Maternal Stress as a Risk Factor for ADHD in School-Aged Children

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ABSTRACT

Background: Attention deficit hyperactivity disorder (ADHD) is one of the most commonly diagnosed neurodevelopmental disorders in the youth population, with a prevalence of 6-12% in North America. The disease negatively impacts academic and social functioning in childhood, as well as occupational achievements in adulthood. The etiology is highly multifactorial and embraces genetics, prenatal exposures to tobacco smoke and alcohol, and postnatal factors such as parenting style.

Objective: To examine the association between maternal stress during pregnancy and the development of ADHD in school-aged children.

Methodology: A systematic review was completed to investigate the relationship between maternal stress and ADHD symptomatology in offspring by using PubMed, Google Scholar, and Cochrane Library databases. Both quantitative and qualitative publications within the past twenty years were searched using keywords such as maternal stress, pregnancy, ADHD, behavioural disorder, and risk factor. The articles were screened for extraneous variables such as maternal age at conception to minimize biases.

Results: Epidemiological studies have indicated an association between maternal stress and behavioural disturbances in offspring, persisting until the ages of four and six. The "excess glucocorticoid" theory suggests that severe maternal stress saturates the enzyme 11β-hydroxysteroid dehydrogenase type II responsible for deactivating cortisol in the placenta during pregnancy, allowing excess hormone to reach the fetus.

Conclusion: Determining preventable risk factors early in life leads to new strategies and treatment options to reduce diagnostics of the disease, improve the quality of life of children at risk, and dramatically reduce health care costs. Further investigation is needed to establish causation.

OBJECTIVE

To examine the association between maternal stress during pregnancy and the development of ADHD in school-aged children.

BACKGROUND

Attention deficit hyperactivity disorder is one of the most commonly diagnosed neurodevelopmental disorders in the youth population.

Symptoms of ADHD include:
- Inattentiveness
- Impulsivity
- Hyperactivity

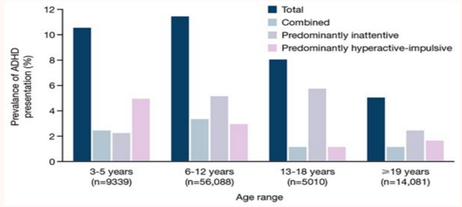


Figure 1. Prevalence rate of ADHD in various age groups.

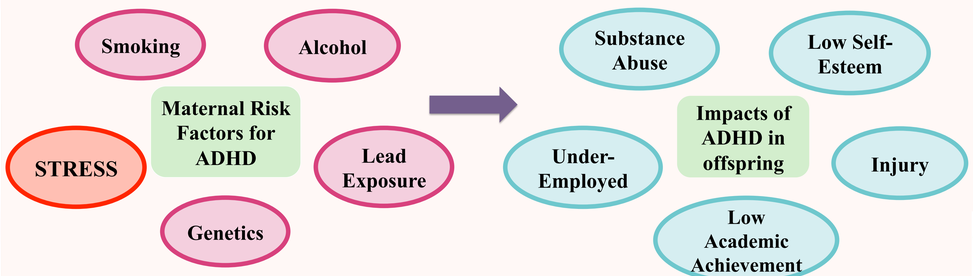


Figure 2. Risk factors during pregnancy and impacts of ADHD in offspring.

Mechanism of action:
- "Excess glucocorticoid theory"

severe maternal stress saturates enzyme 11β-hydroxysteroid dehydrogenase type II → excess hormone reaches fetus

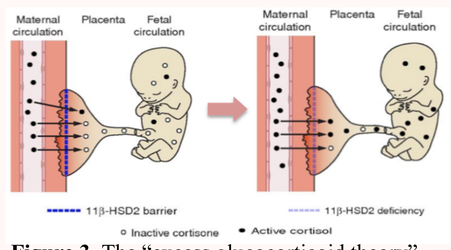
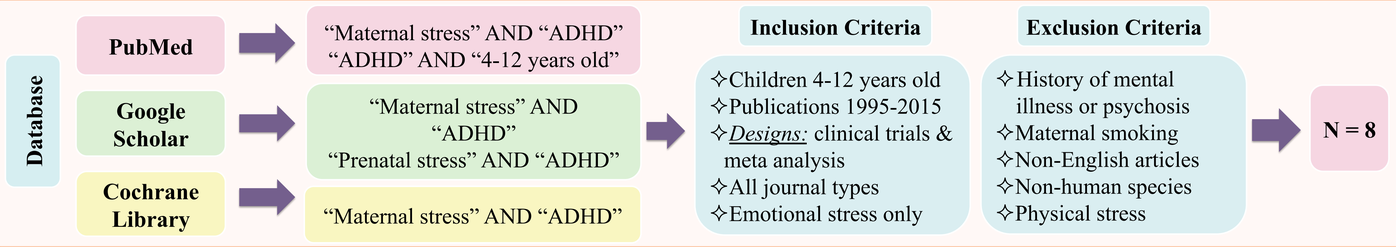


Figure 3. The "excess glucocorticoid theory"

METHODOLOGY



RESULTS

Study	Population	Methodology & Design	Findings
Grizenko et al. (2015)[1]	410 children with ADHD 6-12 years old	**Retrospective study** ▪ Child Behavior Checklist ▪ Conners Global Index for Parents & Teachers	↑MSDP associated with: ↑ CBCL internalizing scores (β=4.2, p<.01) ↑ CBCL externalizing scores (β=1.9, p=.04) ↑ CGI-P restless-impulsive scores (β=2.6, p=.01) ↑ CGI-P emotional ability scores (β=3.1, p=.02) ↑ CGI-T restless-impulsive scores (β=2.2, p=.05)
Lee et al. (2015)[2]	60 children with ADHD & 60 children without ADHD 4-12 years old	**Retrospective case-control study** Questionnaire completed by biological mothers about marital adaptation, marital satisfaction, and incidence of stressful life events during pregnancy	▪ ↓ incidence of positive life events, marital adaptation & marital satisfaction during pregnancy in cases ▪ Marital adaptation & pregnancy before marriage = risk factors for ADHD
Peng et al. (2014)[3]	1765 mother-infant pairs clinically diagnosed with ADHD 4-5 years old	**Prospective longitudinal study** ▪ Prenatal Life Events Checklist ▪ Revised Chinese Edition of the Social Support Scale ▪ Coping Style Questionnaire ▪ Conners' Hyperactivity Index	▪ Mothers experienced SLE in 2nd trimester = twice likely to have significant symptoms of ADHD (OR: 2.41, p: .041) ▪ Middle or 2nd half of pregnancy = sensitive period for PMS (β=0.56, p=.025) ▪ Correlation exists between prenatal SLE, social support, and coping styles on ADHD
Grizenko et al. (2012)[4]	71 children with ADHD & 71 non-ADHD siblings 6-12 years old	**Retrospective study** ▪ Kinney Medical & Gynecological Questionnaire ▪ Child Behavior Checklist ▪ Conners Global Index for Parents	▪ Mothers' experience of ↑ stress during pregnancy leads to ↑chance of ADHD in offspring (OR: 6.3, p=.01)
Grizenko et al. (2008)[5]	203 children with ADHD 6-12 years old	**Double-blind, two weeks RCT** ▪ Kinney Medical & Gynecological Questionnaire ▪ Child Behavior Checklist ▪ Conners Global Index for Parents & Teachers	▪ Severity of stress during pregnancy & ADHD symptoms in offspring ▪ Prenatal stress causes ↑ severity of ADHD symptomatology ▪ Children experience ↑externalizing disorder & internalizing disorders
Van den Bergh et al. (2004)[6]	71 women & 72 firstborns 8-9 years old	**Prospective study** ▪ State Trait Anxiety Inventory ▪ Child Behavior Checklist ▪ Teacher's Report Form ▪ Externalizing Problems Scale (aggressive & delinquent behaviors subscale) ▪ Attention Problems Scale	▪ ↑ maternal anxiety correlates to childhood disorders (controlled for: gender, birth weight, parental education, smoking during pregnancy, postnatal maternal anxiety) ▪ Maternal anxiety explains 9-22% variance in childhood disorders ▪ 12 to 22 weeks gestation = vulnerable period for development of ADHD
Markusse et al. (2003)[7]	N = 5 on psychosocial stress (1973-2002), N = 1 on MSDP and ADHD & N = 4 on ADHD subgroups	**Narrative approach and meta-analysis** PubMed, MEDLINE, EMBASE, and PsychINFO	▪ MSDP associated with ↑ prevalence of congenital malformations & fetal levels of cortisol ▪ Mothers of children with ADHD reported ↑ psychological MSDP ▪ Statistical association with disturbances in attention and activity
O'Connor et al. (2002)[8]	7448 pregnant women living in Avon, UK who delivered babies between April 1991 and December 1992 & their children at 4 years old	**Prospective study** Multiple antenatal and postnatal assessments of maternal anxiety and depression, antenatal and obstetric risks, psychosocial risks and children's behavioral/emotional problems	▪ Antenatal maternal anxiety predicted behavioral problems in boys (OR: 2.14) & girls (OR: 1.88) ▪ Maternal anxiety up to 33 months postnatal predicts problems in boys (OR: 1.56) & girls (OR: 1.51)

DISCUSSION

Confounding factors
→ overestimation of association
(*e.g.* maternal smoking, genetics)

Subjectivity of emotional stress
→ different impacts on different individuals & **Information Bias**

Recall Bias
Questionnaire & checklist rely on mothers' memory

Inconsistent sample sizes in studies
→ sample specific results & **selective attrition**

Further research should investigate:
- Other environmental factors that affect cognition & behavior in children with ADHD
- Potential use of genotyping in predicting risk of attaining ADHD
- Support for mothers whose children have higher risk of developing ADHD symptoms

CONCLUSION

- ADHD prevalence is high in school-aged children
- Mechanism of action follows "excess glucocorticoid theory"
- Literature review of N=8 shows:

Maternal stress during pregnancy is a risk factor for the development of ADHD in school-aged children.

- Further investigation required to establish causation between the two variables ✓

ACKNOWLEDGMENT

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