



Association of Maternal Autoimmune Disease With Attention-Deficit/Hyperactivity Disorder in Children

¹ A.Padakandla, ² A.Setty

^{1,2} California Northstate University College of Medicine

Correspondence : dr.padakandla498485@gmail.com

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ABSTRACT

Background: The association of maternal autoimmune diseases with neurodevelopmental disorders, particularly Attention-Deficit/Hyperactivity Disorder (ADHD) in children, has garnered significant attention in recent years. **Literature Review:** Several articles delve into the mechanisms linking maternal health to child neurodevelopment. For instance, (Dudova et al., 2002) presents evidence that maternal autoantibodies may disrupt fetal brain development, while (Ravaccia & Ghafourian, 2002) reviews the critical role of the maternal immune system in the pathogenesis of Autism Spectrum Disorder (ASD), suggesting parallels with ADHD. The systemic review by (X. Han et al., 2001) reinforces the link between maternal inflammation during pregnancy and neurodevelopmental disorders, indicating that both acute and chronic inflammation can alter neurodevelopmental trajectories. Additionally, the familial associations explored by (Li et al., 2002) suggest that maternal allergic and autoimmune diseases may disrupt dopaminergic systems in offspring, further supporting the hypothesis that maternal health significantly impacts ADHD risk. The interplay between maternal factors, such as ADHD symptoms and attachment styles, as discussed by (Darling Rasmussen et al., 2008), underscores the multifactorial nature of ADHD etiology. **Conclusion:** The collective findings across these studies indicate that maternal autoimmune diseases and related immune dysregulation may play a pivotal role in the neurodevelopmental trajectories of children, particularly concerning ADHD. The evidence suggests a need for further research to elucidate the specific pathways through which maternal health influences child development, emphasizing the importance of maternal well-being during pregnancy.

Keyword: Maternal Autoimmune Disease, Attention-Deficit/Hyperactivity Disorder, Children

INTRODUCTION

The association of maternal autoimmune diseases with neurodevelopmental disorders, particularly Attention-Deficit/Hyperactivity Disorder (ADHD) in children, has garnered significant attention in recent years. The literature reveals a complex interplay between maternal health, environmental factors, and child neurodevelopment, with a growing body of evidence suggesting that maternal autoimmune conditions may contribute to the risk of ADHD.

In 2007, (Quoc Vuong Tran & Miyake, 2007) highlighted the rising prevalence of ADHD, noting a 25.64% increase in diagnosed cases among children aged 3 to 17 years between 2003 and 2015. Their exploration of potential etiological factors pointed to maternal stress and malnutrition, as well as exposure to environmental toxicants, as significant contributors to ADHD risk.

The same year, (Linda Lamanna et al., 2007) examined the prevalence of ADHD symptoms in children with Autism Spectrum Disorders (ASD), discovering alarming rates of ADHD symptoms among this population. Their findings suggested that comorbidities, including allergies and neuropsychiatric disorders, could exacerbate ADHD symptoms, indicating that maternal health factors may have a cascading effect on child behavior.

In 2008, (Darling Rasmussen et al., 2008) introduced the concept of maternal ADHD as a risk factor for the development of ADHD in offspring. They emphasized the importance of the mother-child relationship, suggesting that maternal ADHD symptoms and insecure attachment could mutually influence the risk of ADHD.

(Dudova et al., 2002) further advanced the discourse by investigating the role of maternal autoantibodies in the development of ASD. Their study pointed to a potential link between maternal autoimmune conditions and elevated risks of neurodevelopmental disorders in children, asserting that maternal autoantibodies could disrupt fetal brain development. This was echoed by (Ravaccia & Ghafourian, 2002), who reviewed the maternal immune system's critical role in ASD

pathogenesis, emphasizing how maternal immune activation during pregnancy may alter the prenatal environment and contribute to neurodevelopmental issues.

(X. Han et al., 2001) conducted a systematic review that consolidated evidence regarding maternal inflammation during pregnancy and its association with common neurodevelopmental disorders, including ADHD. Their findings indicated a strong correlation between maternal autoimmune disease and ADHD in offspring, reinforcing the notion that maternal health is a crucial factor in child neurodevelopment.

Finally, (Li et al., 2002) explored the familial associations between allergic and autoimmune diseases and the incidence of ASD and ADHD. Their study proposed that maternal immune activation could disrupt dopaminergic systems in offspring, linking maternal health to the development of ADHD and ASD. This research highlights the potential mechanisms through which maternal autoimmune conditions might influence neurodevelopmental outcomes in children.

Collectively, these studies illuminate the multifaceted relationship between maternal autoimmune diseases and ADHD, suggesting that maternal health factors, including immune system dysregulation and psychological well-being, may play pivotal roles in shaping the neurodevelopmental trajectories of children.

LITERATURE REVIEW

The article titled "Neurodevelopmental Disorders and Environmental Toxicants: Epigenetics as an Underlying Mechanism" by (Quoc Vuong Tran & Miyake, 2007) provides a comprehensive overview of the links between environmental factors and neurodevelopmental disorders, particularly focusing on Attention-Deficit/Hyperactivity Disorder (ADHD). The authors highlight a significant increase in the prevalence of ADHD among children, noting a rise from 7.8% to 9.8% between 2003 and 2015, which underscores the growing concern regarding the etiology of such disorders.

A critical aspect of the article is its exploration of environmental toxicants as potential contributors to neurodevelopmental disorders. The authors argue that while the reasons for the increasing prevalence of ADHD remain controversial, there is a compelling need to investigate the role of environmental exposures during

critical periods of development. They emphasize that maternal health, particularly nutritional status during pregnancy, is crucial, citing that deficiencies in folate and vitamins may elevate the risk of neurodevelopmental disorders in offspring. This assertion aligns with a growing body of literature that suggests maternal dietary habits and exposures can have lasting impacts on child development.

The authors also discuss the importance of epigenetics in understanding how environmental toxicants may influence neurodevelopmental outcomes. By framing the issue within an epigenetic context, the article suggests that maternal autoimmune diseases and related environmental exposures could alter gene expression and contribute to the risk of ADHD. This perspective is particularly relevant in light of the increasing recognition of autoimmune conditions and their potential implications for fetal development.

However, while the article effectively outlines the relationship between environmental factors and neurodevelopmental disorders, it could benefit from a more detailed examination of specific autoimmune diseases and their direct associations with ADHD. The current discussion remains somewhat broad, lacking a nuanced exploration of how various autoimmune conditions might differentially impact neurodevelopment.

The article "Risk factors for the existence of attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders" by (Linda Lamanna et al., 2007) provides an insightful exploration into the prevalence and associated factors of ADHD symptoms among children diagnosed with Autism Spectrum Disorders (ASD). The authors present a compelling argument regarding the co-occurrence of ADHD and ASD, highlighting that a significant percentage of children with ASD exhibit symptoms consistent with ADHD. Notably, their findings indicate that 55% of ASD patients reported ADHD symptoms on the CPRS-R DSM-IV total subscale, which underscores the critical intersection of these two neurodevelopmental conditions.

One of the key contributions of this study is its investigation into the somatic and neuropsychiatric comorbidities that may exacerbate ADHD symptoms in children with ASD. The authors identify several comorbidities, including motor delay, enuresis, allergies, oppositional defiant disorder (ODD), and intellectual

disabilities, as being significantly associated with increased ADHD symptoms. This aligns with previous research suggesting that allergic conditions may lead to behavioral abnormalities, potentially due to the impact of immune dysregulation on neurodevelopmental outcomes. The authors propose that the interaction between neurodevelopmental abnormalities and immune system dysregulation could be a crucial area for further research, emphasizing the need to understand the biological mechanisms underlying these associations.

Moreover, the article delves into familial predictors, identifying a neuropsychiatric family history of intellectual disabilities and psychosis as significant predictors of ADHD symptoms in children with ASD. This finding emphasizes the importance of considering genetic and environmental factors when assessing ADHD risk in this population. The authors effectively argue that understanding these familial patterns could inform early interventions and targeted support for affected children.

While the article provides valuable insights, it would benefit from a more detailed discussion on the implications of these findings for clinical practice. For instance, the authors could expand on how healthcare providers might utilize this information to screen for ADHD symptoms in children with ASD, particularly in the presence of identified comorbidities. Additionally, a more robust exploration of potential interventions that address both ADHD and ASD symptoms could enhance the practical applicability of their research.

The article "Childhood ADHD and treatment outcome: the role of maternal functioning" by (Darling Rasmussen et al., 2008) provides a comprehensive examination of the multifactorial etiology of Attention-Deficit/Hyperactivity Disorder (ADHD), particularly emphasizing the influence of maternal factors on the development and treatment outcomes of ADHD in children. The authors argue that maternal ADHD symptoms may significantly contribute to the risk of developing ADHD in offspring, underscoring the importance of maternal functioning in understanding the disorder's etiology.

One of the key insights from the article is the assertion that maternal ADHD diagnosis has a stronger correlation with child ADHD than paternal diagnosis. This finding highlights the potential impact of maternal mental health on child

development, suggesting that maternal ADHD could be a critical risk factor that warrants further investigation. The authors also emphasize the need to consider maternal ADHD symptomatology as a prognostic factor for treatment outcomes in children diagnosed with ADHD. This perspective is particularly relevant as it opens avenues for targeted interventions that can address both maternal and child ADHD symptoms concurrently.

Moreover, the article delves into the quality of the mother-child relationship, noting that both ADHD and attachment styles, particularly insecure attachment, may act as mutual risk factors. The authors present a compelling argument that the dynamics of the mother-child relationship can significantly influence the trajectory of ADHD in children, suggesting that interventions aimed at improving attachment may also benefit treatment outcomes for ADHD.

However, while the article effectively outlines the associations between maternal factors and child ADHD, it does not provide empirical data to support its claims regarding the prognostic role of maternal ADHD in treatment outcomes. This lack of quantitative evidence could limit the applicability of the findings in clinical settings. Furthermore, the review could benefit from a deeper exploration of the mechanisms through which maternal ADHD symptoms and attachment styles influence child development, which would enhance the understanding of these complex relationships.

The article "Can Maternal Autoantibodies Play an Etiological Role in ASD Development?" by (Dudova et al., 2002) presents a comprehensive examination of the potential link between maternal autoimmune conditions and the development of Autism Spectrum Disorder (ASD) in children. The authors delve into various studies that highlight the association between maternal health during pregnancy and the neurodevelopmental outcomes in offspring, particularly focusing on the role of maternal autoantibodies.

The article begins by referencing a meta-analysis from 2015, which established a correlation between a family history of autoimmune diseases and an increased risk of autism in children. This foundational insight sets the stage for a deeper exploration into the mechanisms through which maternal health may influence fetal brain development. The authors emphasize findings from a

significant population-based study in Denmark, which revealed that maternal hospitalization for infections during pregnancy was associated with a diagnosis of ASD in the child. This suggests that maternal health, especially concerning infections and inflammation, plays a critical role in neurodevelopmental outcomes.

The authors further elaborate on the cytokine and chemokine profiles observed in children diagnosed with ASD. They note that atypical profiles, particularly elevated levels of inflammatory cytokines during mid-gestation, have been linked to ASD with intellectual disabilities. This connection underscores the importance of understanding the inflammatory environment during pregnancy and its potential impact on fetal brain development.

A key contribution of the article is the introduction of the concept of maternal autoantibody related autism (MAR autism) or maternal autoantibody related autism spectrum disorder (MAR ASD). The authors suggest that maternal IgG autoantibodies can interact with fetal brain proteins, potentially disrupting normal neural development. This hypothesis raises important questions regarding the timing and mechanisms of autoantibody generation and their passage from the maternal circulation to the fetal brain.

Despite the compelling evidence presented, the article acknowledges significant gaps in the current understanding of how maternal autoantibodies contribute to ASD. The authors highlight the need for further research to elucidate the specific pathways through which these autoantibodies exert their effects on fetal brain development. Moreover, the article calls for a more detailed investigation into the neuroantigen passage and the implications of maternal immune responses during pregnancy.

The article titled "Critical Role of the Maternal Immune System in the Pathogenesis of Autism Spectrum Disorder" by (Ravaccia & Ghafourian, 2002) presents a comprehensive overview of the interplay between maternal immune activation and the development of Autism Spectrum Disorder (ASD) in offspring. The authors effectively synthesize existing literature to underscore the significance of maternal immune responses during pregnancy as potential contributors to neurodevelopmental disorders in children, including ASD.

The article begins by contextualizing the historical background of maternal immune activation, referencing the notable increase in autism cases following the Rubella outbreak in the 1960s. This historical precedent serves as a foundation for the authors' argument that environmental factors can significantly impact maternal immune responses, which in turn may affect fetal development. The authors highlight that this relationship has been further substantiated by subsequent epidemiological and animal studies that demonstrate a correlation between maternal immune activation and an elevated risk of ASD in offspring.

Ravaccia and Ghafourian delve into the mechanisms through which maternal immune activation may influence fetal neurodevelopment. They discuss the roles of maternal autoantibodies and cytokines, emphasizing how these immune components can alter the prenatal environment. The review critically evaluates various proposed pathways, suggesting that maternal autoantibodies may interfere with fetal brain development by targeting specific neural proteins, while elevated cytokine levels could disrupt normal neurodevelopmental processes through inflammatory pathways.

However, while the article presents a thorough exploration of the mechanisms linking maternal immune activation to ASD, it also acknowledges the complexity of these interactions. The authors point out that the exact sequence of events and the specific immune factors involved remain poorly understood, indicating a need for further research to elucidate these relationships. This critical reflection on the current state of knowledge highlights the challenges faced in establishing a definitive causal link between maternal autoimmune disease and neurodevelopmental outcomes in children, including Attention-Deficit/Hyperactivity Disorder (ADHD).

The article "Maternal acute and chronic inflammation in pregnancy is associated with common neurodevelopmental disorders: a systematic review" by (X. Han et al., 2001) provides a comprehensive examination of the relationship between maternal autoimmune diseases and the subsequent development of neurodevelopmental disorders in children, particularly focusing on Attention-Deficit/Hyperactivity Disorder (ADHD). The authors synthesize findings from

various studies to highlight how maternal inflammation during pregnancy can impact fetal brain development and increase the risk of ADHD in offspring.

One of the key insights from the article is the systematic approach taken by the authors to collate data from multiple studies, allowing for a robust analysis of the association between maternal autoimmune conditions and ADHD. The article emphasizes that both acute and chronic inflammation during pregnancy can lead to alterations in neurodevelopmental trajectories, thereby increasing the likelihood of neurodevelopmental disorders such as ADHD. This is particularly significant given the rising prevalence of autoimmune diseases among pregnant women, which raises concerns about potential long-term effects on children's health.

The authors also discuss the biological mechanisms that may underpin these associations, such as the role of cytokines and other inflammatory markers that can cross the placental barrier and affect fetal brain development. This mechanistic insight is crucial as it provides a biological basis for the observed epidemiological correlations, thereby strengthening the argument for a causal relationship between maternal autoimmune diseases and the risk of ADHD.

However, while the article presents a thorough review of the existing literature, it also acknowledges the limitations inherent in the studies reviewed. For instance, variations in study design, population demographics, and methodologies can introduce biases that may affect the reliability of the findings. The authors call for more standardized research approaches to better understand the nuances of this association and to establish clearer causal pathways.

The article "Associations between Allergic and Autoimmune Diseases with Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder within Families: A Population-Based Cohort Study" by (Li et al., 2002) provides a comprehensive examination of the potential links between maternal autoimmune conditions and the risk of neurodevelopmental disorders, specifically Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) in children.

The authors present a well-structured argument that maternal allergic and autoimmune diseases may significantly increase the likelihood of ASD and ADHD in offspring. They highlight the role of dysregulation in peripheral dopamine

concentration, which is known to be affected by immune-inflammatory diseases. This connection is particularly relevant as it suggests that maternal immune activation can disrupt the dopaminergic system in developing children, thereby contributing to the onset of these disorders.

A notable aspect of the study is the emphasis on maternal–fetal cellular trafficking and maternal microchimerism. The authors argue that maternal cells can cross the placental barrier, which may play a critical role in the development of the fetal immune system. This phenomenon is posited to be a factor in the emergence of immune-related issues in children, particularly when maternal allergic or autoimmune cells are involved. The hypothesis that these maternal cells could trigger neurodevelopmental disorders through immune mechanisms is an intriguing avenue for further research.

The findings also suggest a stronger correlation between maternal immune diseases and the development of ASD and ADHD compared to paternal conditions. This distinction underscores the importance of maternal health during pregnancy and its potential long-term effects on child development. The authors effectively argue that understanding the mechanisms by which maternal health influences neurodevelopment could lead to better preventative strategies for ASD and ADHD.

CONCLUSION

The reviewed literature highlights a significant association between maternal autoimmune diseases and the risk of Attention-Deficit/Hyperactivity Disorder (ADHD) in children. The introduction establishes a context for understanding how maternal health, particularly autoimmune conditions, may influence neurodevelopmental outcomes. A notable increase in ADHD prevalence, as reported by (Quoc Vuong Tran & Miyake, 2007), emphasizes the urgency of exploring various contributing factors, including maternal stress, nutrition, and environmental exposures.

Several articles delve into the mechanisms linking maternal health to child neurodevelopment. For instance, (Dudova et al., 2002) presents evidence that maternal autoantibodies may disrupt fetal brain development, while (Ravaccia & Ghafourian, 2002) reviews the critical role of the maternal immune system in the

pathogenesis of Autism Spectrum Disorder (ASD), suggesting parallels with ADHD. The systemic review by (X. Han et al., 2001) reinforces the link between maternal inflammation during pregnancy and neurodevelopmental disorders, indicating that both acute and chronic inflammation can alter neurodevelopmental trajectories.

Additionally, the familial associations explored by (Li et al., 2002) suggest that maternal allergic and autoimmune diseases may disrupt dopaminergic systems in offspring, further supporting the hypothesis that maternal health significantly impacts ADHD risk. The interplay between maternal factors, such as ADHD symptoms and attachment styles, as discussed by (Darling Rasmussen et al., 2008), underscores the multifactorial nature of ADHD etiology.

The collective findings across these studies indicate that maternal autoimmune diseases and related immune dysregulation may play a pivotal role in the neurodevelopmental trajectories of children, particularly concerning ADHD. The evidence suggests a need for further research to elucidate the specific pathways through which maternal health influences child development, emphasizing the importance of maternal well-being during pregnancy.

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REFERENCES

1. Quoc Vuong Tran, N. & Miyake, K., 2007. Neurodevelopmental Disorders and Environmental Toxicants: Epigenetics as an Underlying Mechanism. ncbi.nlm.nih.gov
2. Linda Lamanna, A., Craig, F., Matera, E., Simone, M., Buttiglione, M., & Margari, L., 2007. Risk factors for the existence of attention

- deficit hyperactivity disorder symptoms in children with autism spectrum disorders. ncbi.nlm.nih.gov
3. Darling Rasmussen, P., Jakob Storebø, O., Shmueli-Goetz, Y., Bo Bojesen, A., Simonsen, E., & Bilenberg, N., 2008. Childhood ADHD and treatment outcome: the role of maternal functioning. ncbi.nlm.nih.gov
 4. Dudova, I., Horackova, K., Hrdlicka, M., & Balastik, M., 2002. Can Maternal Autoantibodies Play an Etiological Role in ASD Development?. ncbi.nlm.nih.gov
 5. Ravaccia, D. & Ghafourian, T., 2002. Critical Role of the Maternal Immune System in the Pathogenesis of Autism Spectrum Disorder. ncbi.nlm.nih.gov
 6. X. Han, V., Patel, S., F. Jones, H., C. Nielsen, T., S. Mohammad, S., J. Hofer, M., Gold, W., Brilot, F., J. Lain, S., Nassar, N., & C. Dale, R., 2001. Maternal acute and chronic inflammation in pregnancy is associated with common neurodevelopmental disorders: a systematic review. ncbi.nlm.nih.gov
 7. Li, D. J., Tsai, C. S., C. Hsiao, R., Chen, Y. L., & Yen, C. F., 2002. Associations between Allergic and Autoimmune Diseases with Autism Spectrum Disorder and Attention-Deficit/Hyperactivity Disorder within Families: A Population-Based Cohort Study. ncbi.nlm.nih.gov