Prenatal Exposure to SSRI Antidepressants and the Risk of Autism Spectrum Disorder (ASD) in Children

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Abstract

**Background:** Selective Serotonin Reuptake Inhibitors (SSRIs) are the most commonly prescribed antidepressant and are continuously used during pregnancy. Some studies reported an increased risk of neurodevelopmental delays such as autism spectrum disorder (ASD) in children who have been exposed to SSRIs during pregnancy. Multiple findings of elevated prevalence of autism spectrum levels in roughly one third of children with ASD have lead many to believe that impaired serotonin levels may be associated to the disorder. Since serotonin is crucial for development in the fetal brain, there exists many concerns regarding prenatal exposure to medications such as SSRIs.

**Objective:** This study aims to examine the association between maternal use of SSRIs during pregnancy and the development of ASD in the offspring.

**Methods:** A structured literature review was conducted through PubMed and Medline databases. Relevant articles were retrieved using the keywords “antidepressants or SSRIs or selective serotonin reuptake inhibitors”, “autism spectrum disorder or ASD”, and “pregnancy”. Selected articles were peer-reviewed and published in English within the last 17 years.

**Results:** The original search using these keywords identified 577 relevant reports which were screened against the exclusion criteria and reviewed to obtain 9 relevant articles.

**Conclusion:** The evidence supports the possibility of an increase in the risk of ASD in children with mothers exposed to SSRIs, however, the observed results may be subject to confounding by indication and the severity of the mental illness. Further studies are needed to determine causality.

**Introduction**

According to the centre for disease control and prevention (CDC) 1 in 68 children have been identified with a form of ASD[1]. Autism spectrum disorder includes a group of developmental disorders with a wide range of symptoms, skills, and levels of disabilities[1]. The severity of the condition varies from individual with mild impairments, while others are severely disabled. Individuals with ASD often display ongoing social problems such as difficulties with communicating and interacting with others, symptoms that hurt their ability to function socially at work or school, as well as repetitive behaviours[1]. Although the specific cause of ASD is unknown many studies have found that the development of the disorder seems to rely on the interaction of genetic, environmental, and biological factors[2]. Children with children diagnosed with autism spectrum disorders are at lower birth weight, with smaller head circumferences, and lower scores on assessments of maternal depression, anxiety, and stress[3].

Pregnancy is a period of high vulnerability to depression; it's most prevalent psychiatric disorder during pregnancy[4]. Up to now, antidepressants are considered safe to use in the treatment of depression in pregnant women. However, since serotonin plays an important role in embryonic development, especially of the nervous system, it is of importance to explore the association between prenatal intake of SSRIs and the development of neurodevelopmental delays such as ASD in the offspring.

**Research Question**

Is the maternal prenatal intake of SSRIs associated with an increased risk of ASD in children?

**Methods**

**Inclusion criteria:**
- English
- Peer reviewed
- After 2013

**Exclusion criteria:**
- No mention of keywords in title
- Before 2014
- Non-English
- Duplicates

**PubMed and Medline search with keywords:** “antidepressants OR SSRIs OR selective serotonin reuptake inhibitors”,”autism spectrum disorder OR ASD”, and “pregnancy”.

**Figure 1. Flow-chart demonstrating the methodology process used to select studies for our structured literature review.**

**Table 1. Summary of findings of structured literature review examining the association between exposure to SSRIs during pregnancy and ASD development in offspring.**

**Discussion**

**Key Findings**
- 5 studies indicate no association that supports the possibility of an increase of the risk of ASD in children with mothers exposed to SSRI, while 4 studies showed an association
- The use of antidepressants such as SSRIs during 2nd and 3rd trimester was statistically associated with an increased risk of ASD in some of the studies
- After confounder adjustment, SSRI exposure and association to ASD was not significant in studies indicating no association
- The reviewing revelation no associations suggest that any risk associated with the use of SSRIs during pregnancy may be related to the indications for their use rather than effect of these drugs

**Limitations of our methods**
- Limited to human studies measuring SSRIs and no other types of antidepressants
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**Limitations within studies**
- Lack of coverage of the variety of depression during pregnancy and physical health, genetic predispositions for ASD, as well as insufficient control for maternal mental health - Recall Bias
- Discontinuation of antidepressants before and after pregnancy, including self-report and medical records were not generated in most studies, nor the analogy of different antidepressant treatment regimens
- Limited to Northern European countries

**Conclus:** We are not surprised by the inconsistency within the results since:
1) The quality of depression and individual differences between mothers (control) during pregnancy varies
2) The reliability of this disorder is not well understood; it is therefore understandable that the results aren't conclusive

**Future Research**
- Conduct more studies in different countries to get more representative data
- Mother's physical health should be taken into consideration to determine possible risk in offspring
- Future research should have larger samples and follow children in all the way up to their late teens
- Studies should consider physical environmental factors

**More research is needed to determine the biological gradient of the exposure and the outcome**

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<table>
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