investigators.

"There is some literature suggesting a family history of mental health conditions among individuals with [ASDs], but no prior studies have been able to look at both the mental health condition and the treatment for the condition at the same time," said Dr. Croen.

For this study, the investigators evaluated medical records of 298 children with ASD (82.9% male; 54.7% white, 13.4% Hispanic, 9.4% Asian, 9.1% black) and 1507 healthy controls (80.6% male; 46.4% white, 20.4% Hispanic, 9.9% Asian, 10% black) from the Childhood Autism Perinatal Study. All were born between January 1995 and June 1999 at a KPNC facility.

Mothers' prescriptions were identified by using the Pharmacy Information Management System. For this study, 3 classifications of antidepressants were assessed: SSRIs, dual-action antidepressants, and tricyclic antidepressants. The SSRI class included citalopram hydrobromide, fluoxetine, fluvoxamine maleate, paroxetine hydrochloride, and sertraline hydrochloride.

Maternal psychiatric conditions for any time before delivery were identified by using inpatient and outpatient KPNC databases.

Modest Increase

Results showed that 6.7% of the children with ASD (n = 20) and 3.3% of the healthy controls (n = 50) had prenatal exposure to at least 1 antidepressant.

The risk for ASD was significantly increased for those with exposure to any SSRI during the year before their delivery (adjusted odds ratio [AOR], 2.2; 95% confidence interval [CI], 1.2 - 4.3) and was even higher when the exposure occurred during the first trimester (AOR, 3.8; 95% CI, 1.8 - 7.8).

There was no increased risk among those with mothers who had a mental illness but did not take SSRIs during pregnancy.

"We were a bit surprised to find that there was really no association between a history of mental health disorders in moms and autism, once we controlled for the contribution of the treatment [SSRI use] for the condition," said Dr. Croen.

"That said, it is possible that the association we found between maternal SSRI use and autism is in fact explained by the underlying condition for which the woman took the medication."

She noted that a possibility for this could be a genetic predisposition to depression — and that those same genes might be involved with autism.

"This is speculation at this point, so it needs to be tested in future studies."

The investigators note that limitations of the study include the "modest number" of women who took an SSRI during pregnancy and that "the proportion of children with ASD in this population that can be statistically attributed to prenatal SSRI exposure is quite low."

Still, the results suggest that "prenatal exposure to SSRIs, especially during the first trimester, may modestly increase the risk of ASD," they write.

Dr. Croen reported that the investigators are conducting 2 multicenter, epidemiologic studies "that will enable us to replicate and extend these intriguing findings."

The [Early Autism Risk Longitudinal Investigation](#) study is funded by the National Institutes of Health, and the [Study to Explore Early Development](#) is funded by the Centers for Disease Control and Prevention.

'Vast Majority' Not At Risk

"We already know there is an association between depression in the family unit and the presence of autism. What this paper suggests is that the use of SSRIs is also associated — but it doesn't tell us why," Max Wiznitzer, MD, associate professor of pediatrics and neurology at Case Western Reserve University in Cleveland, Ohio, and pediatric neurologist at Rainbow Babies and Children's Hospital, told *Medscape Medical News*.

Dr. Wiznitzer, who is also the neurology liaison to the Autism Subcommittee for the American Academy of Pediatrics, noted that "it was interesting" that the investigators did not find the association with tricyclic antidepressants because their mechanism of action is serotonin-based as well as catecholamine-based.

When asked if this was because so few of the study moms used tricyclics, he said that was a problem with the whole study.

"We're only talking about 20 children who had exposure to any antidepressant, and that's an awfully small number on which to make a firm conclusion. Instead, I'd say that if this data is true, this would only be a signal that would suggest you need to study this further to determine why."

Dr. Wiznitzer said that clinicians have to consider the benefits and risks of treatment for any pregnant woman, or one who is planning to become pregnant soon.

"And we can argue that the risk of severe depression with its attendant physical and psychological stressors may be worse for the fetus than a putative, still-needing-to-be-replicated, modest association of medication to autism."

"They found that there was only twice or 3 times the risk. That means 97 or 98 out of 100 individuals taking SSRIs didn't have this problem. In other words, the risk of ADS in the general population is 1%. So that means 3 times the risk is still just 3%," he said.

"So the vast majority of women aren't going to be at risk for this problem. And the risk at 3% is no higher than the risk of almost any developmental problem just in a regular pregnancy."



**Dr. Max
Wiznitzer**

Overall, Dr. Wiznitzer said that there are other risks of SSRI use during pregnancy, including withdrawal symptoms. "But with autism? I worry about what I know may happen rather than what might hypothetically happen based on 1 paper."

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