



Association Between Autism Spectrum Disorders and Cardiometabolic Diseases

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 between Autism Spectrum Disorders (ASD) and cardiometabolic diseases is a complex and multifaceted area of research, as evidenced by the growing body of literature examining the interplay between these conditions.

Literature Review: Moreover, (Tye et al., 2009) characterize the prevalence of comorbid conditions, particularly obesity, among individuals with ASD, highlighting systemic barriers to healthcare access that exacerbate health disparities. This necessitates targeted interventions tailored to the unique needs of this population. The discussion is enriched by (E. Glinton & H. Elsea, 2009), who advocate for the identification of metabolic biomarkers, and (Robea et al., 2000), who connect vitamin deficiencies and gastrointestinal issues to ASD symptoms, underscoring the importance of dietary management. Additionally, (Erbescu et al., 2002) discuss immune dysregulation as a significant factor, linking genetic and environmental influences to comorbid conditions. The metabolomic study presented by (Yazdani et al., 2004) illustrates metabolic differences in children with ASD, suggesting potential biomarkers for cardiometabolic diseases.

Conclusion: In conclusion, the synthesis of these findings underscores the necessity for a multidisciplinary approach to understanding and addressing the complex relationships between ASD and cardiometabolic diseases. This includes considering biochemical, environmental, dietary, and healthcare access factors to develop comprehensive strategies aimed at improving health outcomes for individuals with ASD.

Keyword: Autism Spectrum Disorders, Cardiometabolic Diseases

INTRODUCTION

The association between Autism Spectrum Disorders (ASD) and cardiometabolic diseases is a complex and multifaceted area of research, as evidenced by the growing body of literature examining the interplay between these conditions. The foundational work by (K. Griffiths & J. Levy, 2007) provides critical insights into the biochemical underpinnings of ASD, suggesting that mitochondrial dysfunction may play a significant role in the disorder's pathophysiology. This study highlights the importance of mitochondrial health in the central nervous system, which has substantial metabolic demands, thereby linking metabolic processes to neurodevelopmental outcomes.

Building on these biochemical insights, (Carpita et al., 2008) explore the effects of maternal diabetes and obesity on the intrauterine environment, suggesting that these metabolic conditions may increase the risk of ASD in offspring. Their findings indicate that maternal metabolic health prior to and during pregnancy can have long-term implications for the neurodevelopmental trajectory of children, further emphasizing the importance of metabolic factors in understanding ASD.

(Tye et al., 2009) expand this dialogue by characterizing the prevalence of comorbid medical conditions in individuals with ASD, noting a concerning trend of increased obesity and dietary issues among this population. Their integrative review underscores the barriers that hinder access to healthcare services for individuals with ASD, which may exacerbate existing health disparities and contribute to higher mortality rates. The authors advocate for targeted healthcare interventions that address the unique needs of individuals with ASD, emphasizing the necessity of a holistic approach to their care.

(Mohammed Alhowikan et al., 2009) further investigate the environmental and dietary factors influencing ASD, positing that these elements may interact with metabolic conditions such as diabetes to heighten the risk of developing the disorder. This review highlights the intricate relationship between environmental

exposures and metabolic health, suggesting that understanding these connections is vital for elucidating the etiology of ASD.

In the same vein, (E. Ginton & H. Elsea, 2009) delve into the heterogeneity of ASD and the associated economic burdens on families, advocating for the identification of metabolic biomarkers to facilitate earlier diagnosis and tailored interventions. Their focus on untargeted metabolomics represents a promising avenue for future research, as it may unveil critical insights into the metabolic dysfunctions associated with ASD.

(Robea et al., 2000) contribute to this discourse by examining the relationship between vitamin deficiencies and ASD symptoms, revealing that children with ASD often experience gastrointestinal issues that complicate their nutritional intake. Their findings highlight the importance of addressing dietary factors in the management of ASD, particularly in relation to comorbid obesity.

(A. Chernikova et al., 2001) introduce the concept of the brain-gut-microbiome axis, proposing that gut health may significantly impact brain function and behavior in individuals with ASD. This perspective opens new avenues for research into how dietary and microbial factors may influence both neurodevelopment and metabolic health in this population.

(Erbescu et al., 2002) further elaborate on the immune dysregulation observed in ASD, linking genetic and environmental factors to immune system alterations that may predispose individuals to various comorbid conditions. Their review underscores the complexity of ASD as a spectrum of disorders with diverse biological underpinnings, including significant interactions between immune health and metabolic status.

Finally, (Yazdani et al., 2004) present a metabolomic study that seeks to elucidate the metabolic profiles associated with ASD in Jamaican children, thereby contributing to the understanding of how metabolic disruptions may connect genetic and environmental factors in this neurodevelopmental disorder. Their work emphasizes the need for comprehensive analyses that can inform targeted interventions for affected individuals.

The synthesis of these articles reveals a compelling narrative regarding the intricate relationships between ASD and cardiometabolic diseases, highlighting the

necessity for multidisciplinary approaches in research and healthcare to address the diverse needs of affected individuals.

LITERATURE REVIEW

The article by (K. Griffiths & J. Levy, 2007) presents a compelling examination of the potential link between mitochondrial dysfunction and Autism Spectrum Disorder (ASD). The authors provide a thorough overview of how mitochondrial impairments may intersect with the pathophysiology of ASD, emphasizing that while ASD is primarily characterized by social and communication deficits, its underlying biological mechanisms may extend beyond typical neurodevelopmental frameworks.

The critical evaluation of the article highlights several key insights. First, the authors articulate that mitochondria are not merely energy producers; they also play crucial roles in calcium homeostasis, apoptosis regulation, and the formation of reactive oxygen species. This multifaceted functionality of mitochondria suggests that any dysfunction could have wide-ranging implications for cellular health and signaling pathways, which are vital for neurodevelopment. The authors effectively synthesize existing literature to illustrate how mitochondrial dysfunction could lead to neurodevelopmental anomalies, thereby providing a biochemical basis for the observed behavioral symptoms in individuals with ASD.

Furthermore, the article underscores the gender disparity in ASD prevalence, with males being more frequently affected than females. This observation raises important questions about the genetic and environmental factors that may contribute to mitochondrial dysfunction and, consequently, the development of ASD. The authors suggest that a better understanding of these connections could inform future research directions and therapeutic strategies.

However, while the article provides a robust review of the potential biochemical links between mitochondrial dysfunction and ASD, it also indicates that current medical therapies primarily address behavioral symptoms rather than underlying biological causes. This limitation presents a critical gap in treatment approaches and emphasizes the need for further research into targeted interventions that could address mitochondrial health in individuals with ASD.

The article titled "Oxidative Stress, Maternal Diabetes, and Autism Spectrum Disorders" by (Carpita et al., 2008) presents a comprehensive examination of the potential links between maternal metabolic conditions, particularly diabetes and obesity, and the development of autism spectrum disorders (ASD) in offspring. The authors argue that alterations in brain connectivity, which are characteristic of ASD, may be influenced by changes in the intrauterine environment caused by maternal health issues.

One of the key insights from the article is the emphasis on the role of oxidative stress and inflammation in the context of maternal health and ASD. The authors review a growing body of epidemiological evidence suggesting that maternal obesity and diabetes are significant risk factors for not only somatic but also psychiatric disorders, including ASD. This connection is particularly relevant given the rising prevalence of these metabolic conditions globally. The authors effectively highlight the biological pathways that may mediate these associations, such as maternal immune dysregulation and oxidative stress, which are posited to contribute to the neurodevelopmental outcomes in children.

Moreover, the article discusses the implications of early life insults, emphasizing that the intrauterine environment can have lasting effects on the newborn's health. The authors draw on animal model studies, particularly those involving high-fat diets, to elucidate the mechanisms through which maternal metabolic conditions may impact fetal development and contribute to the risk of developing ASD. This approach is commendable as it provides a biological framework that supports the epidemiological findings.

However, while the article presents a thorough overview of the existing literature, it could benefit from a more detailed discussion on the specific biological mechanisms linking oxidative stress and maternal diabetes to ASD. The review touches on the pathways but does not delve deeply into the molecular processes involved, which could provide a clearer understanding of the etiopathogenesis of ASD.

The article "Characterizing the Interplay Between Autism Spectrum Disorder and Comorbid Medical Conditions: An Integrative Review" by (Tye et al., 2009) offers a comprehensive examination of the relationship between Autism

Spectrum Disorder (ASD) and various comorbid medical conditions, particularly focusing on cardiometabolic diseases such as obesity and poor dietary habits. The authors present a compelling argument that individuals with ASD experience higher rates of obesity and related health issues, which are exacerbated by barriers to healthcare access.

One of the pivotal insights from the article is the identification of systemic barriers that hinder individuals with ASD from utilizing general health services. The authors highlight that impaired communication skills and heightened sensory sensitivities significantly impede these individuals' ability to engage with healthcare systems, ultimately leading to inadequate management of comorbid conditions. This finding underscores the necessity for healthcare services that are not only accessible but also tailored to meet the unique needs of individuals with ASD.

Furthermore, the article emphasizes the heterogeneity of ASD, suggesting that the presence of comorbid medical conditions varies widely among individuals. This variability complicates the understanding of how different factors interact to produce the behaviors associated with ASD. The authors call for more integrative research that takes into account the interplay between biological, environmental, and behavioral factors, which could lead to a better understanding of the functional profiles of individuals with ASD.

The review also highlights the importance of addressing dietary habits and obesity within this population. The authors note that poor dietary choices are prevalent among individuals with ASD, potentially due to sensory sensitivities and restricted eating patterns. This aspect is critical as it links directly to the increased risk of cardiometabolic diseases, emphasizing the need for targeted interventions that promote healthier lifestyles.

The article "Impact of environmental pollution, dietary factors and diabetes mellitus on Autism Spectrum Disorder (ASD)" by (Mohammed Alhowikan et al., 2009) provides a comprehensive examination of the multifaceted relationships between environmental and nutritional factors and the risk of developing Autism Spectrum Disorder (ASD). The authors assert that ASD is fundamentally a

neurodevelopmental disorder with biological underpinnings, yet they emphasize the significant role that external factors may play in its etiology.

One of the key insights presented in this review is the potential interplay between environmental pollution, dietary influences, and the incidence of diabetes mellitus, which is posited to be linked with an increased risk of ASD. The authors argue that these factors may act synergistically during critical periods of brain development, thereby heightening the likelihood of ASD manifestation. This perspective aligns with contemporary research suggesting that environmental exposures, particularly during sensitive developmental windows, can influence neurodevelopmental outcomes.

The discussion surrounding diabetes mellitus is particularly noteworthy. The authors highlight a significant correlation between diabetes and ASD, suggesting that individuals with diabetes may have a higher propensity to develop ASD. This connection raises important questions about the underlying biological mechanisms that might explain this association. The authors call for further research to elucidate the biological pathways linking ASD and Type 2 Diabetes Mellitus (T2DM), indicating that understanding these mechanisms is crucial for developing effective interventions and prevention strategies.

The review effectively synthesizes existing literature on the topic, though it also acknowledges the need for additional studies to deepen the understanding of the complex interactions at play. The authors emphasize that more research is needed to validate the therapeutic potential of microbiota modulation in ASD and associated health conditions.

The article "Untargeted Metabolomics for Autism Spectrum Disorders: Current Status and Future Directions" by (E. Ginton & H. Elsea, 2009) provides a comprehensive overview of the complexities associated with Autism Spectrum Disorders (ASD), emphasizing the need for innovative diagnostic approaches, particularly through the lens of metabolomics.

The authors begin by outlining the clinical spectrum of ASD, which is characterized by deficits in social communication, social interaction, and the presence of restrictive and repetitive behaviors. They highlight the heterogeneity of ASD, noting that individuals exhibit a wide range of impairments and associated

medical complications. This variability complicates the understanding and treatment of ASD, as patients can present with differing degrees of intellectual disability and comorbid conditions, including those related to metabolic health.

A significant aspect of the article is the discussion surrounding the prevalence of ASD in the United States, estimated at 16.8 per 1,000 children older than eight years, with some subgroups exhibiting even higher rates. The economic burden of ASD on families is also addressed, with an annual additional cost of approximately \$17,081 attributed to healthcare, education, and therapy services. These insights underscore the societal implications of ASD and highlight the urgency for effective diagnostic and therapeutic strategies.

The authors advocate for the implementation of routine metabolic testing for patients with ASD, particularly in cases where physical examination features or historical details warrant further investigation. They contrast this with the recommendations from the American Academy of Pediatrics, which favors metabolic workups primarily in patients with intellectual disabilities or global developmental delays.

The article "Relationship between Vitamin Deficiencies and Co-Occurring Symptoms in Autism Spectrum Disorder" by (Robea et al., 2000) provides a focused exploration of the intersection between micronutrient deficiencies and the symptoms associated with autism spectrum disorder (ASD). The authors effectively highlight the prevalence of dietary issues among children with ASD, linking these to broader gastrointestinal (GI) problems that may exacerbate the disorder's behavioral manifestations.

A critical evaluation of the article reveals several key insights. First, the authors present compelling evidence that children with ASD frequently exhibit deficiencies in essential vitamins, including B1, B6, B12, A, and D. This aspect is particularly significant, as it underscores the potential role of nutrition in managing ASD symptoms. The acknowledgment of feeding and eating problems as a prominent concern among this population is a valuable contribution to the literature, as these issues have often been overshadowed by the more commonly discussed social and communication deficits associated with ASD.

The article also addresses the alarming prevalence of obesity among children with ASD, noting that these children tend to gain weight more rapidly than their neurotypical peers. This finding is critical, as it suggests a potential link between ASD and cardiometabolic diseases. The authors reference studies indicating that overweight and obesity are more common in children with ASD, which raises concerns about the long-term health implications for this population. However, while the article provides a solid overview of the correlation between ASD and dietary issues, it could benefit from a deeper exploration of the mechanisms underlying these relationships. For instance, how do specific vitamin deficiencies contribute to the behavioral symptoms of ASD, and what interventions might mitigate these effects?

Moreover, the authors mention various factors influencing the prevalence of feeding problems, including parental education and socioeconomic status. This acknowledgment introduces a socio-economic dimension to the discussion, suggesting that interventions targeting these factors may be necessary to improve dietary outcomes for children with ASD. However, the article would be strengthened by more explicit recommendations for addressing these socio-economic barriers in conjunction with nutritional interventions.

The article "The Brain-Gut-Microbiome System: Pathways and Implications for Autism Spectrum Disorder" by (A. Chernikova et al., 2001) presents a comprehensive examination of the interactions between gut microbiota and the neurological aspects of Autism Spectrum Disorder (ASD). The authors argue that the gut microbiome plays a significant role in modulating brain function, which in turn affects social behavior and the symptomatology of ASD. This perspective aligns with the increasing recognition of the gut-brain axis and its influence on neurodevelopmental disorders.

One of the key insights from the article is the examination of the mechanisms by which gut microbiota may impact the development of neural networks related to social and emotional skills. The authors highlight that alterations in gut microbiota composition can lead to the production of metabolites that influence brain function and behavior. This connection is particularly relevant given the rising prevalence of both ASD and cardiometabolic diseases, as the gut

microbiome is increasingly implicated in metabolic processes and inflammatory pathways that could link these two domains.

The review systematically discusses current research findings that support the hypothesis of a brain-gut-microbiome interaction in ASD. The authors provide a critical evaluation of studies that have explored behavioral and neurological impairments in individuals with ASD, suggesting that microbiota-targeted therapies could offer new avenues for intervention. By focusing on the biochemical and physiological pathways that connect gut health with neurodevelopmental outcomes, the authors present a nuanced understanding of how gut microbiota may influence not only ASD symptomatology but also potential comorbid conditions, including cardiometabolic diseases.

However, while the article presents compelling evidence for the role of the gut microbiome in ASD, it also acknowledges the complexity of these interactions. The authors caution that more research is needed to delineate the specific pathways involved and to establish causative relationships. This critical perspective is essential, as it underscores the need for a rigorous scientific approach to validate the therapeutic potential of microbiota modulation in ASD and associated health conditions.

The article "Re-emerging concepts of immune dysregulation in autism spectrum disorders" by (Erbescu et al., 2002) presents a comprehensive exploration of the multifaceted nature of Autism Spectrum Disorder (ASD), particularly emphasizing its neurodevelopmental characteristics and the interplay between genetic and environmental factors. The authors articulate that ASD is not only marked by social interaction deficits and restricted interests but is also intricately linked with various medical conditions, including gastrointestinal and autoimmune disorders.

A critical aspect of the article is its discussion on the prevalence of ASD, which has seen a significant increase, currently estimated to affect at least 1% of children. This statistic underscores the urgency in understanding the underlying mechanisms of ASD, particularly in the context of its comorbidities. The authors effectively categorize ASD based on the DSM-5 criteria into three levels of

severity, which aids in clarifying the spectrum of support needs among individuals diagnosed with the disorder.

The article highlights the strong genetic component associated with ASD, noting that both rare and common genetic variations contribute to the risk of developing the disorder. This insight is crucial as it not only enhances the understanding of the biological underpinnings of ASD but also points towards potential genetic markers that could be pivotal in early diagnosis and intervention. The authors further delve into the immune response as a significant biological pathway involved in ASD, suggesting that immune dysregulation may play a role in the disorder's manifestation.

Moreover, the discussion on environmental factors such as air pollution, heavy metal exposure, and nutritional deficiencies during pregnancy adds another layer of complexity to the understanding of ASD. The interaction between genetic predispositions and environmental influences is particularly noteworthy, as it suggests a multifactorial approach to both the etiology and management of ASD. This perspective is essential for developing targeted therapeutic strategies that consider both genetic and environmental modulations.

The article "Metabolomic profiles in Jamaican children with and without autism spectrum disorder" by (Yazdani et al., 2004) presents a significant investigation into the metabolic differences between children diagnosed with autism spectrum disorder (ASD) and their typically developing (TD) counterparts. This study is particularly relevant in the context of understanding the potential links between ASD and cardiometabolic diseases, as it explores the metabolic profiles that may underlie both conditions.

The authors employed a metabolomic case-control study design, which is a robust approach for identifying biochemical alterations associated with specific health conditions. By analyzing a comprehensive range of metabolites, the researchers aimed to uncover significant differences that could provide insights into the pathophysiology of ASD. The findings revealed notable alterations in metabolite profiles, suggesting that children with ASD may have distinct metabolic signatures compared to TD children.

One critical aspect of the study is its focus on a specific population—Jamaican children—which may limit the generalizability of the findings. While the results are intriguing, it is essential to consider how cultural, dietary, and environmental factors might influence metabolic profiles. The authors do acknowledge this limitation, emphasizing the need for further research across diverse populations to validate their findings.

Moreover, the study's implications extend beyond the realm of autism. The identification of specific metabolites associated with ASD could pave the way for understanding the broader context of cardiometabolic health in these children. For instance, certain metabolites might serve as biomarkers for increased risk of cardiometabolic diseases, which are known to have higher prevalence rates in individuals with neurodevelopmental disorders. This connection warrants further investigation, as it could inform preventative strategies and therapeutic interventions.

CONCLUSION

The literature reviewed presents a comprehensive examination of the intricate relationship between Autism Spectrum Disorders (ASD) and cardiometabolic diseases, revealing a multifaceted interplay of biological, environmental, and dietary factors. The foundational work by (K. Griffiths & J. Levy, 2007) highlights mitochondrial dysfunction as a potential contributor to ASD's pathophysiology, suggesting that metabolic health is crucial for neurodevelopmental outcomes. This biochemical perspective is further supported by (Carpita et al., 2008), who elucidate the impact of maternal diabetes and obesity on the risk of ASD, emphasizing the long-term implications of maternal metabolic conditions on offspring.

Moreover, (Tye et al., 2009) characterize the prevalence of comorbid conditions, particularly obesity, among individuals with ASD, highlighting systemic barriers to healthcare access that exacerbate health disparities. This necessitates targeted interventions tailored to the unique needs of this population. The environmental and dietary influences on ASD are further explored by

(Mohammed Alhowikan et al., 2009), who suggest that these factors may interact with metabolic conditions to increase ASD risk.

The discussion is enriched by (E. Ginton & H. Elsea, 2009), who advocate for the identification of metabolic biomarkers, and (Robea et al., 2000), who connect vitamin deficiencies and gastrointestinal issues to ASD symptoms, underscoring the importance of dietary management. The concept of the brain-gut-microbiome axis introduced by (A. Chernikova et al., 2001) further emphasizes the need to consider gut health in relation to both neurodevelopment and metabolic health.

Additionally, (Erbescu et al., 2002) discuss immune dysregulation as a significant factor, linking genetic and environmental influences to comorbid conditions. The metabolomic study presented by (Yazdani et al., 2004) illustrates metabolic differences in children with ASD, suggesting potential biomarkers for cardiometabolic diseases.

In conclusion, the synthesis of these findings underscores the necessity for a multidisciplinary approach to understanding and addressing the complex relationships between ASD and cardiometabolic diseases. This includes considering biochemical, environmental, dietary, and healthcare access factors to develop comprehensive strategies aimed at improving health outcomes for individuals with ASD.

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