CAL POLY
SAN LUIS OBISPO

Meta-Analysis of the Association Between Prenatal Antidepressant Use and the Development of ASD in the Offspring

Ryan A. Manning[1], Taylor F. Smith, PhD[1,2], Laura Freberg, PhD[1]
1. Department of Psychology and Child Development, California Polytechnic State University, San Luis Obispo, CA USA
2. Division of Behavioral Genetics, Rhode Island Hospital; DPHB, Brown University, Providence, RI USA

Rhode Island Hospital
BROWN Alpert Medical School

Introduction

- Antidepressants are commonly prescribed to women who are pregnant even though it has been proven that such medication passes through the placental barrier
- Antidepressant use during gestation may be a risk factor for the development of ASD. However, the strength of this association varies across studies
- Therefore, it is important to examine if and how strongly SSRI use during pregnancy is associated with the development of ASD in offspring

Objectives

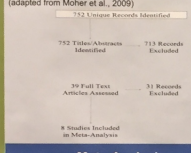
- Meta-analysis examining the strength of the association between maternal antidepressant use during gestation and ASD across studies
- Estimate risk for the development of ASD following antidepressant medication exposure during the 1st, 2nd or 3rd trimester

Methods

- **Databases:** PubMed and Science Direct
- **Search terms:** SSRI OR "selective serotonin reuptake inhibitors" OR "antidepressant drugs" AND "autism spectrum disorder*" OR ASD AND pregnan*
- **Review Process:** Abstract review, full-text review, and data extraction
- **Inclusion Criteria:**
  1. Case-control or cohort study
  2. Maternal use of antidepressants from 30 days before gestation through the third trimester of gestation
  3. ASD diagnostic status and ASD symptom severity based on DSM-III criteria or higher
  4. Sufficient data to calculate effect size between maternal antidepressant use during pregnancy and the development of Autism Spectrum Disorder in the offspring
- **Exclusion Criteria:** Overlapping samples, non-English language publication, ASD diagnosis not based on DSM-III or higher and biased control sample

Study Selection

Figure 1. Flow of information through meta-analytic review (adapted from Moher et al., 2009)



Meta-Analysis

- Random-effects meta-analysis
  - Relative risk (*RR*) was calculated for each sample
- *Q and* I^2 assessed between-study heterogeneity
- Publication bias assessed with Egger's test and visual inspection of funnel plot
- All analyses conducted with CMA.V2

Results

- A total of 8 studies with a pooled population of 1,364,520 were included in the meta-analysis.
- Across all samples the **pooled *RR* = 1.68 (1.20-2.35; p<.01).** Effect sizes were also examined based on the trimester of antidepressant exposure (see Table 1).
- There was significant variability in the strength of association between prenatal antidepressant use and ASD across studies (*Q = 87.08;* df = 7; *p <.01; I^2 = 91.96*).
- Egger's test for publication bias was significant (Egger's intercept = -2.93 *t = .69; df = 6; p <. 05),* suggesting the presence of positive publication bias (see Figure 1).

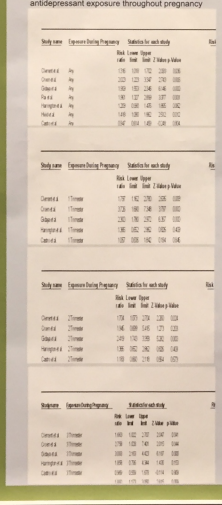
Results (continued)

Table 1. Pooled effect sizes for ASD and antidepressants

		Relative Risk		
Exposure	n	*RR*	CI	p
Prenatal	8	1.68	1.20-2.35	< .01
1st Trimester	5	1.88	1.31-2.70	< .01
2nd Trimester	5	1.78	1.34-2.38	< .01
3rd Trimester	5	1.89	1.17-3.05	< .01

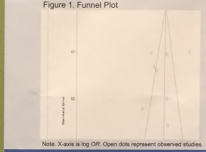
Note. Prenatal antidepressant exposure was defined as thirty days before conception through the third trimester of the gestational period.

Table 2. Forest plots for ASD risk following antidepressant exposure throughout pregnancy



Results (continued)

Figure 1. Funnel Plot



Note: X-axis is log OR. Open dots represent observed studies.

Discussion

- The pooled ***RR* = 1.68**, suggesting that prenatal antidepressant exposure is associated with a 1.67 fold increase in the risk of developing ASD.
- Across samples there is a significant risk related to the association of antidepressant use and the development of ASD by trimester, though more analysis is needed to confirm this association.
- Only raw estimates of the association between prenatal antidepressant medication exposure and ASD were included. Therefore, this analysis is an overestimate of the true association between antidepressant medication exposure during pregnancy and ASD development in offspring
- **Limitations**
  - Trimester data is confounded with exposure and varies between stu
  - Publication bias
- **Future Directions**
  - Examine the effectiveness of combination of therapies in tr psychological disorders in co antidepressant medication on mothers
  - Investigate the effect of pren antidepressant use on the c organization and physiologi of the fetal brain
  - Progress towards the devel preventative interventions f individuals exposed to pre