Journal of Neurochemistry

WILEY

SPECIAL ISSUE Autism Spectrum Disorder

Journal of Neurochemistry JNC The Official Journal of the International Society for Neurochemistry

SYSTEMATIC REVIEW OPEN ACCESS

Presymptomatic Biological, Structural, and Functional Diagnostic Biomarkers of Autism Spectrum Disorder

Bonnie M. Wang[1] | Zoe Mills[1,2] | Hannah F. Jones[2,3] | Johanna M. Montgomery[1,2] | Kevin Y. Lee[1,2]

[1]Department of Physiology, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand | [2]Centre for Brain Research, Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand | [3]Department of Neuroservices, Starship Children's Hospital, Auckland, New Zealand

Correspondence: Kevin Y. Lee (kevin.lee2@ucsf.edu)

Received: 29 November 2024 | **Revised:** 26 April 2025 | **Accepted:** 6 May 2025

Funding: This work was supported by the Department of Physiology, University of Auckland, New Zealand (PHYSIOL 399), and the Neurological Foundation of New Zealand (1954 SRF to K.Y.L.).

Keywords: autism spectrum disorder | electroencephalography | magnetic resonance imaging | magnetoencephalography | presymptomatic diagnostic biomarkers | pupillometry

ABSTRACT

Autism spectrum disorder (ASD) is a common neurodevelopmental disorder clinically diagnosed by persistent deficits in three areas of social communication and interaction, plus at least two of four types of restricted repetitive behaviors. ASD has been shown to be caused by genetic predisposition and environmental factors; however, the heterogeneity of ASD complicates its diagnosis and treatment. Early behavioral interventions have shown significant benefits, emphasizing the urgent need for reliable diagnostic biomarkers to enhance long-term outcomes. Here we provide a systematic review that outlines current findings on genetic and neurological biomarkers for presymptomatic ASD diagnoses, assessed prior to the observation of behavioral manifestations. Specifically, we offer insights into the mechanisms of presymptomatic neurological, biological, structural, and functional markers for ASD, compare outcomes across studies, and critically assess their limitations and implications. Recent findings highlight genotype-guided therapeutic strategies in animal models, such as dietary zinc supplementation for reversing ASD-associated behaviors by synaptic deficits. However, the differential efficacy based on underlying genotypes, along with challenges in identifying reliable genomic biomarkers prior to symptom onset, indicates the need for further research. Notably, recent advancements in imaging technologies like magnetic resonance imaging, electroencephalography, and pupillometry have shown promising markers in neonates, and at 3 and 9 months old, respectively. Newer developments in magnetoencephalography hardware can facilitate the much-needed infant ASD studies. It is important to note that many of these biomarker findings are preliminary, and further validation for clinical use is required. Continued research is needed to advance the practicality, reliability, and acceptability of these biomarkers to improve ASD diagnosis and treatment strategies.

1 | Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder typically emerging by 2 years of age that is clinically diagnosed by persistent deficits in three areas of social communication and interaction in addition to at least two of four types of restricted, repetitive patterns of behaviours (RRBs; American Psychiatric Association 2022). ASD causation has a significant

Abbreviations: ASD, autism spectrum disorder; CC, corpus callosum; EEG, electroencephalography; ERPs, event-related potentials; FA, fractional anisotropy; fc, functional connectivity; GA, gestational age; GABA, gamma-aminobutyric acid; GxE, gene-environmental; LC, locus coeruleus; MEG, magnetoencephalography; MRI, magnetic resonance imaging; PAF, peak alpha frequency; SNPs, single nucleotide polymorphisms; TD, typically developing.

genetic contribution, with over 1000 genes implicated (de la Torre-Ubieta et al. 2016). Idiopathic ASD is also common, making ASD a highly complex and heterogeneous disorder of high prevalence. It affects 1 in 100 children globally, and estimates have risen over time (Zeidan et al. 2022). ASD is predominantly diagnosed in males, who are four times more likely to receive an ASD diagnosis than females (Maenner et al. 2020). Individuals with ASD frequently require health, education, and social support services, posing a major fiscal impact on healthcare systems. The impaired quality of life often extends beyond the individuals directly affected, placing a substantial hardship upon their families.

Current diagnostic practices typically rely on a spectrum of behavioural cues culminating over the years as symptoms, which may not always yield consistent or early diagnoses, particularly in young children (American Psychiatric Association 2022). This variability underscores the absence of reliable and objective diagnostic biomarkers for ASD. There is consensus that timely diagnosis and intervention, especially before the full manifestation of behavioural deficits, are crucial for improving the quality of life. Indeed, the benefits of early intervention, such as sensory exposure during critical periods of brain development, can normalise neural activity and improve behavioural outcomes (Dawson et al. 2012). Therefore, the identification of presymptomatic biomarkers that enable early intervention is paramount. In the current review, we explore promising presymptomatic biomarkers, encompassing genetic and neurological indicators as well as environmental influences on them, and non-neurological diagnostic biomarkers. We evaluate their mechanisms, examine their potential and limitations, and propose directions for future development.

2 | Genetic Biomarkers

The genetic aetiology of ASD, like many other psychiatric conditions, is well regarded as profound yet inherently complex due to the significant genetic heterogeneity, pleiotropy, and polygenic nature of the disorder. Genomic biomarkers can be classified into DNA-related markers, including single nucleotide polymorphisms (SNPs), copy number variants (CNVs), cytogenetic rearrangements, and epigenetic modifications; and RNA-related markers, such as mRNA and microRNA (Novelli et al. 2008). Such genetic variation, when conclusively linked to changes in expression, functionality, and regulatory processes involved in pathological conditions or therapeutic responses, serves as a critical biological signal (Novelli et al. 2008). Despite extensive research, no genomic biomarker has yet been validated for clinical use in ASD. However, ongoing efforts to identify such biomarkers hold considerable promise, as their future utility could provide significant predictive power for early presymptomatic diagnosis. Additionally, the identification and stratification of ASD-affected individuals into genetically distinct subpopulations could facilitate the option to tailor treatment strategies to target associated subpopulation-specific deficits.

Early twin studies provided the first compelling evidence for a strong genetic component in autism spectrum disorder (ASD), with concordance rates suggesting a Mendelian inheritance pattern (Folstein and Rutter 1977). This major finding has laid the groundwork for research dedicated to understanding the significant genetic influence underlying ASD, which has been further supported by recent studies showing a heritability rate exceeding 80% (Folstein and Rutter 1977; Sandin et al. 2017; Tick et al. 2016). Today, conservative estimates of 20% (but have been reported as high as 40%) of all ASD cases are considered to have a known underlying cause, typically associated with a genetic syndrome (De Rubeis et al. 2014; Gaugler et al. 2014; Iossifov et al. 2014; Schaefer et al. 2013; Tammimies et al. 2015). The remaining cases with no linkable cause yet found, either genetic or environmental, are deemed "idiopathic" or "primary" ASD. It is well documented that in cases of ASD with an established genetic basis, variation frequently arises through inheritance and as spontaneous mutations. Current estimates attribute ~15%–20% of ASD liability to rare de novo variations and > 50% to common inherited variants (de la Torre-Ubieta et al. 2016; Gaugler et al. 2014; Sanders et al. 2015).

The discovery of the genetic links confirming many secondary ASD cases (i.e., as a result of another underlying medical condition) has been expedited by modern whole genome/exome sequencing studies (Abrahams and Geschwind 2008; De Rubeis et al. 2014; O'Roak et al. 2012; Sanders et al. 2012, 2015; Satterstrom et al. 2020). The Simons Foundation Autism Research Initiative (SFARI) human gene module database now includes over 1200 rare and common variants that are scored and categorized based on the strength of evidence and relevance to ASD risk (Banerjee-Basu and Packer 2010). Syndromic ASD-associated genes are defined as rare monogenic syndromes in which a significant subset of individuals develops ASD. There are 207 syndromic genes in this database, 116 of which are considered both syndromic and high confidence, with an additional 91 genes classified as strong candidates or supported by suggestive evidence to have an association with ASD. The genes that reach the most stringent levels of gene score classification include, in order: *SHANK3* (Phelan-McDermid Syndrome, ~60% ASD prevalence; Synaptic signalling/organisation; (Gergoudis et al. 2020)); *MECP2* (Rett Syndrome, ~50% prevalence; Transcriptional regulation; (Wulffaert et al. 2009)), *PTEN* (PTEN Hamartoma Tumour Syndrome, 25–30% ASD prevalence; Cell growth regulation; (Cummings et al. 2022)), *SYNGAP1* (SYNGAP1-Related Intellectual Disability, 50%–70% ASD prevalence; Synaptic functioning; (Mignot et al. 2016; Wiltrout et al. 2024)), *SCN1A* (Dravet Syndrome; 20%–25% ASD prevalence; Ion channel function; (Brown et al. 2020; He et al. 2018)), *ARID1B* (Coffin-Siris Syndrome, 45% ASD prevalence; Chromatin remodelling; (Vasko and Schrier Vergano 2022)), *ADNP* (Helsmoortel-Van der Aa Syndrome, > 90% ASD prevalence; Chromatin remodelling; (Van Dijck et al. 2019)), *DYRK1A* (DYRK1A-Related Intellectual Disability, 85% ASD prevalence; Kinase activity; (Kurtz-Nelson et al. 2023)), CHD2 (CHD2-Related Syndrome, ~40% ASD prevalence; Chromatin remodelling; (Chen et al. 2020; Thomas et al. 2015)). However, despite extreme genetic heterogeneity and close association with a significant number of monogenic conditions, no ASD-associated genes have been identified with complete penetrance, making it difficult to determine ASD diagnosis based on genetics alone. Furthermore, Down Syndrome is the only monogenic syndrome associated with ASD that is routinely screened prenatally (de Sena Barbosa et al. 2024). The relative rarity of these conditions diminishes the possibility of

standardized prenatal testing such as chorionic venous sampling and amniocentesis.

While rare variants often have a large effect size and can be easily categorized, common variants account for a large proportion of ASD liability (~50% of established Mendelian risk). These variants are SNPs frequently found in the general population, which primarily contribute to normal genetic diversity; however, in combination, the additive effect of these low-effect variants can confer an increased burden of disease susceptibility (Weiner et al. 2017). Polygenic risk scores assess an individual's genome and produce an estimated risk profile according to the presence and combination of these disease-attributable variants. However, there are currently only five ASD-specific genetic loci that have reached genome-wide significance (Anney et al. 2012; Devlin et al. 2011; Grove et al. 2019; Klei et al. 2012). Interestingly, in multiplex families with multiple cases of ASD caused by inherited rare causative mutations, an increased burden of background ASD-related common variants has been reported (Chang et al. 2022; Cirnigliaro et al. 2023; Leppa et al. 2016). This over-transmission points toward a threshold susceptibility model of liability where polygenic risk also affects the penetrance of de novo rare variants and vice versa, and could better inform prognosis in these cases (Cirnigliaro et al. 2023). Clinical implementation of polygenic risk scores into routine practice continues to evolve as accuracy and understanding improve the precision of diagnosis.

Interestingly, high confidence ASD risk genes exhibit significant functional and regulatory overlap, converging in critical neurodevelopmental and synaptic signalling pathways (Bill and Geschwind 2009; Jin et al. 2020; Moyses-Oliveira et al. 2020; Pinto et al. 2014; Quesnel-Vallières et al. 2019; Sestan and State 2018; State and Sestan 2012; Sullivan et al. 2019; Willsey et al. 2022). Many of the affected proteins physically interact within distinct neuronal structures, such as synapses, directly influencing synaptic architecture, transmission, and plasticity. Other examples of converging roles include chromatin remodelling, cytoskeletal regulation, and protein homeostasis (Sullivan et al. 2019; Willsey et al. 2022). ASD risk genes are also known to have indirect influences by acting as upstream regulators affecting transcription and translation networks as well as epigenetic modification of other low-risk genes (De Rubeis et al. 2014; Satterstrom et al. 2018). The nexuses at which these genes overlap have significant clinical and scientific relevance as they are suggestive of common underlying mechanisms that could explain ASD pathogenesis in individuals. Targeting this common mechanism may produce therapeutic targets with broad and efficacious clinical applicability despite the intrinsic genetic and clinical heterogeneity of ASD.

Currently, there is a modest portrayal of genotype-guided therapeutic strategies in the ASD literature. We have recently shown that potential ASD-targeted treatments exhibit differential efficacy based on the underlying genotype, as shown using the same treatment on different genetic models (Lee et al. 2024). Dietary zinc supplementation has been shown to reverse and prevent ASD-associated behaviors in *Shank3*$^{-/-}$ and *TBR1*$^{-/-}$ genetic rodent models by targeting underlying synaptic deficits, indicating zinc's potential therapeutic utility in Phelan-McDermid Syndrome and TBR1-Related Disorder (Fourie et al. 2018; Lee et al. 2022; Vyas et al. 2020). However, in the *Shank2*$^{-/-}$ model, zinc supplementation produced differential effects, failing to achieve comparable behavioral improvements in working memory (Lee et al. 2024). These findings underscore the complexity of treatment responses in ASD and the necessity of considering genotype-specific factors when developing and implementing therapeutic strategies for clinical trials to achieve efficacy to progress through phases.

The genes *OXTR* and *CD38*, which are integral to oxytocin regulation, each have single nucleotide polymorphisms (SNPs) associated with autism spectrum disorder (ASD) that have been shown to modulate responses to oxytocin-based interventions (Frye et al. 2019; Hammock et al. 2012). In healthy individuals, homozygous carriers of the *CD38* SNP rs3796863 exhibited enhanced fusiform gyrus activation and faster reaction times during social matching tasks following intranasal oxytocin (Sauer et al. 2012). This finding suggests that risk genetic variation in *CD38* likely results in a lower baseline of oxytocin, leading to super sensitivity and compensatory mechanisms, influencing the efficacy of oxytocin to augment social cognitive processes in carriers with this variant (Sauer et al. 2012). Similarly, in individuals with ASD, carriers of the *OXTR* SNP rs6791619 demonstrated significant improvements in Clinical Global Impression-Improvement (CGI-I) scores with oxytocin treatment compared to placebo (Kosaka et al. 2016).

Despite the failure to identify genomic biomarkers in ASD to date, future research in this area continues to hold significant promise. Points of convergence and shared molecular mechanisms could provide a framework for classifying ASD subtypes and understanding their complex aetiology. By uncovering these common pathways, through advancing technology and database creation, researchers may bridge decades of inconclusive findings and move toward significant progress in therapeutic development. Furthermore, early detection of ASD through these genetic biomarkers could enable timely interventions targeting these shared mechanisms, ultimately improving treatment outcomes and addressing the diverse needs of individuals on the spectrum.

3 | Environmental Influences

Environmental exposures during pregnancy, particularly during critical neurodevelopmental periods, are implicated in ASD aetiology (Bölte et al. 2019; Yenkoyan et al. 2024). Many known exposures have effects during gestation, delivery, or, in rare cases, the neonatal period (Parellada et al. 2023). Some frequently examined factors in the literature that provide direct evidence of an environmental component in ASD include increased risk following maternal immune activation induced by bacterial or viral infection (Tioleco et al. 2021), autoimmune disease (Chen et al. 2023; Atladóttir et al. 2009), or stress (Abbott et al. 2018); the impact of maternal nutrition and malnutrition due to dietary factors (Zhong et al. 2020), deficiencies of zinc (Alsufiani et al. 2022), magnesium (Skalny et al. 2020) and selenium (Skalny et al. 2018), vitamin D (Wang et al. 2020) and folate (Vasconcelos et al. 2025), or short interpregnancy intervals (Zerbo et al. 2015); pre-existing and concurrent metabolic conditions (Krakowiak et al. 2012); prenatal and early postnatal exposure to heavy

metals (cadmium, lead, arsenic, and mercury; Ding et al. 2023), and air pollutants (e.g., fine particulate matter, nitrogen dioxide; Duque-Cartagena et al. 2024; Lam et al. 2016); medication use, notably valproic acid (Moore et al. 2000), and antidepressants (Croen et al. 2011); birth method (Chen et al. 2024); birthing complications, such as fetal hypoxia (Walker et al. 2015); and gestational age and weight (Guo et al. 2024).

Due to the timeline of exposure, biomarkers of ASD influenced by environmental exposure are good candidates for aiding presymptomatic detection, provided that sufficient maternal medical history is available and can inform screening panels and assays during pre- and peri-natal periods (Frye et al. 2019). The bioaccumulation of environmental agents, such as heavy metals and endocrine-disrupting chemicals (e.g., phthalates and bisphenol A), present in blood, urine, and hair, are reliable biomarkers that indicate prolonged exposure and therefore an increased risk of neurodevelopmental disruptions associated with ASD (Ding et al. 2023). Other potential biomarkers linked to environmental stresses leading to ASD include cytokines, such as interleukin-6 and tumour necrosis factor-alpha (Anastasescu et al. 2024), which increase in expression and are present in the blood for sampling as a result of immune activation and possible dysregulation and inflammation (Xu et al. 2015). However, a recent meta-analysis detailed that the abnormal profile of more than 10 cytokines could serve as potential biomarkers of ASD (Zhao et al. 2021). Additionally, oxidative stress markers, namely lipid peroxidation products and reduced glutathione levels (Liu et al. 2022), and epigenetic modifications, such as DNA methylation patterns (Vogel Ciernia and LaSalle 2016; Bakulski et al. 2021). However, despite the promising collation of evidence and detection of these potential and emerging biomarkers, as with genetic factors, most evidence informing environmentally associated biomarkers has small effect sizes, with no single biomarker exhibiting a consistent exposure-response relationship (Frye et al. 2019; Parellada et al. 2023).

Gene–environment (GxE) interactions in human pathophysiology describe how an individual's genotype can be a determinant of their susceptibility to environmental exposures, influencing their innate predisposition to ASD (Tordjman et al. 2014; Chaste and Leboyer 2012; Cheroni et al. 2020). The influence of epigenetics in ASD is one example of the interconnection between the external environment and an individual's genome (Tordjman et al. 2014). Epigenetic processes dynamically silence or activate genes and regulate the accessibility of transcription machinery to areas of chromatin in response to both genetic mutation and environmental exposures without altering the underlying DNA sequence. This highlights a bidirectional relationship between environmental influences on the genome and vice versa, which influences ASD pathology (Tordjman et al. 2014). The significance of this relationship is reinforced by data from the Simons Foundation Autism Research Initiative (SFARI) database, which identifies numerous genes involved in epigenetic machinery that are directly linked to ASD aetiology (Banerjee-Basu and Packer 2010). Other GxE interactions commonly manifest when specific alleles confer protective or pathogenic effects in response to environmental insults (Wu et al. 2023). A demonstration of this in ASD is seen in the Methylenetetrahydrofolate Reductase (*MTHFR*) gene, where two common polymorphisms, C677T and A1298C, impair folate metabolism (Li et al. 2020). Low maternal folate levels can then exacerbate this effect, leading to differential effects and severity of outcomes in carriers versus noncarriers (Li et al. 2020; El-Baz et al. 2017).

The multifactorial aetiology of ASD suggests that single-factor approaches to biomarker identification are inherently inadequate (Jensen et al. 2022; Mustafa 2024). Understanding how gene–environment interactions shape ASD phenotypes will be crucial for developing early diagnostic tools and potential intervention strategies and improving the relevancy of biomarkers (Mustafa 2024). These interactions may also explain a substantial portion of incomplete penetrance in ASD-associated genetic syndromes and contribute to the variable burden of common variants in the population (Tordjman et al. 2014; Chaste and Leboyer 2012; Cheroni et al. 2020).

4 | Neurological Biomarkers

4.1 | Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) generates high-resolution 3D anatomical images using magnetic fields that align bodily protons (Baranger et al. 2021). MRI provides both quantitative and qualitative information on brain structure and function. Functional MRI images the changes in neural activity via its detection of blood oxygen level-dependent alterations (Baranger et al. 2021). Functional connectivity (fc) MRI can show the temporal relationships between neurological events that are spatially apart (Pickler et al. 2017). A compelling case is made for the cost-effectiveness of using MRI to identify ASD in presymptomatic at-risk infants in the context of United states, if an intervention is implemented (Williamson et al. 2020).

4.1.1 | Functional MRI Studies of ASD

Abnormal neural organisations at local and global levels of brain architecture and function have been implicated in ASD (Table 1). Manifestations of ASD include both increased (Bos et al. 2014; Butera et al. 2023; Carper et al. 2015; Doyle-Thomas et al. 2015; Gabrielsen et al. 2018; Green et al. 2016; Linke et al. 2018; Mash et al. 2020; Nair et al. 2015; Solomon et al. 2014; Uddin et al. 2013) and decreased (Bai et al. 2023; Bos et al. 2014; Doyle-Thomas et al. 2015; Fishman et al. 2018; Gabrielsen et al. 2018; Keehn et al. 2021; Long et al. 2016; Nair et al. 2015; Shen et al. 2016; Supekar et al. 2021; Wood et al. 2021) fc across various brain regions and networks. A more specific example is the increased fc in sensorimotor and vision regions, but reduced fc in social and cognition regions in children with ASD (Chen et al. 2018). Overconnectivity primarily involves frontotemporal networks and the basal ganglia, related to social development and RRBs in ASD, respectively (Conti et al. 2017). The connectivity patterns in ASD can differentiate from other developmental disorders involving intellectual and language impairments in toddlers (Conti et al. 2017). Sex differences for fc in ASD are also observed (Alaerts et al. 2016; Lawrence et al. 2020; Smith et al. 2019; Ypma et al. 2016). Hyperconnectivity and reduced differentiability between task-evoked and resting brain states seen in children with ASD are thought to contribute to

TABLE 1 | Functional magnetic resonance imaging biomarkers for < 2 year olds.

No.	Author	Region	Population	Findings
1	McKinnon et al. (2019)	United states—Part of Infant Brain Imaging Study (IBIS)	Infants 12 and 24 months old $n = 167$ (22/16, male/female with data at both time points)	Alterations in fc between different long- and short-range networks were associated with elevated RRBs
2	Emerson et al. (2017)	United states—Part of IBIS	Infants 6 months old $n = 59$ (41/18, male/female)	Hyper- and hypo-connected circuits predicted later ASD diagnosis at age 2 with 96.6% classification accuracy and 100% positive predictive value
3	Ciarrusta et al. (2020)	United Kingdom	Newborns with a first-degree ASD relative $n = 20$ (14/6, male/female)	Local hyperconnectivity but no difference in long-range connectivity
4	Lewis et al. (2017)	United states—Part of IBIS	Infants at 6 and 12 months old $n = 260$ (79/37, male/female with data at both time points)	Poorer network efficiencies in regions for low-level processing (e.g., audition, vision and motor cortices), sensory integration and higher-level processing (e.g., Broca's area).
5	Liu et al. (2020)	United states	Infants 1.5 to 9 months old $n = 65$ at 1.5 months (38/27, male/female) $n = 60$ at 9 months (34/26, male/female)	1. Disrupted interhemispheric fc of left Heschl's gyrus and right somatosensory region found at 1.5 months old 2. Increased intrahemispheric fc between left Heschl's gyrus and left sensory cortex 3. Static development trajectories
6	Liu et al. (2021)	United states	Infants 9 months old $n = 43$ (26/17, male, female; 28/13/2, white/non-white/missing race)	Reduced learning-related signals in left temporal regions related to poorer expressive language at 36 months
7	Blasi et al. (2015)	United Kingdom	Infants 7 months old $n = 33$ (17/16, male, female)	Weaker sensitivity signals to sad vocalisations in the left hippocampus and right fusiform gyrus
8	Nair et al. (2021)	United states	Infants 1.5 months old $n = 52$ (29/23, male/female; 35/17, white/non-white)	1. Thalamic-occipital and -motor hyperconnectivity predicted atypical social development 2. Thalamic hypoconnectivity of prefrontal regions
9	Wagner et al. (2023)	United states	Infants 1.5 to 9 months old $n = 77$ at 1.5 months (46/31, male/female) $n = 72$ at 9 months (42/30, male/female)	1. Thalamic-motor hypoconnectivity at 9 months old 2. Thalamic hypoconnectivity of prefrontal regions 3. Thalamic-limbic hyperconnectivity at 1.5 months 4. Inverse relationship for thalamic connectivity to sensory cortices/basal ganglia and higher-order associative regions that associated with SOR symptom severity

(Continues)

TABLE 1 | (Continued)

No.	Author	Region	Population	Findings
10	Hawks et al. (2023)	United states—Part of IBIS	Infants 6 to 24 months old $n = 94$ (68/26, male/female)	1. No relationship between 6-month cerebro-cerebellar fc with later ASD behaviours 2. fcMRI enrichment identified correlations between DMN and RRBs at 12 and 24 months
11	Okada et al. (2022)	United states	Infants 9 months old $n = 119$ (68/51, male/female)	Hypoconnectivity of the right Crus I prior to behavioural deficit onset
12	Scheinost et al. (2022)	United states	High-risk neonates mean $n = 44$ weeks postmenstrual age $n = 53$ (29/24, male/female)	Hypoconnectivity between left anterior insula and left amygdala associated with poorer social communication behaviour scores 12 to 18 months later
13	Thomason et al. (2021)	United states	Foetuses 24 to 39 weeks GA $n = 109$ (Did not describe sex distribution)	1. Increased amygdala-prefrontal and -sensorimotor connectivity 2. Decreased anterior insula-cerebellum connectivity 3. Sex interactions in inferior prefrontal and striatal regions
14	Liu et al. (2024)	United states—part of IBIS	Infants 12 months old $n = 87$ (57/30, male/female)	Poor connectivity between the left amygdala and right anterior cingulate cortex, and right amygdala and left visual cortex. The latter is associated with poorer motor and communication ability
15	Tsang et al. (2024)	United states	Infants 6 weeks old $n = 53$ (30/28, male/female)	Stronger salience-sensorimotor connectivity at the expense of weaker salience-prefrontal connectivity

impaired behavioural flexibility (Uddin et al. 2015, 2013) and social deficit severity (Supekar et al. 2013).

4.1.1.1 | Behaviour. In at-risk infants aged from 12 to 24 months, alterations in fc between different long- and short-range networks were associated with elevated RRBs (McKinnon et al. 2019). Assessment of the hyper- and hypo-connected circuits in 6-month-old high-risk infants as a predictive measure of later ASD diagnosis at age 2 yielded 96.6% accuracy with a positive predictive value of 100% (Emerson et al. 2017). In contrast, although at-risk newborn infants showed local hyperconnectivity, there was no difference in long-range connectivity compared to the low-risk group (Ciarrusta et al. 2020). Although there is no behavioral outcome data available for this study (Ciarrusta et al. 2020), taken together, this suggests local connectivity alterations might precede the atypicalities in long-range connectivity.

4.1.1.2 | Language. Poorer network efficiencies in primary and secondary auditory cortices related to low-level processing are found in at-risk 6-month-old infants and were associated with symptom severity at 24 months (Lewis et al. 2017). By 12 months, inefficiencies in other regions for low-level processing (e.g., vision and motor cortices), sensory integration, and higher-level processing (e.g., Broca's area) also became associated with symptom severity at 24 months. These findings agree with previous work on 24-month-old at-risk infants (Lewis et al. 2014). This aligns with the hypothesis that low-level sensory processing deficits occur earlier in the ASD development trajectory than higher-level processes (Belmonte et al. 2004) and sets up a cascade that leads to the deficits in higher-level processes. As intensive auditory behavioral training in rodents has been shown to reverse ASD-like deficits in the primary auditory cortex, interventions could perhaps halt the cascade toward inefficiencies in higher-level regions (Zhou et al. 2015).

More recently, disruptions in interhemispheric fc of networks between the left Heschl's gyrus and right somatosensory region needed for auditory and motor integration, and thus language development, are found in high-risk infants as early as 1.5 months old (Liu et al. 2020). At 9 months, these infants show increased intrahemispheric connectivity between the left Heschl's gyrus and left sensory cortex, whereas low-risk infants show hyperconnectivity between auditory and higher-order temporal regions. High-risk infants also showed more static development trajectories, lacking the increasing long-range connectivity (e.g., fronto-temporal language regions) and decreasing short-range connectivity (e.g., temporal-thalamic) seen in low-risk infants from 1.5 to 9 months (Liu et al. 2020). Weaker interhemispheric fc in language areas is only evident in toddlers with autism, not in toddlers solely with language delays (Dinstein et al. 2011). Furthermore, lower increases in learning-related signals within the left temporal regions while listening to a speech at 9 months are related to poorer expressive language outcomes at 36 months (Liu et al. 2021), and weaker sensitivity signals to sad vocalisations in the left hippocampus and right fusiform gyrus were found in high-risk 4 to 7-month-old infants (Blasi et al. 2015).

Interhemispheric auditory hypoconnectivity and temporal-thalamic hyperconnectivity are associated with social symptoms in youth (aged 8–17; Linke et al. 2018), and temporal-thalamic hyperconnectivity was the only exception to an overall thalamocortical hypoconnectivity in children with ASD (aged 12–17; Nair et al. 2013). However, thalamocortical hyperconnectivity is more commonly reported (Cerliani et al. 2015; Tomasi and Volkow 2019; Woodward et al. 2017), and thalamic-occipital and -motor hyperconnectivity in 1.5-month-old high-risk infants is predicted to later atypical social development (Nair et al. 2021). Although findings on thalamic hypoconnectivity with prefrontal regions are consistent (Nair et al. 2021; Wagner et al. 2023), in contrast, thalamic-motor hypoconnectivity was seen in 9-month-old high-risk infants (Wagner et al. 2023). Thalamic-limbic hyperconnectivity was also seen at 1.5 months of age (Wagner et al. 2023). Thalamocortical hyperconnectivity could reflect how reduced thalamic inhibition constitutes impaired filtering of sensory information reaching the cortex, which interferes with attention and contributes to sensory oversensitivity (SOR) in ASD (Baran et al. 2023).

4.1.1.3 | Cerebellum Networks. Studies of cerebro-cerebellar fc in children with ASD showed cerebellar hyperconnectivity to sensorimotor networks, at the expense of hypoconnectivity in supramodal cognition (e.g., prefrontal cortex; (Khan et al. 2015)), and together, these might contribute to more severe SOR symptoms (Cakar et al. 2024; Oldehinkel et al. 2019). Although no relationship was found between 6-month cerebro-cerebellar (e.g., fronto-parietal network and DMN) fc with ASD behaviors at 24 months, fcMRI enrichment identified correlations between DMN and RRBs at 12 and 24 months (Hawks et al. 2023). Hypoconnectivity of the right Crus I, implicated in social communication, is found in high-risk 9-month-old infants prior to overt deficit onset (Okada et al. 2022). Atypical right Crus I connectivity was also found in the Purkinje neuron *Tsc1* ASD mouse model, and stimulation of this cerebellar area's activity rescued social impairments but not the RRBs (Stoodley et al. 2017). Rapamycin (an mTOR-specific inhibitor) therapy also rescues cerebellar-mediated social dysfunction in mutant *Tsc1* mice but does not ameliorate the RRBs thought to be mediated by rapamycin-insensitive cerebellar domains (Tsai et al. 2018).

4.1.1.4 | Salience Network. Across the commonly identifiable large-scale brain networks, salience network hyperconnectivity has shown the highest accuracy in differentiating ASD and typically developing (TD) children and predicted RRB scores (Uddin et al. 2013). The anterior insula, amygdala, and anterior cingulate cortex are key nodes in the salience network (Uddin et al. 2013). fcMRI in high-risk neonates (full-term, postmenstrual age matched; mean 44 weeks) showed hypoconnectivity between the left anterior insula and the left amygdala, which was associated with poorer social communication behavior scores 12 to 18 months later (Scheinost et al. 2022). As these two areas coactivate during the final trimester of pregnancy, ASD prediction is potentially possible prenatally (Scheinost et al. 2022). This remains to be investigated. Nonetheless, increased amygdala-prefrontal and -sensorimotor connectivity and decreased anterior insula-cerebellum connectivity were associated with later ASD diagnosis in fetuses (24–39 weeks gestational age (GA); Thomason et al. 2021). High-risk 12-month-old infants display poorer connectivity between the left amygdala and right anterior cingulate cortex, and right amygdala and left visual cortex. The latter is associated with poorer motor and communication ability (Liu et al. 2024).

Moreover, stronger salience-sensorimotor connectivity at the expense of weaker salience-prefrontal connectivity in 6-week-old high-risk infants is suggested to underlie the balance between greater attention to basic sensory information over socially relevant sensory information (Tsang et al. 2024). A similar inverse relationship is seen for thalamic connectivity to sensory cortices/basal ganglia and higher-order associative regions, in association with SOR symptom severity in 9-month-old infants (Wagner et al. 2023). Interestingly, SOR is more strongly associated with salience-primary sensory network hyperconnectivity in male children, but salience-prefrontal network hyperconnectivity in female children, which unveils potential sex-specific connectivity differences in ASD manifestations (Cummings et al. 2020). These sex differences are yet to be studied in infants.

Ultimately, atypical fc is present as early as 4–6 weeks old in infants at high risk of ASD (Scheinost et al. 2022; Tsang et al. 2024). Salience network connectivity differences are even observable in utero (Thomason et al. 2021). Alterations as early as 1.5 months (Nair et al. 2021) and 6 months (Emerson et al. 2017; Hawks et al. 2023; Lewis et al. 2017) are predictive of ASD behaviors (e.g., RRBs) at 24 months. Further extrapolation of presymptomatic sex differences and understanding the potential of prenatal ASD predictions is warranted (Scheinost et al. 2022). As non-replication of fc differences in ASD has been noted in older children and young adults (He et al. 2020), examination of replicability is needed before we can progress to validating these biomarkers for clinical use.

4.1.2 | Structural MRI

Aside from network fc, some studies have used structural MRI (Table 2). Atypical structural connectivity of large-scale brain networks is implicated in children aged from 2 to 4 with ASD, with sex-by-diagnosis differences in structural covariance compared to TD counterparts (Zielinski et al. 2022). Beyond neural circuitry, abnormalities in regional brain thickness (Dierker et al. 2015; Levman et al. 2019; Libero et al. 2015) and volume (Eilam-Stock et al. 2016; Levman et al. 2018; Maier et al. 2015; Xiao et al. 2014) are implicated in ASD, with abnormal alterations changing with age (Zuo et al. 2019).

4.1.2.1 | Amygdala. Infants that later develop ASD show a typical amygdala size at 6 months old but a larger volume by 12 months due to faster growth of the amygdala from 6 to 24 months. This increased growth was associated with greater social impairment at 24 months and differentiated ASD from infants with fragile X syndrome (Shen et al. 2022). Enlarged amygdala volume was only seen in highly impaired ASD children, which had a higher proportion of females and an association with internalising behaviour only in females (Nordahl et al. 2020). This suggests sex-specific pathology and subsequent symptoms.

4.1.2.2 | Cortex. Cortex hyper-expansion in sensory processing areas from 6 to 12 months old preceded the brain volume overgrowth seen at 12 to 24 months, and predicted later ASD diagnoses in high-risk infants with 88% sensitivity and 95% specificity (Hazlett et al. 2017). The initiation and severity of brain volume growth were respectively correlated to the onset and extent of social impairment, signifying brain overgrowth as the ignition to a cascade of social-related neural atypicalities (Hazlett et al. 2017). Brain overgrowth is seen in ASD with known genetic contributors like CHD8 (Bernier et al. 2014) and 16p11 deletions (Qureshi et al. 2014). However, megalencephaly might only be attributed to a subset of children with ASD, particularly boys who have more severe deficits (Amaral et al. 2017; Nordahl et al. 2011; Ohta et al. 2016).

4.1.2.3 | Insula Cortex. The insula is involved in social attention and sensory processing, among other capabilities (Odriozola et al. 2016). Although insula volumes are decreased in children and adults with ASD (Kosaka et al. 2010; Parellada et al. 2017), findings of increased insular cortex volume using in utero MRI in foetuses later diagnosed with ASD could be explained by age-related changes, thereby potentially providing a promising foetal biomarker (Ortug et al. 2024). Using controlled protocols in a larger sample size, prospective studies identifying any sex differences are needed to further delineate these foetal observations.

4.1.2.4 | Corpus Callosum. Increased area and thickness of the corpus callosum (CC) at 6 months correlated to RRBs at 2 years, and the ability to distinguish ASD from CC size diminished by 2 years (Wolff et al. 2015). CC volumes remained higher in children aged 2 to 4 with ASD, albeit more significant in females than males with ASD (Zhang et al. 2023). This enlargement is thought to be underpinned by overgrowth of axons and myelin sheaths (Boger-Megiddo et al. 2006), which would also coincide with brain volume overgrowth (Hazlett et al. 2017). By adulthood, there is a smaller CC volume in ASD due to reduced age-related volume increases, where larger volumes were related to better Autism Diagnostic Observation Schedule scores (Prigge et al. 2021).

Greater than typical fractional anisotropy (FA; index of white matter integrity) in the splenium (Wolff et al. 2015) and genu (Wolff et al. 2017) at 6 months predicted RRBs and subsequent ASD diagnosis at 2 years and positively associated with symptom severity (Wolff et al. 2017). Similarly, higher FA and rightward lateralization of the left superior longitudinal fasciculus in high-risk 6-week-old infants were related to language development and ASD symptoms at 18 and 36 months, respectively (Liu et al. 2019). No FA difference is seen in thalamic-cortical tracts between high- and low-risk 6-week-old infants, though mean diffusivity was significantly higher for thalamic-occipital tracts in the high-risk group (Nair et al. 2021). Interestingly, FA is then lower in various white matter tracts of 2-year-old toddlers with ASD (Wolff et al. 2012) and in particular, differences in FA of the CC are not observed in toddlers aged from 3 to 5 with ASD (Nordahl et al. 2015). Reduced FA is seen in older children and adults with ASD (Ameis et al. 2016; Aoki et al. 2013; Chiang et al. 2017; Fishman et al. 2015; Im et al. 2018). However, increased FA of various white matter tracts in toddlers aged from 2 to 4 is still observed (Andrews et al. 2019; Solso et al. 2016; Xiao et al. 2014). These findings suggest that atypical ASD FA measures transition from an increased to decreased state between 30 and 40 months of age (Andrews et al. 2019), where

TABLE 2 | Structural magnetic resonance imaging biomarkers for < 2 years olds.

No	Author	Region	Population	Findings
1	Shen et al. (2022)	United States — part of IBIS	Infants 6 to 24 months old $n = 408$ (254/154, male/female)	1. Infants with later ASD diagnosis have typical amygdala size at 6-months-old, but a larger volume at 12 months from faster growth of the amygdala from 6 to 24 months. 2. Faster growth associated with greater social impairment at 24 months, and differentiated ASD from infants with fragile X syndrome
2	Hazlett et al. (2017)	United States— part of IBIS	Infants 6 to 24 months old $n = 435$ (269/166, male/female)	1. Cortex hyper-expansion in sensory processing areas preceded brain volume overgrowth, and predicted later ASD diagnoses with 88% sensitivity and 95% specificity 2. Initiation and severity of brain volume growth, respectively, correlated to the onset and extent of social impairment
3	Ortug et al. (2024)	United states	Foetuses 18 to 36 weeks GA $n = 39$ (33/6, male/female)	Increased insular cortex volume using in utero MRI in foetuses later diagnosed with ASD
4	Wolff et al. (2015)	United States — part of IBIS	Infants 6 to 24 months old $n = 378$ (235/143, male/female)	1. Increased area and thickness of the corpus callosum at 6 months correlated to RRBs at 2 years 2. Ability to distinguish ASD using CC size diminished by 2 years 3. Greater FA in splenium
5	Wolff et al. (2017)	United States— part of IBIS	Infants 6 to 24 months old $n = 217$ (139/78, male/female)	Greater FA in genu predicted RRBs, later ASD diagnosis, and positively associated with symptom severity
6	Liu et al. (2019)	United states	Infants 6 weeks old $n = 34$ (21/13, male/female)	Higher FA and rightward lateralization of the left superior longitudinal fasciculus related to language development and ASD symptoms at 18 and 36 months, respectively
7	Nair et al. (2021)	United States	Infants 6 weeks old $n = 52$ (29/23, male/female)	1. No FA difference in thalamic-cortical tracts between high- and low-risk infants 2. Mean diffusivity significantly higher for thalamic-occipital tracts in the high-risk group
8	Pote et al. (2019)	United Kingdom	Infants 4 to 6 months-old $n = 50$ (23/27, male/female)	Increased cerebellar and subcortical volumes in were associated with increased RRBs at 36 months
9	Shiohama et al. (2022)	United States	Presymptomatic toddlers under 3 years $n = 162$ (gender-matched)	Smaller nucleus accumbens and larger cerebral ventricles in the infant period
10	Shen et al. (2013) and Shen et al. (2017)	United States	Infants 6 to 9 months old $n = 64$ (43/21, male/female; Shen et al. 2013) $n = 343$ (213/130, male/female; Shen et al. 2017)	Increased extra-axial cerebrospinal fluid, where its presence and amount respectively predicted ASD diagnosis and motor symptom severity

presymptomatic diagnostic measures need to consider distinct timeframes to prevent false negatives.

While both male and female preschool-aged children (aged 3–5 years) with ASD had smaller regions projecting to the superior frontal cortex, males had a smaller region of callosal fibers projecting to the orbitofrontal cortex, whereas females had a smaller callosal region projecting to the anterior frontal cortex (Nordahl et al. 2015). Increased mean, axial, and radial diffusivity relative to TD counterparts was also only observed in females with ASD (Andrews et al. 2019; Nordahl et al. 2015), whereas males showed decreased axial diffusivity relative to TD counterparts (Andrews et al. 2019). These alterations did not differ based on age, suggesting they were established before 3 years of age (Nordahl et al. 2015). These diffusion alterations could reflect poor axon myelination or membrane integrity (Alexander et al. 2007; Song et al. 2002, 2005).

Children with ASD show slower FA development in multiple areas, including the splenium, where slower FA development in the sagittal stratum was seen in autistic children who increased in severity across childhood (Andrews et al. 2021). Interestingly, individuals with ASD exposed to parent-managed behavioral interventions had higher and lower FA in regions of the CC, which followed a dose–response relationship to the intensity of intervention (Virues-Ortega et al. 2022). Thus, differences in white matter development could potentially predict prognosis and treatment effects. Future randomized controlled trials may use this study as a basis for estimating statistical powers needed.

4.1.2.5 | Other Volume Changes and EA-CSF. Increased cerebellar and subcortical volumes in 4- to 6-month-old high-risk infants were associated with increased RRBs at 36 months (Pote et al. 2019). Smaller nucleus accumbens and larger cerebral ventricles in presymptomatic toddlers under 3 years of age were observed in the infant period (Shiohama et al. 2022). Reduced nucleus accumbens size might mediate ASD pathology as oxytocin treatment, shown to improve social symptoms in ASD, enhances serotonin release via actions on nucleus accumbens oxytocin receptors (Gordon et al. 2016; Kruppa et al. 2019; Walsh et al. 2018; Yamasue et al. 2020). Moreover, Shiohama et al. (2022) used Infant FreeSurfer, which is optimized for T1-weighted neuroimaging data of infants < 2 years (Zöllei et al. 2020). Future infantile studies might consider this over the original FreeSurfer.

Interestingly, infants aged 6–9 months show increased extra-axial cerebrospinal fluid (EA-CSF), where its presence and amount respectively predicted ASD diagnosis and motor symptom severity (Shen et al. 2017, 2013). Elevated EA-CSF persists into childhood, predicts ASD diagnosis with 78% accuracy, and is associated with sleep disturbances (Shen et al. 2018). Sleep normally drives increased CSF clearance of neurotoxic metabolic byproducts that accumulate during wakefulness and can contribute to neuropathology (Johanson et al. 2008; Xie et al. 2013). Moreover, although increased EA-CSF volume was not observed in a previous study (Pote et al. 2019), it is likely due to the younger and smaller study population and different MR slicing. Thus, we do not know the earliest emergence of increased EA-CSF and if this phenomenon is specific to ASD, or whether it extends to other neurodevelopmental disorders.

Structural changes in volume, FA, and connectivity of the cortex and other regions are found in ASD. Notably, differences in CC (Wolff et al. 2015), cerebellar and subcortical (Pote et al. 2019), and EA-CSF (Shen et al. 2017, 2013) volumes are present by 6 months. Atypical lateralization of dorsal language tracts is present as early as 6 weeks (Liu et al. 2019), and increased insular cortex volume is a promising fetal biomarker that warrants investigation (Ortug et al. 2024). Moreover, findings are pending from an ongoing 6-year follow-up cohort study on preterm infants using comprehensive neonatal MRI, EEG, and clinical biomarkers at 32 weeks PMA to predict neurodevelopmental outcomes in Australia (George et al. 2020). Nevertheless, while the use of MRI for ASD diagnosis is promising, it is not yet ready for clinical application due to uncertainty in its generalizability, and the inherent heterogeneity of ASD that is further complicated by the heterogeneity in study participants and protocols (Schielen et al. 2024).

5 | Electroencephalography

Electroencephalography (EEG) provides a non-invasive continuous recording of cerebral electrical activity (Baranger et al. 2021). Event-related potentials (ERPs) derived from EEG represent the electrical activity of a neuronal population in response to a particular stimulus (Cygan et al. 2014). EEG is an easy-to-use, readily available, and low-cost tool that could be routinely implemented for infants (Bosl et al. 2018). EEG has been used to investigate ASD in high-risk infants (Table 3).

5.1 | Power and Frontal Alpha Asymmetry

In infants and toddlers with ASD, early intervention has been shown to shift the P400 response and theta and alpha power closer to that of TD counterparts in response to social stimuli and was associated with improved social behavior (Dawson et al. 2012; Jones et al. 2017). High-risk infants show reduced power of all frequency bands from delta to gamma at 3 months and steeper age-related power increases in spectral power till 3 years (Gabard-Durnam et al. 2015; Huberty et al. 2021; Piazza et al. 2023; Tierney et al. 2012). Moreover, from 6 to 18 months, TD infants display greater right-sided frontal alpha asymmetry (FAA) that shifts left, whereas high-risk infants have greater left-sided FAA that shifts right (Gabard-Durnam et al. 2015). Although this reversed FAA pattern is consistent with findings in preschoolers with ASD in response to direct versus downward gaze (Lauttia et al. 2019) and older children in response to open versus closed eyes (Kylliäinen et al. 2012), the above studies did not predict ASD-specific outcomes.

Recently, a comparison of EEG signal features in 3-month-old infants predicted later ASD diagnosis and severity with over 95% accuracy (Bosl et al. 2018). Steeper delta and gamma band power trajectories across the first 12 months also consistently differentiated high- and low-risk infants (Bosl et al. 2018). Further changes in frontal power through 36 months differentiated infants with ASD diagnosis from those without, indicating the importance of EEG trajectory in understanding ASD pathophysiology and classification (Gabard-Durnam et al. 2019). Peak

TABLE 3 | Electroencephalography biomarkers for < 2 years olds.

No.	Author	Region	Population	Findings
1	Tierney et al. (2012)	United States	Infants 6 to 24 months old $n = 122$ (Did not describe sex distribution)	1. Spectral power was lower across all bands in high-risk infants 2. Different developmental trajectories of spectral power change
2	Gabard-Durnam et al. (2015)	United States	Infants 6 to 18 months old $n = 108$ (Approximately 50% males and 50% females)	High-risk infants have greater left-sided FAA that shifts right, whereas TD infants display greater right-sided FAA that shifts left
3	Huberty et al. (2021)	United States and United Kingdom	Infants 3 to 36 months old $n = 397$ (208/189, male/female)	1. Spectral power was lower across all bands in high-risk infants 2. Steeper developmental trajectories of spectral power change
4	Piazza et al. (2023)	Northern Italy	Infants 6 to 12 months old $n = 284$ (137/144, male/female)	1. Reduced power in the low-frequency bands differentiated high-risk 6-month-old infants with later ASD from those infants later diagnosed with language learning impairment 2. Higher power in the high-frequency bands increased risk of learning language impairment
5	Bosl et al. (2018)	United states	Infants 3 to 36 months old $n = 188$ (Did not describe sex distribution)	1. Comparison of EEG signal features at 3 months predicted later ASD diagnosis and severity with over 95% accuracy 2. Steeper delta and gamma band power trajectories across the first 12 months differentiated high- and low-risk infants
6	Gabard-Durnam et al. (2019)	United States	Infants 3 to 36 months old $n = 171$ (93/78, male/female)	Delta and gamma frequency power trajectories till 36 months differentiates infants with and without ASD
7	Carter Leno et al. (2021)	United States and United Kingdom	Infants 12 to 36 months old $n = 151$ (Did not describe sex distribution)	Peak alpha frequency does not predict ASD in 12-month-old infants
8	Jones et al. (2020)	United States	Infants 12 to 36 months old Cohort 1—$n = 14$ (Did not describe sex distribution) Cohort 2—$n = 34$ (Did not describe sex distribution)	Theta changes predicted non-verbal and verbal skills, and the changes explain over 80% of variance in non-verbal skills in infants with later ASD at 3 years
9	Haartsen et al. (2022)	United Kingdom	Infants 14 months old $n = 101$ (48/53, male/female)	Theta modulations in power and connectivity while viewing social content is not different to TD counterparts
10	Levin et al. (2017)	United States	Infants 3 to 36 months old $n = 39$ (23/16, male/female)	Reduced frontal alpha and beta power at 3 months associated with reduced expensive language at 12 months

(Continues)

TABLE 3 | (Continued)

No.	Author	Region	Population	Findings
11	De Ridder et al. (2020)	Part of EPISTOP project	Infants < 48 weeks GA with tuberous sclerosis complex $n = 64$ (35/29, male/female)	Dysmature EEG in infants was associated with higher likelihood of ASD traits and lower language abilities at 24 months with 86% specificity
12	Jones et al. (2016)	Part of Early Connections project	Infants 6 and 12 months old $n = 88$ (54/34, male/female)	1. Faster but less prolonged P400 ERPs when viewing faces versus non-social stimuli in infants with later ASD 2. This difference was less apparent at 12 months
13	Elsabbagh et al. (2012)	United Kingdom	Infants 6 to 10 months old $n = 104$ (42/62, male/female)	1. Faster but less prolonged P400 ERPs when viewing faces versus noise stimuli in infants with later ASD 2. Lack of differential P400 amplitude in response to gaze toward versus away in at-risk infants who did develop ASD
14	Guy et al. (2018)	United States	Infants 12 months old $n = 57$ (42/15, male/female)	No difference in P400 latency between high- and low-risk groups
15	Elsabbagh et al. (2015)	United Kingdom	Infants 7 months old $n = 92$ (38/54, male/female)	At-risk infants with more positive affect show faster responses to gaze toward versus away
16	Abou-Abbas et al. (2021)	United Kingdom—Part of BASIS	Infants 6 months old $n = 94$ (35/59, male/female)	Classification of infants into high-risk with later ASD versus no ASD using a gaze toward/away model yielded 88.44% accuracy
17	Keehn et al. (2015)	United States	Infants 6 and 12 months old 95 infants contributed 127 data sets $n = 58$ at 6 months (27/31, male/female) $n = 69$ at 12 months (38/31, male/female)	Greater leftward lateralization of intrahemispheric gamma coherence to faces in infants with later ASD
18	Orekhova et al. (2014)	United Kingdom—Part of BASIS	Infants 14 months old $n = 54$ (22/32, male/female)	1. Frontal and central hyperconnectivity in alpha frequencies when viewing social videos in those with later ASD 2. Degree of hyperconnectivity associated positively with severity of RRBs at 3 years
19	Haartsen et al. (2019)	United Kingdom	Infants 14 months old $n = 101$ (58/43, male/female)	1. Hyperconnectivity in alpha frequencies when viewing social videos in those with later ASD 2. Degree of hyperconnectivity associated positively with severity of RRBs at 3 years 3. Association was strongest for the circumscribed interest subcategory of RRBs

(Continues)

TABLE 3 | (Continued)

No.	Author	Region	Population	Findings
20	Tran et al. (2021)	United States	Infants 3 months old $n = 63$ (40/23, male/female)	Reduced left fronto-central phase coherence in theta and alpha frequency bands during language processing in those with later ASD symptoms
21	Righi et al. (2014)	United States	Infants 6 and 12 months old $n = 54$ (Did not describe sex distribution)	Lower fronto-parietal fc when listening to speech sounds in those with later ASD
22	Dickinson et al. (2021)	United States	Infants 3 months old $n = 65$ (41/24, male/female)	Lower frontal connectivity and higher right temporoparietal connectivity predicted greater ASD severity

alpha frequency, however, is not a predictor of ASD in 12-month infants (Carter Leno et al. 2021). Moreover, FAA and frontal alpha power only correlated with externalizing behaviors in male but not female youth with ASD (Neuhaus et al. 2023). These sex differences are yet to be replicated in infants.

Infant theta changes have been shown to predict non-verbal and verbal skills, and the changes explain over 80% of the variance in non-verbal skills in infants with later ASD (Jones et al. 2020). However, theta modulations in power and connectivity while viewing social content are not different from TD counterparts at 14 months (Haartsen et al. 2022). High-risk infants are reported to have reduced frontal alpha and beta power at 3 months, which was associated with reduced expressive language at 12 months (Levin et al. 2017). Interestingly, lower power of low-frequency bands differentiated high-risk 6-month-old infants later diagnosed with ASD from those infants later diagnosed with language learning impairment (LLI), where the risk for LLI increased with higher power of high-frequency bands (Piazza et al. 2023). Higher power in higher frequencies is also related to lower ASD risk and higher socioemotional competence, though this is only significant for males (Brito et al. 2019). Nevertheless, this indicates the potential to differentiate ASD from other neurodevelopmental language disorders as early as 6 months. Dysmature EEG (i.e., abnormal discontinuity, slow delta waves, inappropriate waveforms for GA, etc.) in infants less than 48 weeks GA with tuberous sclerosis complex was associated with a higher likelihood of ASD traits at 24 months with 86% specificity, and lower language abilities (De Ridder et al. 2020). Moreover, children with Dup15q syndrome who have a high risk of neurodevelopmental disorders like ASD show excessive beta frequency activity (Urraca et al. 2013). It remains unknown whether this EEG pattern could predict clinical ASD outcomes in this subgroup.

5.2 | Event-Related Potentials—Face Processing

P400 ERPs describe the semantic aspects of processing face information (de Haan et al. 2003). In 6-month-old infants with later ASD diagnosis, faster but less prolonged P400 ERPs are observed when viewing faces versus non-social stimuli (Elsabbagh et al. 2012; Jones et al. 2016). This is thought to reflect reduced attentional engagement to and processing depth of social stimuli. This difference was also less apparent at 12 months, suggesting this biomarker is specific to earlier windows (Guy et al. 2018; Jones et al. 2016). A lack of differential P400 amplitude in response to gaze toward versus away in 6- to 10-month-old infants with later ASD is also seen (Elsabbagh et al. 2012), where 7-month-old at-risk infants with more positive moods show faster responses to gaze toward versus away (Elsabbagh et al. 2015). Classification of 6-month-old infants into high-risk with later ASD versus no ASD using a gaze toward/away model yielded 88.44% accuracy (Abou-Abbas et al. 2021).

In addition, high-risk infants with later ASD diagnosis show greater leftward lateralization of intrahemispheric gamma coherence to faces, whereas TD infants showed rightward lateralization (Keehn et al. 2015). Blunted lateralization of face and name processing, and delayed N170 ERP (related to early encoding of face structure; Bentin and Deouell 2000; Eimer 2000),

where females are more impacted are reported in children and adults with ASD (Coffman et al. 2015; Cygan et al. 2014; McPartland et al. 2011). Valproic acid-exposed zebrafish also exhibit atypical social-visual lateralization via genetic effects (Messina et al. 2024). Since it is hypothesized that atypical lateralization stems from insufficient neural visual specialization (Behrmann et al. 2006), and purposeful early exposure to social stimuli, thus repeated engagement of these circuits may encourage specialization. This needs to be evaluated longitudinally, considering both sex and prediagnostic infantile stages.

5.3 | Connectivity

High-risk infants with later ASD diagnosis show frontal and central hyperconnectivity in alpha frequencies when viewing social videos at 14 months, and the degree of hyperconnectivity is associated positively with the severity of RRBs at 3 years (Orekhova et al. 2014). Findings were replicated and further showed the association was strongest for the circumscribed interest subcategory of RRBs (Haartsen et al. 2019). Reduced left fronto-central phase coherence in theta and alpha frequency bands during language processing is also seen in 3-month-old infants with ASD symptoms at 18 months (Tran et al. 2021), and lower fronto-parietal fc is implicated in 12-month-old high-risk infants with later ASD diagnosis when listening to speech sounds (Righi et al. 2014). Greater ASD severity was predicted by lower frontal connectivity and higher right temporoparietal connectivity at 3 months (Dickinson et al. 2021).

Ultimately, multiple EEG changes can be detected as early as 3 months (Bosl et al. 2018; Dickinson et al. 2021; Gabard-Durnam et al. 2019; Huberty et al. 2021; Levin et al. 2017; Tran et al. 2021) in high-risk infants, and dysmature EEG in infants <48 weeks GA with tuberous sclerosis complex was associated with a higher likelihood of ASD traits at 24 months. Extrapolation of sex differences in FAA and frontal alpha power correlations with externalizing behaviors is yet to be replicated in infants (Neuhaus et al. 2023). Nevertheless, while further research is needed to validate EEG findings before clinical application, ongoing work in developing robust measurements of EEG biomarkers by the Eurosibs consortium has shown that EEG findings hold great promise for research efforts in diverse populations (Jones et al. 2019). EEG as a portable neuroimaging tool has also provided access into rural settings for the Brain Imaging for Global Health (BRIGHT) project on neurodevelopment, highlighting its potential for increasing the representation of diverse ethnicities and geographical locations (Lloyd-Fox et al. 2024).

6 | Magnetoencephalography

Magnetoencephalography (MEG) maps brain activity directly by recording the magnetic fields mainly arising from postsynaptic currents in cortical neurons (Chen et al. 2019). This allows MEG to capture the rapid dynamics of brain processes with millisecond precision, offering both high temporal and spatial resolution, surpassing that of EEG, especially in spatial capabilities (Chen et al. 2019). Although expensive, MEG may stand superior to MRI due to the absence of loud noises and limited bodily space of MRI machines that could be unpleasant for infants and young children, particularly those with ASD who possess sensory hyperarousal and overstimulation tendencies (Cakar et al. 2024; Oldehinkel et al. 2019; Wagner et al. 2023).

6.1 | Auditory Processing

Both stronger and weaker cerebro-cerebellar fc patterns that are correlated with ASD severity are seen in children with ASD during speech processing (Alho et al. 2023). Alpha-band event-related desynchronisation, related to attention, is bilaterally reduced in the auditory cortex during audio stimuli (Arutiunian, Arcara, Buyanova, Buivolova, et al. 2023). More interestingly, multiple findings agree on a clinically significant delay in auditory-evoked M50 and M100 latency in children and adults with ASD, which correspond to the neural response of the superior temporal gyrus, a region containing the primary and secondary auditory cortices (Berman et al. 2016; Edgar et al. 2015; Matsuzaki et al. 2019; Port et al. 2016; Roberts et al. 2019). M100 latency delay is associated with greater ASD severity (Berman et al. 2016; Port et al. 2016), and it persists irrespective of the expected age-based maturations (Port et al. 2016). Importantly, these studies only required passive listening to auditory sounds, so they can be performed in minimally verbal or non-verbal children with ASD (Kuschner et al. 2021).

It has been hypothesised that this latency delay signifies disrupted simple auditory encoding, arising from an altered developmental trajectory of the neural components, such as synaptic function and white matter conductivity within the auditory nerves in ASD. In primary auditory tonotopic maps of valproic acid-ASD models, there is over-representation of higher frequencies, greater intensity thresholds, and reduced receptive field tuning (Anomal et al. 2015). However, they observed shorter neural latencies using EEG (Anomal et al. 2015). MEF2C point mutations (McChesney et al. 2022) and overexpression of methyl-CpG binding protein 2 (Zhou et al. 2019) in mice are also implicated in synaptic function, auditory latency delays, and increased intensity thresholds. In addition to macroencephaly, 16p11.2 locus deletion carriers also show MEG M100 latency delays; however, this was present in both carriers with and without ASD (Jenkins III et al. 2015), and 16p11.2 deletion consequences on white matter microstructure do not explain the conduction delay completely (Berman et al. 2016). Furthermore, Lower gamma-aminobutyric acid (GABA) concentration is also found in conjunction with delayed M50 latencies in ASD (Roberts et al. 2020).

GABA concentration is thought to underlie gamma band power (Balz et al. 2016). Reduced auditory steady-state response (ASSR), particularly in the gamma band, was associated with language impairment in ASD children and adolescents (Arutiunian, Arcara, Buyanova, Davydova, et al. 2023; Samoylov et al. 2024; Seymour et al. 2020). Localization of the auditory response was superior and posterior in TD children (Samoylov et al. 2024). However, ASSR findings are inconsistent, where several studies reported no difference between ASD and TD children (Ahlfors et al. 2024; Edgar et al. 2016; Ono et al. 2020; Stroganova et al. 2020). On top of a typical auditory gamma despite reduced GABA concentration, a lack of typical age-related increase in

GABA concentration and gamma band coherence maturation is also reported (Port et al. 2017). Therefore, as the above studies used different ages, the differences in age-related gamma maturation could underlie the mixed results of ASSR.

Hearing impairments from genetic or environmental origins can predispose infants to less, or altered early auditory experiences that have a contemporaneous relationship with auditory circulatory maturation and myelination (Long et al. 2018). As audition is closely related to language and learning, auditory alterations may pose important implications for ASD manifestations. To date, there are no infant MEG studies on auditory processing for ASD. Further research is warranted, given the mostly unanimous findings that make M100 a promising biomarker.

6.2 | Face Processing

MEG alterations in face processing have also been implicated in ASD. Reduced and absent gamma responses in visual and facial emotion processing areas have been reported in children with ASD (Hasegawa et al. 2023; Wright et al. 2012). Functional connectivity network alterations in emotional face processing are also implicated (Mamashli et al. 2018, 2021; Safar et al. 2021, 2018), with increased alpha phase synchronisation for happy faces that correlates to ASD severity (Safar et al. 2018) and a decrease in age-related gamma connectivity to emotional face that markedly opposes the expected age-related increases in TD (Safar et al. 2021).

6.3 | Resting-State Measures

At resting state, children and adolescents with ASD show increased frontal lobe connectivity but decreased connectivity of other lobes, which are inversely related to the entropy-based signal complexity of these areas (Ghanbari et al. 2015). Increased local gamma connectivity but reduced long-range gamma connectivity are associated with ASD severity (Kitzbichler et al. 2015; Lajiness-O'Neill et al. 2018). Significant correlations between connectivity strength in large-scale brain networks with severity of RRBs and social impairment in children (aged 2–6 years) are also reported (Taddei et al. 2024). Recently, self-supervised machine learning of resting-state MEG features accurately distinguished between ASD and TD children (aged 4–7 years; Barik et al. 2024). Sub-threshold ASD can also be detected using graph theory, where individuals who probably have ASD, based on their autistic traits in the Social Responsiveness Scale, show significantly lower small-worldness across frequency bands than those unlikely to have ASD (Constantino 2021; Shiota et al. 2022). Perhaps, this system could be used in MEG studies of high-risk infants to predict later ASD outcomes.

Although a lack of age-related increase in peak alpha frequency (PAF) is found, where adults with ASD have lower PAF, a higher PAF in younger male children (< 10 years) is reported (Edgar et al. 2019; Shen et al. 2024). This suggests PAF could be a marker more sensitive for earlier ASD development. However, no difference in PAF of children within the same age range is also reported (Kameya et al. 2024). Given PAF in EEG was not a predictor of ASD at 12 months (Carter Leno et al. 2021), further investigation into PAF as an ASD marker in male and female infantile ages greater than 12 months is recommended.

Ultimately, there remains a gap in MEG studies investigating potential neurological markers of ASD in young children, let alone high-risk infants, to enable presymptomatic ASD diagnosis and, ultimately, early intervention. Recent developments of MEG hardware like the BabyMEG (Okada et al. 2016) and Artemis 123 (Roberts et al. 2014) that are optimized for these groups will hopefully make this more accessible.

7 | Pupillometry

Pupillometry is a non-invasive measure of changes in pupil diameter in response to stimuli that have been used to investigate ASD (Table 4; Amiez and Procyk 2019). Hyperarousal to the environment is a symptom of ASD. It has been hypothesised that this signifies an imbalance in autonomic regulation, due to altered cortical development, where there is reduced baseline parasympathetic activity (Neuhaus et al. 2014). As pupillometry describes activity in the locus coeruleus (LC), it acts as a descriptor of autonomic function via the induction of the pupillary light reflex (PLR; Granovetter et al. 2020). PLR describes the changes in pupil diameter in response to retinal light alterations. It is mediated by efferent cranial nerve III that synapses on the ciliary ganglion, which houses axons that innervate the pupillary muscles, constricting and dilating them in response to light and dark, respectively (Amiez and Procyk 2019; Loewenfeld and Lowenstein 1993). The pupil constrictor muscle called the iris sphincter receives parasympathetic drive, whereas the pupil dilator muscle receives sympathetic drive (Loewenfeld and Lowenstein 1993). Multiple trials can be conducted efficiently within minutes, granting feasibility for use in infants (Granovetter et al. 2020).

7.1 | Latency

Longer latencies for pupil constriction are seen in children (Daluwatte et al. 2013, 2015; Dinalankara et al. 2017) and adolescents (Lynch et al. 2018). Differentiation between ASD and TD was achieved with 73% accuracy (Lynch et al. 2018). Latency delays could be explained by alterations in neural transduction, synaptic function, neuronal connectivity, and myelination, which are all implicated in ASD (Bourgeron 2015; Hull et al. 2017; Weinstein et al. 2011). In contrast, however, a faster and stronger hypersensitive PLR was observed in 9 to 10-month-old high-risk infants with later ASD diagnosis (Nyström et al. 2018, 2015). Inconsistencies might arise from different methods and testing conditions (e.g., room lighting and light stimuli intervals) that can affect PLR response (Bitsios et al. 1996). Moreover, age-dependent reductions in PLR latency in those TD are reported as present (Kercher et al. 2020), absent (Daluwatte et al. 2013), or diminished (Dinalankara et al. 2017) in ASD. Interestingly, high-risk infants have shown slower latency reductions from 9 to 14 months, but faster latency reductions from 14 to 24 months in infants later diagnosed with ASD (Fish et al. 2021).

TABLE 4 | Pupillometry biomarkers for < 2 years olds.

No.	Author	Region	Population	Findings
1	Nyström et al. (2015)	Sweden	Infants 10 months old $n = 44$ (21/23, male/female)	1. Faster and stronger hypersensitive PLR in those with later ASD diagnosis 2. No difference in pupil size
2	Nyström et al. (2018)	Sweden and United Kingdom — Part of BASIS	Infants 9 to 10 months old $n = 187$ (98/89, male/female)	1. Faster and stronger hypersensitive PLR in those with later ASD diagnosis 2. Reduced constriction amplitudes 3. Age-related increases in amplitude for TD infants is reversed in those later diagnosed with ASD
3	Kercher et al. (2020)	United States	Infants 6 to 24 months old $n = 42$ (Approximately 50% males and 50% females)	1. Age-dependent reductions in PLR latency 2. Reduced constriction amplitudes 3. Age-related increases in amplitude for TD infants is reversed in those later diagnosed with ASD 4. Larger pupil sizes
4	Fish et al. (2021)	United Kingdom — Part of BASIS and STAARS	Infants 9 to 24 months old $n = 264$ (121/143, male/female)	1. Slower PLR latency reductions from 9 to 14 months, but faster latency reductions from 14 to 24 months in infants later diagnosed ASD 2. Age-related increases in amplitude for TD infants is reversed in those later diagnosed with ASD

7.2 | Amplitude

Reduced constriction amplitudes are reported in high-risk infants (Kercher et al. 2020; Nyström et al. 2018) and children with ASD (Daluwatte et al. 2013, 2015). Reduced constriction amplitude, signifying reduced parasympathetic modulation, was corroborated by a greater resting heart rate and was associated with poorer sensory behaviors (Daluwatte et al. 2015). Interestingly, this observation was not significant for ASD children co-diagnosed with Asperger's (Daluwatte et al. 2015). Therefore, PLR parameters may be able to differentiate between different sub-groups on the autism spectrum to tailor intervention. Furthermore, age-related increases in amplitude for TD infants in the first year of life are reversed in those later diagnosed with ASD (Fish et al. 2021; Kercher et al. 2020; Nyström et al. 2018).

The LC mediates neural gain during attention to tasks (Aston-Jones and Cohen 2005; Eldar et al. 2013). With high tonic, thus low phasic LC activity seen in ASD (Aston-Jones and Cohen 2005; Bast et al. 2023; DiCriscio and Troiani 2021; Granovetter et al. 2020; Kim et al. 2022), stemming from an imbalance in cortical excitation and inhibition, results in heightened cortical neural gain and thus neural responsivity (Aston-Jones and Cohen 2005). The result is increased distractibility and reduced task engagement from a reduced ability to shift attention away from task-irrelevant information in ASD (Aston-Jones and Cohen 2005; Gilzenrat et al. 2010). This may explain the behaviors like fixations, selective attention, and SOR (Bouret and Sara 2002; Keehn et al. 2013; Remington et al. 2009).

Indeed, in a group of age- and sex-matched adults with ASD, lower task-evoked PLR amplitudes that demonstrate decreased phasic responsiveness were observed in the presence of distractors (Granovetter et al. 2020). The opposite profile would be expected during increased attentional demand for those TD. The amplitude difference was sufficient to differentiate ASD from TD participants based on data alone (Granovetter et al. 2020). However, more recently, ADHD, but not ASD symptoms, were related to tonic and phasic LC indices (Kim et al. 2022). They hypothesised that atypical LC activity may not be ASD-specific but rather reflects the genetic overlap between ASD and other neurological disorders (Cristino et al. 2014; Geschwind 2011). Nonetheless, these findings reinforce the importance of underpinning differences in the developmental trajectory of autonomic function for those with ASD. Delineation of potential overlap with other neurological disorders is needed to yield ASD-specific measures that can allow more targeted screening.

7.3 | Resting Pupil Size

Aside from PLR, studies have sought to investigate pupillary anatomical differences in children with ASD but have raised inconsistent findings. High-risk infants have shown larger pupil sizes (Kercher et al. 2020), and no difference (Nyström et al. 2015). Larger (Bast et al. 2023; Kim et al. 2022), smaller (Martineau et al. 2011), and no difference (Bleimeister et al. 2024; Daluwatte et al. 2013; Granovetter et al. 2020; Nuske et al. 2014; Zhao et al. 2022) in pupil sizes are also reported in children with ASD. Each of these studies looked at different ages, so perhaps the controversial findings lie in age-dependent changes. Indeed, a study observed that pupil size increases with age in TD but not ASD children, who instead have decreasing age trends. Children aged under 4 with ASD had a larger pupil size, whereas those

older than 4 had a smaller pupil size than those TD (Dinalankara et al. 2017). Increased sympathetic drive would result in large pupil sizes and increased sweating (Daluwatte et al. 2013; Ellaway et al. 2010). Therefore, (Dinalankara et al. 2017) hypothesised that these ASD pupil size disparities may result from sympathetic dysregulation. However, they did not find an association between larger pupil size and sweat levels in ASD children, despite an association being confirmed in TD children.

These pupillometry studies point to both latency and amplitude changes, underlined by parasympathetic and possible sympathetic dysregulation. These highlight the importance of understanding the mechanisms behind autonomic dysfunction as a neurological biomarker. To improve comparability, consistent and replicable pupillometry methods and conditions are advised for future studies. Participant comfort also needs to be considered as anxiety signaling sympathetic activity could interfere with PLR interpretation reliability (Keil et al. 2018). Given the gap in infant studies and the existing studies yielding distinct differences to older autistic children, more infant studies are needed to validate the earliest PLR markers for ASD to delineate potential presymptomatic ASD diagnosis.

8 | Others

Eye-tracking measures have emerged as a cost-effective neurophysiological method for early ASD diagnosis, particularly notable for its utility in large-scale studies (Frazier et al. 2018). Preference for non-social stimuli in a subtype of ASD has been shown in a large sample of 1863 toddlers (Wen et al. 2022). This preference was associated with increased symptom severity (Pierce et al. 2016), suggesting potential for enhancing diagnostic accuracy (Keehn et al. 2024). Moreover, reduced social-visual engagement has been proven to be a reliable diagnostic biomarker in children younger than 3 years old (Jones, Klaiman, Richardson, Aoki, et al. 2023; Jones, Klaiman, Richardson, Lambha, et al. 2023). Recent studies in small samples of infants that examined gaze following, specifically on tracking eyes and mouth during word learning, underscore the utility of eye-tracking for early ASD detection (Camero et al. 2023; Fu et al. 2024). Furthermore, atypical visual attention disengagement in infants has been highlighted as a potential early indicator of ASD risk (Bryson et al. 2018; Elison et al. 2013; Elsabbagh et al. 2013; Keehn et al. 2024). However, the specific behavior of attentional disengagement has shown varied efficacy, being more pronounced in predicting ASD in boys (Bedford et al. 2016). These preliminary findings stress the potential of integrating eye-tracking indices to aid early ASD diagnosis, pending further validation and practical application considerations.

Ultrasonography has shown that ASD children more frequently present with fetal anomalies compared to their TD peers, with notable differences between genders in ASD, where females display more anomalies (Regev et al. 2022). These anomalies have been linked to genetic variants, particularly loss-of-function mutations, emphasizing the importance of genetic screening in understanding ASD severity (Regev et al. 2024). Recently, machine learning applied to prenatal anatomical ultrasounds has demonstrated a 77% positive predictive value in distinguishing ASD cases, with significant biomarkers identified from common pregnancy screenings such as maternal family history, femur length, and white blood cell count in the 3rd trimester (Caly et al. 2021). Other emerging physiological biomarkers include infant electrocardiography signal features such as heart rate variability (Tilwani et al. 2023), and infant vocal characteristics (e.g., F0, phonation, amplitude; Pusil et al. 2025), offering new avenues for early detection, potentially accessible and scalable across various settings.

9 | Non-Neurological Biomarkers

While this review outlines the genetic and neurological markers of ASD, there is a variety of non-neurological biomarkers that also display potential for presymptomatic detection and early intervention. These include metabolic, protein, and peptide-based markers that can be identified through simple blood and saliva tests.

Among the promising developments, a study has linked several newborn (7 of 36) blood screening analytes, including 17 17-hydroxyprogesterone, phenylalanine/tyrosine, and acylcarnitines, with a later diagnosis of ASD, highlighting their potential to contribute to early intervention strategies (Canfield et al. 2019). Furthermore, an algorithm has been developed to classify children aged 5 to 12 years old into ASD or typically developing (TD) groups based on blood test features, including plasma protein glycation, oxidation, and nitration adduct markers (Al-Saei et al. 2024; Anwar et al. 2018). However, lowering the minimum inclusion age from 5 years in the discovery study (Anwar et al. 2018) to 1.5 years reduced the accuracy for classifying whether children had ASD or were typically developing (Al-Saei et al. 2024). In addition, salivary biomarkers, such as early postnatal testosterone levels, have been examined in 1- to 3-month-old infants, but have shown no significant correlation with later autistic trait scores (Kung et al. 2016). While a range of protein-, peptide-, and metabolite-based biomarkers have been identified (see review Shen et al. 2020), there remains insufficient research on these markers in very young children (< 5 years), and even more so for infants (< 2 years). Nonetheless, these biomarkers present a practical, less costly alternative to advanced diagnostic technologies such as MRI, making them particularly valuable in resource-limited settings.

10 | Ethical and Social Implications of Presymptomatic Testing and ASD Diagnosis

The prospect of presymptomatic diagnosis of ASD raises important ethical and practical issues for researchers, autistic individuals and their families, and society, which are largely beyond the scope of this review (MacDuffie et al. 2021; Wolff and Piven 2021). Factors to be considered include, but are not limited to, the optimal age and population to screen, for example, high-risk populations compared with general population screening; the impact of false positive and false negative diagnoses on children, their families and available resources; the heterogeneity of ASD and the positive contribution of neurodiversity to society; the need to establish early diagnosis of ASD to progress with clinical trials and the development of more effective intervention; and the resource implications of presymptomatic intervention

when early intervention therapies are often constrained. Early qualitative research into parental opinions regarding predictive testing indicates that parents generally favor an earlier diagnosis (Vanaken et al. 2023; Washington et al. 2024), but careful consultation with consumers and community stakeholders will be required before the implementation of proven presymptomatic diagnostic methods in the clinical setting.

11 | Limitations and Considerations

The current review acknowledges several limitations that warrant consideration when interpreting the findings. We focused on physiological biomarkers, which, while potentially transformative for presymptomatic diagnosis of ASD, present challenges in terms of cost and accessibility. Unlike metabolic or genetic markers, which are typically utilized after an ASD diagnosis has been established based on clinical symptoms, physiological biomarkers offer the advantage of potentially identifying ASD before behavioral symptoms fully manifest. However, the higher costs and limited accessibility of technologies required for measuring such biomarkers, including MRI, EEG, and MEG, may restrict their widespread application, particularly in resource-limited settings. Furthermore, the current study's scope is limited by its population size and geographic coverage. The majority of the data stems from specific regions, primarily the United States and European nations, which do not fully represent global populations and often underrepresent less researched and more vulnerable countries. This concern necessitates future research involving larger and more diverse international participants to ensure the findings are broadly applicable. Any generalization from the results of this study to broader ASD populations should therefore be approached with caution until more expansive studies are conducted.

While the majority of studies discussed in this review feature cohorts with comparable numbers of male and female participants, the significant sex differences observed in normal brain development underline the importance of targeted studies on these variations. Research has shown that males and females exhibit distinct patterns of brain growth and maturation, such as differences in frontal white matter volume asymmetry and occipital lobe surface measured by MRI imaging (Studholme et al. 2020). Longitudinal studies showed different developmental trajectories in brain regions heavily influenced by sex steroid receptors, such as the basal ganglia, hippocampus, and amygdala (Giedd et al. 2012; Lenroot and Giedd 2010). Moreover, functional MRI and EEG studies have revealed distinct cognitive and neural processing patterns between males and females, for instance, in microstate dynamics (Zhang et al. 2020; Tomescu et al. 2018). Furthermore, genetic studies suggest that the genetic makeup contributing to ASD risk may differ by sex, with females potentially requiring a higher genetic load to manifest ASD (Jacquemont et al. 2014). These findings underscore the complexity of developing ASD biomarkers that are reflective of the underlying pathology and not merely indicative of normal sex differences. Indeed, it has been suggested that females with ASD may exhibit less overt symptoms and different neuroanatomical patterns compared to males, necessitating the development of sex-specific biomarkers or the adjustment of existing biomarkers to account for these differences (Halladay et al. 2015). Future biomarker development efforts must, therefore, include balanced sex representation and consider sex as a critical variable in both the research and application phases of biomarker validation.

12 | Conclusion and Future Directions

At present, the biomarkers developed for presymptomatic detection of ASD are still largely in experimental stages. The efficacy of these biomarkers is complicated by the heterogeneous nature of ASD, compounded by limitations in environmental factors and variability in study designs, including limitations related to participant age, sex, geographical location, and sample size. Relative to other biomarkers, MRI and EEG appear promising for early, presymptomatic identification of ASD, especially in high-risk infants. Studies suggest that abnormalities in brain connectivity and structure detectable by these methods as early as 6 months old may predict later ASD diagnoses and behavioral outcomes with notable accuracy. Genetic biomarkers, despite extensive research and the identification of numerous ASD-associated genes, face challenges in clinical application as presymptomatic diagnostic tools due to their complexity and heterogeneity of genetic influences on ASD. Standardized prenatal testing to target genetic markers presymptomatically remains challenging in clinical practice. Similarly, metabolic and non-neurological biomarkers, such as those derived from blood or saliva analyses, are still in preliminary stages of research and lack the extensive validation required for widespread clinical implementation as presymptomatic tools at this stage.

Future studies should aim to incorporate large equal-sex longitudinal infant participants across all risk levels to determine commonalities among those who do and do not receive a diagnosis of ASD. In addition, meta-analyses of diagnostic accuracies and evaluation of appropriate guidelines are warranted to understand the absolute feasibility of implementing biomarker screening in practice. Moreover, a continued understanding of the underlying biological and genetic processes of these biomarkers is required for a comprehensive grasp of ASD origin and consequences. Multimodal research, including behavioural, genetic, and neuroimaging/electrophysiological participant data, will be of fundamental relevance to this objective.

Author Contributions

Bonnie M. Wang: writing – original draft, writing – review and editing, conceptualization. **Zoe Mills:** conceptualization, writing – original draft, writing – review and editing. **Hannah F. Jones:** writing – review and editing, writing – original draft. **Johanna M. Montgomery:** conceptualization, supervision, writing – review and editing. **Kevin Y. Lee:** conceptualization, supervision, writing – original draft, writing – review and editing, project administration.

Acknowledgements

This work was supported by the Department of Physiology, University of Auckland, New Zealand (PHYSIOL 399), and the Neurological Foundation of New Zealand (1954 SRF to K.Y.L.). The figure was created in BioRender. Lee, K (2025), https://BioRender.com/m76m126. Open access publishing facilitated by The University of Auckland, as part of the Wiley - The University of Auckland agreement via the Council of Australian University Librarians.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data in this study will be shared by the corresponding author upon request.

Peer Review

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/jnc.70088.

References

Abbott, P. W., S. B. Gumusoglu, J. Bittle, D. Q. Beversdorf, and H. E. Stevens. 2018. "Prenatal Stress and Genetic Risk: How Prenatal Stress Interacts With Genetics to Alter Risk for Psychiatric Illness." *Psychoneuroendocrinology* 90: 9–21. https://doi.org/10.1016/j.psyneuen.2018.01.019.

Abou-Abbas, L., S. van Noordt, J. A. Desjardins, M. Cichonski, and M. Elsabbagh. 2021. "Use of Empirical Mode Decomposition in ERP Analysis to Classify Familial Risk and Diagnostic Outcomes for Autism Spectrum Disorder." *Brain Sciences* 11, no. 4: 409. https://doi.org/10.3390/brainsci11040409.

Abrahams, B. S., and D. H. Geschwind. 2008. "Advances in Autism Genetics: On the Threshold of a New Neurobiology." *Nature Reviews. Genetics* 9: 341–355.

Ahlfors, S. P., S. Graham, H. Bharadwaj, et al. 2024. "No Differences in Auditory Steady-State Responses in Children With Autism Spectrum Disorder and Typically Developing Children." *Journal of Autism and Developmental Disorders* 54, no. 5: 1947–1960. https://doi.org/10.1007/s10803-023-05907-w.

Alaerts, K., S. P. Swinnen, and N. Wenderoth. 2016. "Sex Differences in Autism: A Resting-State fMRI Investigation of Functional Brain Connectivity in Males and Females." *Social Cognitive and Affective Neuroscience* 11, no. 6: 1002–1016. https://doi.org/10.1093/scan/nsw027.

Alexander, A. L., J. E. Lee, M. Lazar, and A. S. Field. 2007. "Diffusion Tensor Imaging of the Brain." *Neurotherapeutics* 4, no. 3: 316–329. https://doi.org/10.1016/j.nurt.2007.05.011.

Alho, J., J. G. Samuelsson, S. Khan, et al. 2023. "Both Stronger and Weaker Cerebro-Cerebellar Functional Connectivity Patterns During Processing of Spoken Sentences in Autism Spectrum Disorder." *Human Brain Mapping* 44, no. 17: 5810–5827. https://doi.org/10.1002/hbm.26478.

Al-Saei, A. N. J. M., W. Nour-Eldine, K. Rajpoot, et al. 2024. "Validation of Plasma Protein Glycation and Oxidation Biomarkers for the Diagnosis of Autism." *Molecular Psychiatry* 29, no. 3: 653–659. https://doi.org/10.1038/s41380-023-02357-9.

Alsufiani, H. M., A. S. Alkhanbashi, N. A. B. Laswad, et al. 2022. "Zinc Deficiency and Supplementation in Autism Spectrum Disorder and Phelan-McDermid Syndrome." *Journal of Neuroscience Research* 100, no. 4: 970–978.

Amaral, D. G., D. Li, L. Libero, et al. 2017. "In Pursuit of Neurophenotypes: The Consequences of Having Autism and a Big Brain." *Autism Research* 10, no. 5: 711–722. https://doi.org/10.1002/aur.1755.

Ameis, S. H., J. P. Lerch, M. J. Taylor, et al. 2016. "A Diffusion Tensor Imaging Study in Children With ADHD, Autism Spectrum Disorder, OCD, and Matched Controls: Distinct and Non-Distinct White Matter Disruption and Dimensional Brain-Behavior Relationships." *American Journal of Psychiatry* 173, no. 12: 1213–1222. https://doi.org/10.1176/appi.ajp.2016.15111435.

American Psychiatric Association. 2022. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association. https://doi.org/10.1176/appi.books.9780890425787.

Amiez, C., and E. Procyk. 2019. "Chapter 4—Midcingulate Somatomotor and Autonomic Functions." In *Handbook of Clinical Neurology*, edited by B. A. Vogt, vol. 166, 53–71. Elsevier. https://doi.org/10.1016/B978-0-444-64196-0.00004-2.

Anastasescu, C. M., V. Gheorman, E. C. Stoicanescu, F. Popescu, V. Gheorman, and I. Udriștoiu. 2024. "Immunological Biomarkers in Autism Spectrum Disorder: The Role of TNF-Alpha and Dependent Trends in Serum IL-6 and CXCL8." *Life* 14, no. 9: 1201.

Andrews, D. S., J. K. Lee, D. J. Harvey, et al. 2021. "A Longitudinal Study of White Matter Development in Relation to Changes in Autism Severity Across Early Childhood." *Biological Psychiatry* 89, no. 5: 424–432. https://doi.org/10.1016/j.biopsych.2020.10.013.

Andrews, D. S., J. K. Lee, M. Solomon, S. J. Rogers, D. G. Amaral, and C. W. Nordahl. 2019. "A Diffusion-Weighted Imaging Tract-Based Spatial Statistics Study of Autism Spectrum Disorder in Preschool-Aged Children." *Journal of Neurodevelopmental Disorders* 11, no. 1: 32. https://doi.org/10.1186/s11689-019-9291-z.

Anney, R., L. Klei, D. Pinto, et al. 2012. "Individual Common Variants Exert Weak Effects on the Risk for Autism Spectrum Disorders." *Human Molecular Genetics* 21, no. 21: 4781–4792.

Anomal, R. F., E. de Villers-Sidani, J. A. Brandão, R. Diniz, M. R. Costa, and R. N. Romcy-Pereira. 2015. "Impaired Processing in the Primary Auditory Cortex of an Animal Model of Autism." *Frontiers in Systems Neuroscience* 9: 158. https://doi.org/10.3389/fnsys.2015.00158.

Anwar, A., P. M. Abruzzo, S. Pasha, et al. 2018. "Advanced Glycation Endproducts, Dityrosine and Arginine Transporter Dysfunction in Autism—A Source of Biomarkers for Clinical Diagnosis." *Molecular Autism* 9: 3. https://doi.org/10.1186/s13229-017-0183-3.

Aoki, Y., O. Abe, Y. Nippashi, and H. Yamasue. 2013. "Comparison of White Matter Integrity Between Autism Spectrum Disorder Subjects and Typically Developing Individuals: A Meta-Analysis of Diffusion Tensor Imaging Tractography Studies." *Molecular Autism* 4, no. 1: 25. https://doi.org/10.1186/2040-2392-4-25.

Arutiunian, V., G. Arcara, I. Buyanova, et al. 2023. "Event-Related Desynchronization of MEG Alpha-Band Oscillations During Simultaneous Presentation of Audio and Visual Stimuli in Children With Autism Spectrum Disorder." *Brain Sciences* 13, no. 9: 1313. https://doi.org/10.3390/brainsci13091313.

Arutiunian, V., G. Arcara, I. Buyanova, et al. 2023. "Neuromagnetic 40 Hz Auditory Steady-State Response in the Left Auditory Cortex Is Related to Language Comprehension in Children With Autism Spectrum Disorder." *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 122: 110690. https://doi.org/10.1016/j.pnpbp.2022.110690.

Aston-Jones, G., and J. D. Cohen. 2005. "An Integrative Theory of Locus Coeruleus-Norepinephrine Function: Adaptive Gain and Optimal Performance." *Annual Review of Neuroscience* 28: 403–450. https://doi.org/10.1146/annurev.neuro.28.061604.135709.

Atladóttir, H. Ó., M. G. Pedersen, P. Thorsen, et al. 2009. "Association of Family History of Autoimmune Diseases and Autism Spectrum Disorders." *Pediatrics* 124, no. 2: 687–694.

Bai, C., Y. Wang, Y. Zhang, et al. 2023. "Abnormal Gray Matter Volume and Functional Connectivity Patterns in Social Cognition-Related Brain Regions of Young Children With Autism Spectrum Disorder." *Autism Research* 16, no. 6: 1124–1137. https://doi.org/10.1002/aur.2936.

Bakulski, K. M., J. F. Dou, J. I. Feinberg, et al. 2021. "Autism-Associated DNA Methylation at Birth From Multiple Tissues Is Enriched for Autism Genes in the Early Autism Risk Longitudinal Investigation." *Frontiers in Molecular Neuroscience* 14: 775390.

Balz, J., J. Keil, Y. Roa Romero, et al. 2016. "GABA Concentration in Superior Temporal Sulcus Predicts Gamma Power and Perception in the Sound-Induced Flash Illusion." *NeuroImage* 125: 724–730. https://doi.org/10.1016/j.neuroimage.2015.10.087.

Banerjee-Basu, S., and A. Packer. 2010. "Sfari Gene: An Evolving Database for the Autism Research Community." *Disease Models & Mechanisms* 3: 133–135. https://doi.org/10.1242/dmm.005439.

Baran, B., Q. T. H. Nguyen, D. Mylonas, S. L. Santangelo, and D. S. Manoach. 2023. "Increased Resting-State Thalamocortical Functional Connectivity in Children and Young Adults With Autism Spectrum Disorder." *Autism Research* 16, no. 2: 271–279. https://doi.org/10.1002/aur.2875.

Baranger, J., O. Villemain, M. Wagner, et al. 2021. "Brain Perfusion Imaging in Neonates." *NeuroImage: Clinical* 31: 102756. https://doi.org/10.1016/j.nicl.2021.102756.

Barik, K., S. Dey, K. Watanabe, et al. 2024. "Self-Supervised Machine Learning Approach for Autism Detection in Young Children Using MEG Signals." *Biomedical Signal Processing and Control* 98: 106671. https://doi.org/10.1016/j.bspc.2024.106671.

Bast, N., S. Boxhoorn, H. Supér, et al. 2023. "Atypical Arousal Regulation in Children With Autism but Not With Attention-Deficit/Hyperactivity Disorder as Indicated by Pupillometric Measures of Locus Coeruleus Activity." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 8, no. 1: 11–20. https://doi.org/10.1016/j.bpsc.2021.04.010.

Bedford, R., E. J. H. Jones, M. H. Johnson, A. Pickles, T. Charman, and T. Gliga. 2016. "Sex Differences in the Association Between Infant Markers and Later Autistic Traits." *Molecular Autism* 7, no. 1: 21. https://doi.org/10.1186/s13229-016-0081-0.

Behrmann, M., C. Thomas, and K. Humphreys. 2006. "Seeing It Differently: Visual Processing in Autism." *Trends in Cognitive Sciences* 10, no. 6: 258–264. https://doi.org/10.1016/j.tics.2006.05.001.

Belmonte, M. K., E. H. Cook Jr., G. M. Anderson, et al. 2004. "Autism as a Disorder of Neural Information Processing: Directions for Research and Targets for Therapy." *Molecular Psychiatry* 9, no. 7: 646–663. https://doi.org/10.1038/sj.mp.4001499.

Bentin, S., and L. Y. Deouell. 2000. "Structural Encoding and Identification in Face Processing: Erp Evidence for Separate Mechanisms." *Cognitive Neuropsychology* 17, no. 1: 35–55. https://doi.org/10.1080/026432900380472.

Berman, J. I., D. Chudnovskaya, L. Blaskey, et al. 2016. "Relationship Between M100 Auditory Evoked Response and Auditory Radiation Microstructure in 16p11.2 Deletion and Duplication Carriers." *American Journal of Neuroradiology* 37, no. 6: 1178–1184. https://doi.org/10.3174/ajnr.A4687.

Bernier, R., C. Golzio, B. Xiong, et al. 2014. "Disruptive CHD8 Mutations Define a Subtype of Autism Early in Development." *Cell* 158, no. 2: 263–276. https://doi.org/10.1016/j.cell.2014.06.017.

Bill, B. R., and D. H. Geschwind. 2009. "Genetic Advances in Autism: Heterogeneity and Convergence on Shared Pathways." *Current Opinion in Genetics & Development* 19, no. 3: 271–278.

Bitsios, P., R. Prettyman, and E. Szabadi. 1996. "Changes in Autonomic Function With Age: A Study of Pupillary Kinetics in Healthy Young and Old People." *Age and Ageing* 25, no. 6: 432–438. https://doi.org/10.1093/ageing/25.6.432.

Blasi, A., S. Lloyd-Fox, V. Sethna, et al. 2015. "Atypical Processing of Voice Sounds in Infants at Risk for Autism Spectrum Disorder." *Cortex* 71: 122–133. https://doi.org/10.1016/j.cortex.2015.06.015.

Bleimeister, I., I. Avni, M. Granovetter, et al. 2024. "Idiosyncratic Pupil Regulation in Autistic Children." bioRxiv. https://doi.org/10.1101/2024.01.10.575072.

Boger-Megiddo, I., D. W. Shaw, S. D. Friedman, et al. 2006. "Corpus Callosum Morphometrics in Young Children With Autism Spectrum Disorder." *Journal of Autism and Developmental Disorders* 36, no. 6: 733–739. https://doi.org/10.1007/s10803-006-0121-2.

Bölte, S., S. Girdler, and P. B. Marschik. 2019. "The Contribution of Environmental Exposure to the Etiology of Autism Spectrum Disorder." *Cellular and Molecular Life Sciences* 76: 1275–1297.

Bos, D. J., T. R. van Raalten, B. Oranje, et al. 2014. "Developmental Differences in Higher-Order Resting-State Networks in Autism Spectrum Disorder." *NeuroImage. Clinical* 4: 820–827. https://doi.org/10.1016/j.nicl.2014.05.007.

Bosl, W. J., H. Tager-Flusberg, and C. A. Nelson. 2018. "EEG Analytics for Early Detection of Autism Spectrum Disorder: A Data-Driven Approach." *Scientific Reports* 8, no. 1: 6828. https://doi.org/10.1038/s41598-018-24318-x.

Bouret, S., and S. J. Sara. 2002. "Locus Coeruleus Activation Modulates Firing Rate and Temporal Organization of Odour-Induced Single-Cell Responses in Rat Piriform Cortex." *European Journal of Neuroscience* 16, no. 12: 2371–2382. https://doi.org/10.1046/j.1460-9568.2002.02413.x.

Bourgeron, T. 2015. "From the Genetic Architecture to Synaptic Plasticity in Autism Spectrum Disorder." *Nature Reviews. Neuroscience* 16, no. 9: 551–563. https://doi.org/10.1038/nrn3992.

Brito, N. H., A. J. Elliott, J. R. Isler, et al. 2019. "Neonatal EEG Linked to Individual Differences in Socioemotional Outcomes and Autism Risk in Toddlers." *Developmental Psychobiology* 61, no. 8: 1110–1119. https://doi.org/10.1002/dev.21870.

Brown, A., M. Arpone, A. L. Schneider, S. Micallef, V. A. Anderson, and I. E. Scheffer. 2020. "Cognitive, Behavioral, and Social Functioning in Children and Adults With Dravet Syndrome." *Epilepsy & Behavior* 112: 107319.

Bryson, S., N. Garon, T. McMullen, et al. 2018. "Impaired Disengagement of Attention and Its Relationship to Emotional Distress in Infants at High-Risk for Autism Spectrum Disorder." *Journal of Clinical and Experimental Neuropsychology* 40, no. 5: 487–501.

Butera, C., J. Kaplan, E. Kilroy, et al. 2023. "The Relationship Between Alexithymia, Interoception, and Neural Functional Connectivity During Facial Expression Processing in Autism Spectrum Disorder." *Neuropsychologia* 180: 108469. https://doi.org/10.1016/j.neuropsychologia.2023.108469.

Cakar, M. E., N. J. Okada, K. K. Cummings, et al. 2024. "Functional Connectivity of the Sensorimotor Cerebellum in Autism: Associations With Sensory Over-Responsivity." *Frontiers in Psychiatry* 15: 1337921. https://doi.org/10.3389/fpsyt.2024.1337921.

Caly, H., H. Rabiei, P. Coste-Mazeau, et al. 2021. "Machine Learning Analysis of Pregnancy Data Enables Early Identification of a Subpopulation of Newborns With ASD." *Scientific Reports* 11, no. 1: 6877. https://doi.org/10.1038/s41598-021-86320-0.

Camero, R., C. Gallego, and V. Martínez. 2023. "Gaze Following as an Early Diagnostic Marker of Autism in a New Word Learning Task in Toddlers." *Journal of Autism and Developmental Disorders* 54, no. 9: 3211–3224. https://doi.org/10.1007/s10803-023-06043-1.

Canfield, M. A., P. H. Langlois, G. W. Rutenberg, et al. 2019. "The Association Between Newborn Screening Analytes and Childhood Autism in a Texas Medicaid Population, 2010–2012." *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 180, no. 5: 291–304. https://doi.org/10.1002/ajmg.b.32728.

Carper, R. A., S. Solders, J. M. Treiber, I. Fishman, and R. A. Müller. 2015. "Corticospinal Tract Anatomy and Functional Connectivity of Primary Motor Cortex in Autism." *Journal of the American Academy of Child and Adolescent Psychiatry* 54, no. 10: 859–867. https://doi.org/10.1016/j.jaac.2015.07.007.

Carter Leno, V., A. Pickles, S. van Noordt, et al. 2021. "12-Month Peak Alpha Frequency Is a Correlate but Not a Longitudinal Predictor of Non-Verbal Cognitive Abilities in Infants at Low and High Risk for Autism Spectrum Disorder." *Developmental Cognitive Neuroscience* 48: 100938. https://doi.org/10.1016/j.dcn.2021.100938.

Cerliani, L., M. Mennes, R. M. Thomas, A. Di Martino, M. Thioux, and C. Keysers. 2015. "Increased Functional Connectivity Between Subcortical and Cortical Resting-State Networks in Autism Spectrum

Disorder." *JAMA Psychiatry* 72, no. 8: 767–777. https://doi.org/10.1001/jamapsychiatry.2015.0101.

Chang, T. S., M. Cirnigliaro, S. A. Arteaga, et al. 2022. "The Contributions of Rare Inherited and Polygenic Risk to ASD in Multiplex Families." medRxiv. https://doi.org/10.1101/2022.04.05.22273459.

Chaste, P., and M. Leboyer. 2012. "Autism Risk Factors: Genes, Environment, and Gene-Environment Interactions." *Dialogues in Clinical Neuroscience* 14, no. 3: 281–292.

Chen, C.-C., C.-H. Lin, and M.-C. Lin. 2023. "Maternal Autoimmune Disease and Risk of Offspring Autism Spectrum Disorder – A Nationwide Population-Based Cohort Study." *Frontiers in Psychiatry* 14: 1254453.

Chen, H., J. Wang, L. Q. Uddin, et al. 2018. "Aberrant Functional Connectivity of Neural Circuits Associated With Social and Sensorimotor Deficits in Young Children With Autism Spectrum Disorder." *Autism Research* 11, no. 12: 1643–1652. https://doi.org/10.1002/aur.2029.

Chen, J., J. Zhang, A. Liu, et al. 2020. "CHD2-Related Epilepsy: Novel Mutations and New Phenotypes." *Developmental Medicine and Child Neurology* 62, no. 5: 647–653.

Chen, M., Y. Lin, C. Yu, et al. 2024. "Effect of Cesarean Section on the Risk of Autism Spectrum Disorders/Attention Deficit Hyperactivity Disorder in Offspring: A Meta-Analysis." *Archives of Gynecology and Obstetrics* 309, no. 2: 439–455.

Chen, Y.-H., J. Saby, E. Kuschner, W. Gaetz, J. C. Edgar, and T. P. L. Roberts. 2019. "Magnetoencephalography and the Infant Brain." *NeuroImage* 189: 445–458. https://doi.org/10.1016/j.neuroimage.2019.01.059.

Cheroni, C., N. Caporale, and G. Testa. 2020. "Autism Spectrum Disorder at the Crossroad Between Genes and Environment: Contributions, Convergences, and Interactions in ASD Developmental Pathophysiology." *Molecular Autism* 11, no. 1: 69.

Chiang, H. L., Y. J. Chen, H. Y. Lin, W. I. Tseng, and S. S. Gau. 2017. "Disorder-Specific Alteration in White Matter Structural Property in Adults With Autism Spectrum Disorder Relative to Adults With ADHD and Adult Controls." *Human Brain Mapping* 38, no. 1: 384–395. https://doi.org/10.1002/hbm.23367.

Ciarrusta, J., R. Dimitrova, D. Batalle, et al. 2020. "Emerging Functional Connectivity Differences in Newborn Infants Vulnerable to Autism Spectrum Disorders." *Translational Psychiatry* 10, no. 1: 131. https://doi.org/10.1038/s41398-020-0805-y.

Cirnigliaro, M., T. S. Chang, S. A. Arteaga, et al. 2023. "The Contributions of Rare Inherited and Polygenic Risk to ASD in Multiplex Families." *Proceedings of the National Academy of Sciences of the United States of America* 120, no. 31: e2215632120.

Coffman, M. C., L. C. Anderson, A. J. Naples, and J. C. McPartland. 2015. "Sex Differences in Social Perception in Children With ASD." *Journal of Autism and Developmental Disorders* 45, no. 2: 589–599. https://doi.org/10.1007/s10803-013-2006-5.

Constantino, J. N. 2021. "Social Responsiveness Scale." In *Encyclopedia of Autism Spectrum Disorders*, 4457–4467. Springer.

Conti, E., J. Mitra, S. Calderoni, et al. 2017. "Network Over-Connectivity Differentiates Autism Spectrum Disorder From Other Developmental Disorders in Toddlers: A Diffusion MRI Study." *Human Brain Mapping* 38, no. 5: 2333–2344. https://doi.org/10.1002/hbm.23520.

Cristino, A. S., S. M. Williams, Z. Hawi, et al. 2014. "Neurodevelopmental and Neuropsychiatric Disorders Represent an Interconnected Molecular System." *Molecular Psychiatry* 19, no. 3: 294–301. https://doi.org/10.1038/mp.2013.16.

Croen, L. A., J. K. Grether, C. K. Yoshida, R. Odouli, and V. Hendrick. 2011. "Antidepressant Use During Pregnancy and Childhood Autism Spectrum Disorders." *Archives of General Psychiatry* 68: 1104–1112.

Cummings, K., A. Watkins, C. Jones, R. Dias, and A. Welham. 2022. "Behavioural and Psychological Features of PTEN Mutations: A Systematic Review of the Literature and Meta-Analysis of the Prevalence of Autism Spectrum Disorder Characteristics." *Journal of Neurodevelopmental Disorders* 14, no. 1: 1.

Cummings, K. K., K. E. Lawrence, L. M. Hernandez, et al. 2020. "Sex Differences in Salience Network Connectivity and Its Relationship to Sensory Over-Responsivity in Youth With Autism Spectrum Disorder." *Autism Research* 13, no. 9: 1489–1500. https://doi.org/10.1002/aur.2351.

Cygan, H. B., P. Tacikowski, P. Ostaszewski, I. Chojnicka, and A. Nowicka. 2014. "Neural Correlates of Own Name and Own Face Detection in Autism Spectrum Disorder." *PLoS One* 9, no. 1: e86020. https://doi.org/10.1371/journal.pone.0086020.

Daluwatte, C., J. H. Miles, S. E. Christ, D. Q. Beversdorf, T. N. Takahashi, and G. Yao. 2013. "Atypical Pupillary Light Reflex and Heart Rate Variability in Children With Autism Spectrum Disorder." *Journal of Autism and Developmental Disorders* 43, no. 8: 1910–1925. https://doi.org/10.1007/s10803-012-1741-3.

Daluwatte, C., J. H. Miles, J. Sun, and G. Yao. 2015. "Association Between Pupillary Light Reflex and Sensory Behaviors in Children With Autism Spectrum Disorders." *Research in Developmental Disabilities* 37: 209–215. https://doi.org/10.1016/j.ridd.2014.11.019.

Dawson, G., E. J. Jones, K. Merkle, et al. 2012. "Early Behavioral Intervention Is Associated With Normalized Brain Activity in Young Children With Autism." *Journal of the American Academy of Child and Adolescent Psychiatry* 51, no. 11: 1150–1159. https://doi.org/10.1016/j.jaac.2012.08.018.

de Haan, M., M. H. Johnson, and H. Halit. 2003. "Development of Face-Sensitive Event-Related Potentials During Infancy: A Review." *International Journal of Psychophysiology* 51, no. 1: 45–58. https://doi.org/10.1016/s0167-8760(03)00152-1.

de la Torre-Ubieta, L., H. Won, J. L. Stein, and D. H. Geschwind. 2016. "Advancing the Understanding of Autism Disease Mechanisms Through Genetics." *Nature Medicine* 22, no. 4: 345–361. https://doi.org/10.1038/nm.4071.

De Ridder, J., M. Lavanga, B. Verhelle, et al. 2020. "Prediction of Neurodevelopment in Infants With Tuberous Sclerosis Complex Using Early EEG Characteristics." *Frontiers in Neurology* 11: 582891. https://doi.org/10.3389/fneur.2020.582891.

De Rubeis, S., X. He, A. P. Goldberg, et al. 2014. "Synaptic, Transcriptional and Chromatin Genes Disrupted in Autism." *Nature* 515: 209–215.

de Sena Barbosa, M. G., R. L. V. de Souza, L. G. G. Cherain, et al. 2024. "Biomarkers for Autism Spectrum Disorder: A Short Review." *Annals of Medicine and Surgery* 86: 7227–7231.

Devlin, B., N. Melhem, and K. Roeder. 2011. "Do Common Variants Play a Role in Risk for Autism? Evidence and Theoretical Musings." *Brain Research* 1380: 78–84.

Dickinson, A., M. Daniel, A. Marin, et al. 2021. "Multivariate Neural Connectivity Patterns in Early Infancy Predict Later Autism Symptoms." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 6, no. 1: 59–69. https://doi.org/10.1016/j.bpsc.2020.06.003.

DiCriscio, A. S., and V. Troiani. 2021. "Resting and Functional Pupil Response Metrics Indicate Features of Reward Sensitivity and ASD in Children." *Journal of Autism and Developmental Disorders* 51, no. 7: 2416–2435. https://doi.org/10.1007/s10803-020-04721-y.

Dierker, D. L., E. Feczko, J. R. Pruett Jr., et al. 2015. "Analysis of Cortical Shape in Children With Simplex Autism." *Cerebral Cortex* 25, no. 4: 1042–1051. https://doi.org/10.1093/cercor/bht294.

Dinalankara, D. M. R., J. H. Miles, T. Nicole Takahashi, and G. Yao. 2017. "Atypical Pupillary Light Reflex in 2–6-Year-Old Children With Autism Spectrum Disorders." *Autism Research* 10, no. 5: 829–838. https://doi.org/10.1002/aur.1745.

Ding, M., S. Shi, S. Qie, J. Li, and X. Xi. 2023. "Association Between Heavy Metals Exposure (Cadmium, Lead, Arsenic, Mercury) and Child Autistic Disorder: A Systematic Review and Meta-Analysis." *Frontiers in Pediatrics* 11: 1169733.

Dinstein, I., K. Pierce, L. Eyler, et al. 2011. "Disrupted Neural Synchronization in Toddlers With Autism." *Neuron* 70, no. 6: 1218–1225. https://doi.org/10.1016/j.neuron.2011.04.018.

Doyle-Thomas, K. A., W. Lee, N. E. Foster, et al. 2015. "Atypical Functional Brain Connectivity During Rest in Autism Spectrum Disorders." *Annals of Neurology* 77, no. 5: 866–876. https://doi.org/10.1002/ana.24391.

Duque-Cartagena, T., M. D. B. Dalla, E. Mundstock, et al. 2024. "Environmental Pollutants as Risk Factors for Autism Spectrum Disorders: A Systematic Review and Meta-Analysis of Cohort Studies." *BMC Public Health* 24, no. 1: 2388.

Edgar, J. C., M. Dipiero, E. McBride, et al. 2019. "Abnormal Maturation of the Resting-State Peak Alpha Frequency in Children With Autism Spectrum Disorder." *Human Brain Mapping* 40, no. 11: 3288–3298. https://doi.org/10.1002/hbm.24598.

Edgar, J. C., C. L. t. Fisk, S. Liu, et al. 2016. "Translating Adult Electrophysiology Findings to Younger Patient Populations: Difficulty Measuring 40-Hz Auditory Steady-State Responses in Typically Developing Children and Children With Autism Spectrum Disorder." *Developmental Neuroscience* 38, no. 1: 1–14. https://doi.org/10.1159/000441943.

Edgar, J. C., S. Y. Khan, L. Blaskey, et al. 2015. "Neuromagnetic Oscillations Predict Evoked-Response Latency Delays and Core Language Deficits in Autism Spectrum Disorders." *Journal of Autism and Developmental Disorders* 45, no. 2: 395–405. https://doi.org/10.1007/s10803-013-1904-x.

Eilam-Stock, T., T. Wu, A. Spagna, L. J. Egan, and J. Fan. 2016. "Neuroanatomical Alterations in High-Functioning Adults With Autism Spectrum Disorder." *Frontiers in Neuroscience* 10: 237. https://doi.org/10.3389/fnins.2016.00237.

Eimer, M. 2000. "Event-Related Brain Potentials Distinguish Processing Stages Involved in Face Perception and Recognition." *Clinical Neurophysiology* 111, no. 4: 694–705. https://doi.org/10.1016/s1388-2457(99)00285-0.

El-Baz, F., M. Abd El-Aal, T. M. Kamal, A. A. Sadek, and A. A. Othman. 2017. "Study of the C677T and 1298AC Polymorphic Genotypes of MTHFR Gene in Autism Spectrum Disorder." *Electronic Physician* 9, no. 9: 5287–5293.

Eldar, E., J. D. Cohen, and Y. Niv. 2013. "The Effects of Neural Gain on Attention and Learning." *Nature Neuroscience* 16, no. 8: 1146–1153. https://doi.org/10.1038/nn.3428.

Elison, J. T., S. J. Paterson, J. J. Wolff, et al. 2013. "White Matter Microstructure and Atypical Visual Orienting in 7-Month-Olds at Risk for Autism." *American Journal of Psychiatry* 170, no. 8: 899–908. https://doi.org/10.1176/appi.ajp.2012.12091150.

Ellaway, P. H., A. Kuppuswamy, A. Nicotra, and C. J. Mathias. 2010. "Sweat Production and the Sympathetic Skin Response: Improving the Clinical Assessment of Autonomic Function." *Autonomic Neuroscience* 155, no. 1–2: 109–114. https://doi.org/10.1016/j.autneu.2010.01.008.

Elsabbagh, M., R. Bruno, M. W. Wan, T. Charman, M. H. Johnson, and J. Green. 2015. "Infant Neural Sensitivity to Dynamic Eye Gaze Relates to Quality of Parent-Infant Interaction at 7-Months in Infants at Risk for Autism." *Journal of Autism and Developmental Disorders* 45, no. 2: 283–291. https://doi.org/10.1007/s10803-014-2192-9.

Elsabbagh, M., J. Fernandes, S. Jane Webb, G. Dawson, T. Charman, and M. H. Johnson. 2013. "Disengagement of Visual Attention in Infancy Is Associated With Emerging Autism in Toddlerhood." *Biological Psychiatry* 74, no. 3: 189–194. https://doi.org/10.1016/j.biopsych.2012.11.030.

Elsabbagh, M., E. Mercure, K. Hudry, et al. 2012. "Infant Neural Sensitivity to Dynamic Eye Gaze Is Associated With Later Emerging Autism." *Current Biology* 22, no. 4: 338–342. https://doi.org/10.1016/j.cub.2011.12.056.

Emerson, R. W., C. Adams, T. Nishino, et al. 2017. "Functional Neuroimaging of High-Risk 6-Month-Old Infants Predicts a Diagnosis of Autism at 24 Months of Age." *Science Translational Medicine* 9, no. 393: eaag2882. https://doi.org/10.1126/scitranslmed.aag2882.

Fish, L. A., P. Nyström, T. Gliga, et al. 2021. "Development of the Pupillary Light Reflex From 9 to 24 Months: Association With Common Autism Spectrum Disorder (ASD) Genetic Liability and 3-Year ASD Diagnosis." *Journal of Child Psychology and Psychiatry* 62, no. 11: 1308–1319. https://doi.org/10.1111/jcpp.13518.

Fishman, I., M. Datko, Y. Cabrera, R. A. Carper, and R. A. Müller. 2015. "Reduced Integration and Differentiation of the Imitation Network in Autism: A Combined Functional Connectivity Magnetic Resonance Imaging and Diffusion-Weighted Imaging Study." *Annals of Neurology* 78, no. 6: 958–969. https://doi.org/10.1002/ana.24533.

Fishman, I., A. C. Linke, J. Hau, R. A. Carper, and R. A. Müller. 2018. "Atypical Functional Connectivity of Amygdala Related to Reduced Symptom Severity in Children With Autism." *Journal of the American Academy of Child and Adolescent Psychiatry* 57, no. 10: 764–774.e763. https://doi.org/10.1016/j.jaac.2018.06.015.

Folstein, S., and M. Rutter. 1977. "Infantile Autism: A Genetic Study of 21 Twin Pairs." *Journal of Child Psychology and Psychiatry* 18: 297–321.

Fourie, C., Y. Vyas, K. Lee, Y. Jung, C. C. Garner, and J. M. Montgomery. 2018. "Dietary Zinc Supplementation Prevents Autism Related Behaviors and Striatal Synaptic Dysfunction in Shank3 Exon 13–16 Mutant Mice." *Frontiers in Cellular Neuroscience* 12: 374.

Frazier, T. W., E. W. Klingemier, S. Parikh, et al. 2018. "Development and Validation of Objective and Quantitative Eye Tracking–Based Measures of Autism Risk and Symptom Levels." *Journal of the American Academy of Child & Adolescent Psychiatry* 57, no. 11: 858–866. https://doi.org/10.1016/j.jaac.2018.06.023.

Frye, R. E., S. Vassall, G. Kaur, C. Lewis, M. Karim, and D. Rossignol. 2019. "Emerging Biomarkers in Autism Spectrum Disorder: A Systematic Review." *Annals of Translational Medicine* 7, no. 23: 792.

Fu, X., E. Platt, F. Shic, and J. Bradshaw. 2024. "Infant Social Attention Associated With Elevated Likelihood for Autism Spectrum Disorder: A Multi-Method Comparison." *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-024-06360-z.

Gabard-Durnam, L., A. L. Tierney, V. Vogel-Farley, H. Tager-Flusberg, and C. A. Nelson. 2015. "Alpha Asymmetry in Infants at Risk for Autism Spectrum Disorders." *Journal of Autism and Developmental Disorders* 45, no. 2: 473–480. https://doi.org/10.1007/s10803-013-1926-4.

Gabard-Durnam, L. J., C. Wilkinson, K. Kapur, H. Tager-Flusberg, A. R. Levin, and C. A. Nelson. 2019. "Longitudinal EEG Power in the First Postnatal Year Differentiates Autism Outcomes." *Nature Communications* 10, no. 1: 4188. https://doi.org/10.1038/s41467-019-12202-9.

Gabrielsen, T. P., J. S. Anderson, K. G. Stephenson, et al. 2018. "Functional MRI Connectivity of Children With Autism and Low Verbal and Cognitive Performance." *Molecular Autism* 9, no. 1: 67. https://doi.org/10.1186/s13229-018-0248-y.

Gaugler, T., L. Klei, S. J. Sanders, et al. 2014. "Most Genetic Risk for Autism Resides With Common Variation." *Nature Genetics* 46: 881–885.

George, J. M., A. M. Pagnozzi, S. Bora, et al. 2020. "Prediction of Childhood Brain Outcomes in Infants Born Preterm Using Neonatal MRI and Concurrent Clinical Biomarkers (PREBO-6): Study Protocol for a Prospective Cohort Study." *BMJ Open* 10, no. 5: e036480. https://doi.org/10.1136/bmjopen-2019-036480.

Gergoudis, K., A. Weinberg, J. Templin, et al. 2020. "Psychometric Study of the Social Responsiveness Scale in Phelan–McDermid Syndrome." *Autism Research* 13, no. 8: 1383–1396.

Geschwind, D. H. 2011. "Genetics of Autism Spectrum Disorders." *Trends in Cognitive Sciences* 15, no. 9: 409–416. https://doi.org/10.1016/j.tics.2011.07.003.

Ghanbari, Y., L. Bloy, J. Christopher Edgar, L. Blaskey, R. Verma, and T. P. Roberts. 2015. "Joint Analysis of Band-Specific Functional Connectivity and Signal Complexity in Autism." *Journal of Autism and Developmental Disorders* 45, no. 2: 444–460. https://doi.org/10.1007/s10803-013-1915-7.

Giedd, J. N., A. Raznahan, K. L. Mills, and R. K. Lenroot. 2012. "Review: Magnetic Resonance Imaging of Male/Female Differences in Human Adolescent Brain Anatomy." *Biology of Sex Differences* 3, no. 1: 19. https://doi.org/10.1186/2042-6410-3-19.

Gilzenrat, M. S., S. Nieuwenhuis, M. Jepma, and J. D. Cohen. 2010. "Pupil Diameter Tracks Changes in Control State Predicted by the Adaptive Gain Theory of Locus Coeruleus Function." *Cognitive, Affective, & Behavioral Neuroscience* 10, no. 2: 252–269. https://doi.org/10.3758/cabn.10.2.252.

Gordon, I., A. Jack, C. M. Pretzsch, et al. 2016. "Intranasal Oxytocin Enhances Connectivity in the Neural Circuitry Supporting Social Motivation and Social Perception in Children With Autism." *Scientific Reports* 6: 35054. https://doi.org/10.1038/srep35054.

Granovetter, M. C., C. S. Burlingham, N. M. Blauch, N. J. Minshew, D. J. Heeger, and M. Behrmann. 2020. "Uncharacteristic Task-Evoked Pupillary Responses Implicate Atypical Locus Ceruleus Activity in Autism." *Journal of Neuroscience* 40, no. 19: 3815–3826. https://doi.org/10.1523/jneurosci.2680-19.2020.

Green, S. A., L. Hernandez, S. Y. Bookheimer, and M. Dapretto. 2016. "Salience Network Connectivity in Autism Is Related to Brain and Behavioral Markers of Sensory Overresponsivity." *Journal of the American Academy of Child and Adolescent Psychiatry* 55, no. 7: 618–626.e611. https://doi.org/10.1016/j.jaac.2016.04.013.

Grove, J., S. Ripke, and T. D. Als. 2019. "Identification of Common Genetic Risk Variants for Autism Spectrum Disorder." *Nature Genetics* 51, no. 3: 431–444.

Guo, B. Q., H. B. Li, D. S. Zhai, and L. Q. Yang. 2024. "Prevalence of Autism Spectrum Disorder Diagnosis by Birth Weight, Gestational Age, and Size for Gestational Age: A Systematic Review, Meta-Analysis, and Meta-Regression." *European Child & Adolescent Psychiatry* 33, no. 7: 2035–2049.

Guy, M. W., J. E. Richards, B. L. Tonnsen, and J. E. Roberts. 2018. "Neural Correlates of Face Processing in Etiologically-Distinct 12-Month-Old Infants at High-Risk of Autism Spectrum Disorder." *Developmental Cognitive Neuroscience* 29: 61–71. https://doi.org/10.1016/j.dcn.2017.03.002.

Haartsen, R., T. Charman, G. Pasco, M. H. Johnson, and E. J. H. Jones. 2022. "Modulation of EEG Theta by Naturalistic Social Content Is Not Altered in Infants With Family History of Autism." *Scientific Reports* 12, no. 1: 20758. https://doi.org/10.1038/s41598-022-24870-7.

Haartsen, R., E. J. H. Jones, E. V. Orekhova, T. Charman, and M. H. Johnson. 2019. "Functional EEG Connectivity in Infants Associates With Later Restricted and Repetitive Behaviours in Autism; a Replication Study." *Translational Psychiatry* 9, no. 1: 66. https://doi.org/10.1038/s41398-019-0380-2.

Halladay, A. K., S. Bishop, J. N. Constantino, et al. 2015. "Sex and Gender Differences in Autism Spectrum Disorder: Summarizing Evidence Gaps and Identifying Emerging Areas of Priority." *Molecular Autism* 6, no. 1. https://doi.org/10.1186/s13229-015-0019-y.

Hammock, E., J. Veenstra-VanderWeele, Z. Yan, et al. 2012. "Examining Autism Spectrum Disorders by Biomarkers: Example From the Oxytocin and Serotonin Systems." *Journal of the American Academy of Child & Adolescent Psychiatry* 51, no. 7: 712–721.

Hasegawa, C., T. Ikeda, Y. Yoshimura, et al. 2023. "Reduced Gamma Oscillation During Visual Processing of the Mother's Face in Children With Autism Spectrum Disorder: A Pilot Study." *Psychiatry and Clinical Neurosciences Reports* 2, no. 1: e68. https://doi.org/10.1002/pcn5.68.

Hawks, Z. W., A. Todorov, N. Marrus, et al. 2023. "A Prospective Evaluation of Infant Cerebellar-Cerebral Functional Connectivity in Relation to Behavioral Development in Autism Spectrum Disorder." *Biological Psychiatry Global Open Science* 3, no. 1: 149–161. https://doi.org/10.1016/j.bpsgos.2021.12.004.

Hazlett, H. C., H. Gu, B. C. Munsell, et al. 2017. "Early Brain Development in Infants at High Risk for Autism Spectrum Disorder." *Nature* 542, no. 7641: 348–351. https://doi.org/10.1038/nature21369.

He, N., B. M. Li, Z. X. Li, et al. 2018. "Few Individuals With Lennox-Gastaut Syndrome Have Autism Spectrum Disorder: A Comparison With Dravet Syndrome." *Journal of Neurodevelopmental Disorders* 10: 1–8.

He, Y., L. Byrge, and D. P. Kennedy. 2020. "Nonreplication of Functional Connectivity Differences in Autism Spectrum Disorder Across Multiple Sites and Denoising Strategies." *Human Brain Mapping* 41, no. 5: 1334–1350. https://doi.org/10.1002/hbm.24879.

Huberty, S., V. Carter Leno, S. van Noordt, et al. 2021. "Association Between Spectral Electroencephalography Power and Autism Risk and Diagnosis in Early Development." *Autism Research* 14: 1390–1403. https://doi.org/10.1002/aur.2518.

Hull, J. V., L. B. Dokovna, Z. J. Jacokes, C. M. Torgerson, A. Irimia, and J. D. Van Horn. 2017. "Resting-State Functional Connectivity in Autism Spectrum Disorders: A Review." *Frontiers in Psychiatry* 7: 205. https://doi.org/10.3389/fpsyt.2016.00205.

Im, W. Y., J. H. Ha, E. J. Kim, K.-A. Cheon, J. Cho, and D.-H. Song. 2018. "Impaired White Matter Integrity and Social Cognition in High-Function Autism: Diffusion Tensor Imaging Study." *Psychiatry Investigation* 15, no. 3: 292–299. https://doi.org/10.30773/pi.2017.08.15.

Iossifov, I., B. J. O'Roak, S. J. Sanders, et al. 2014. "The Contribution of De Novo Coding Mutations to Autism Spectrum Disorder." *Nature* 515: 216–221.

Jacquemont, S., P. C. Bradley, M. Hersch, et al. 2014. "A Higher Mutational Burden in Females Supports a 'Female Protective Model' in Neurodevelopmental Disorders." *American Journal of Human Genetics* 94, no. 3: 415–425. https://doi.org/10.1016/j.ajhg.2014.02.001.

Jenkins, J., III, V. Chow, L. Blaskey, et al. 2015. "Auditory Evoked M100 Response Latency Is Delayed in Children With 16p11.2 Deletion but Not 16p11.2 Duplication." *Cerebral Cortex* 26, no. 5: 1957–1964. https://doi.org/10.1093/cercor/bhv008.

Jensen, A. R., A. L. Lane, B. A. Werner, S. E. McLees, T. S. Fletcher, and R. E. Frye. 2022. "Modern Biomarkers for Autism Spectrum Disorder: Future Directions." *Molecular Diagnosis & Therapy* 26, no. 5: 483–495.

Jin, X., S. K. Simmons, A. Guo, et al. 2020. "In Vivo Perturb-Seq Reveals Neuronal and Glial Abnormalities Associated With Autism Risk Genes." *Science* 370: eaaz6063.

Johanson, C. E., J. A. Duncan 3rd, P. M. Klinge, T. Brinker, E. G. Stopa, and G. D. Silverberg. 2008. "Multiplicity of Cerebrospinal Fluid Functions: New Challenges in Health and Disease." *Cerebrospinal Fluid Research* 5, no. 10: 10. https://doi.org/10.1186/1743-8454-5-10.

Jones, E. J. H., G. Dawson, J. Kelly, A. Estes, and S. J. Webb. 2017. "Parent-Delivered Early Intervention in Infants at Risk for ASD: Effects on Electrophysiological and Habituation Measures of Social Attention." *Autism Research* 10, no. 5: 961–972. https://doi.org/10.1002/aur.1754.

Jones, E. J. H., A. Goodwin, E. Orekhova, et al. 2020. "Infant EEG Theta Modulation Predicts Childhood Intelligence." *Scientific Reports* 10, no. 1: 11232. https://doi.org/10.1038/s41598-020-67687-y.

Jones, E. J. H., L. Mason, J. B. Ali, et al. 2019. "Eurosibs: Towards Robust Measurement of Infant Neurocognitive Predictors of Autism Across Europe." *Infant Behavior and Development* 57: 101316. https://doi.org/10.1016/j.infbeh.2019.03.007.

Jones, E. J. H., K. Venema, R. Earl, et al. 2016. "Reduced Engagement With Social Stimuli in 6-Month-Old Infants With Later Autism Spectrum Disorder: A Longitudinal Prospective Study of Infants at High Familial Risk." *Journal of Neurodevelopmental Disorders* 8, no. 1: 7. https://doi.org/10.1186/s11689-016-9139-8.

Jones, W., C. Klaiman, S. Richardson, et al. 2023. "Eye-Tracking–Based Measurement of Social Visual Engagement Compared With Expert Clinical Diagnosis of Autism." *JAMA* 330, no. 9: 854–865. https://doi.org/10.1001/jama.2023.13295.

Jones, W., C. Klaiman, S. Richardson, et al. 2023. "Development and Replication of Objective Measurements of Social Visual Engagement to Aid in Early Diagnosis and Assessment of Autism." *JAMA Network Open* 6, no. 9: e2330145. https://doi.org/10.1001/jamanetworkopen.2023.30145.

Kameya, M., T. Hirosawa, D. Soma, et al. 2024. "Relationships Between Peak Alpha Frequency, Age, and Autistic Traits in Young Children With and Without Autism Spectrum Disorder." *Frontiers in Psychiatry* 15: 1419815. https://doi.org/10.3389/fpsyt.2024.1419815.

Keehn, B., P. Monahan, B. Enneking, T. Ryan, N. Swigonski, and R. M. Keehn. 2024. "Eye-Tracking Biomarkers and Autism Diagnosis in Primary Care." *JAMA Network Open* 7, no. 5: e2411190. https://doi.org/10.1001/jamanetworkopen.2024.11190.

Keehn, B., R. A. Müller, and J. Townsend. 2013. "Atypical Attentional Networks and the Emergence of Autism." *Neuroscience and Biobehavioral Reviews* 37, no. 2: 164–183. https://doi.org/10.1016/j.neubiorev.2012.11.014.

Keehn, B., V. Vogel-Farley, H. Tager-Flusberg, and C. A. Nelson. 2015. "Atypical Hemispheric Specialization for Faces in Infants at Risk for Autism Spectrum Disorder." *Autism Research* 8, no. 2: 187–198. https://doi.org/10.1002/aur.1438.

Keehn, R. J. J., E. B. Pueschel, Y. Gao, et al. 2021. "Underconnectivity Between Visual and Salience Networks and Links With Sensory Abnormalities in Autism Spectrum Disorders." *Journal of the American Academy of Child and Adolescent Psychiatry* 60, no. 2: 274–285. https://doi.org/10.1016/j.jaac.2020.02.007.

Keil, V., R. Hepach, S. Vierrath, et al. 2018. "Children With Social Anxiety Disorder Show Blunted Pupillary Reactivity and Altered Eye Contact Processing in Response to Emotional Faces: Insights From Pupillometry and Eye Movements." *Journal of Anxiety Disorders* 58: 61–69. https://doi.org/10.1016/j.janxdis.2018.07.001.

Kercher, C., L. Azinfar, D. M. R. Dinalankara, T. N. Takahashi, J. H. Miles, and G. Yao. 2020. "A Longitudinal Study of Pupillary Light Reflex in 6- to 24-Month Children." *Scientific Reports* 10, no. 1: 1205. https://doi.org/10.1038/s41598-020-58254-6.

Khan, A. J., A. Nair, C. L. Keown, M. C. Datko, A. J. Lincoln, and R. A. Müller. 2015. "Cerebro-Cerebellar Resting-State Functional Connectivity in Children and Adolescents With Autism Spectrum Disorder." *Biological Psychiatry* 78, no. 9: 625–634. https://doi.org/10.1016/j.biopsych.2015.03.024.

Kim, Y., G. Kadlaskar, R. M. Keehn, and B. Keehn. 2022. "Measures of Tonic and Phasic Activity of the Locus Coeruleus-Norepinephrine System in Children With Autism Spectrum Disorder: An Event-Related Potential and Pupillometry Study." *Autism Research* 15, no. 12: 2250–2264. https://doi.org/10.1002/aur.2820.

Kitzbichler, M. G., S. Khan, S. Ganesan, et al. 2015. "Altered Development and Multifaceted Band-Specific Abnormalities of Resting State Networks in Autism." *Biological Psychiatry* 77, no. 9: 794–804. https://doi.org/10.1016/j.biopsych.2014.05.012.

Klei, L., S. J. Sanders, M. T. Murtha, et al. 2012. "Common Genetic Variants, Acting Additively, Are a Major Source of Risk for Autism." *Molecular Autism* 3, no. 1: 9.

Kosaka, H., Y. Okamoto, T. Munesue, et al. 2016. "Oxytocin Efficacy Is Modulated by Dosage and Oxytocin Receptor Genotype in Young Adults With High-Functioning Autism: A 24-Week Randomized Clinical Trial." *Translational Psychiatry* 6: e872. https://doi.org/10.1038/tp.2016.152.

Kosaka, H., M. Omori, T. Munesue, et al. 2010. "Smaller Insula and Inferior Frontal Volumes in Young Adults With Pervasive Developmental Disorders." *NeuroImage* 50, no. 4: 1357–1363. https://doi.org/10.1016/j.neuroimage.2010.01.085.

Krakowiak, P., C. K. Walker, A. A. Bremer, et al. 2012. "Maternal Metabolic Conditions and Risk for Autism and Other Neurodevelopmental Disorders." *Pediatrics* 129, no. 5: e1121–e1128.

Kruppa, J. A., A. Gossen, E. Oberwelland Weiß, et al. 2019. "Neural Modulation of Social Reinforcement Learning by Intranasal Oxytocin in Male Adults With High-Functioning Autism Spectrum Disorder: A Randomized Trial." *Neuropsychopharmacology* 44, no. 4: 749–756. https://doi.org/10.1038/s41386-018-0258-7.

Kung, K. T., M. Constantinescu, W. V. Browne, R. M. Noorderhaven, and M. Hines. 2016. "No Relationship Between Early Postnatal Testosterone Concentrations and Autistic Traits in 18 to 30-Month-Old Children." *Molecular Autism* 7, no. 1: 15. https://doi.org/10.1186/s13229-016-0078-8.

Kurtz-Nelson, E. C., H. M. Rea, A. C. Petriceks, et al. 2023. "Characterizing the Autism Spectrum Phenotype in DYRK1A-Related Syndrome." *Autism Research* 16, no. 8: 1488–1500. https://doi.org/10.1002/aur.2995.

Kuschner, E. S., M. Kim, L. Bloy, M. Dipiero, J. C. Edgar, and T. P. L. Roberts. 2021. "MEG-PLAN: A Clinical and Technical Protocol for Obtaining Magnetoencephalography Data in Minimally Verbal or Nonverbal Children Who Have Autism Spectrum Disorder." *Journal of Neurodevelopmental Disorders* 13, no. 1: 8. https://doi.org/10.1186/s11689-020-09350-1.

Kylliäinen, A., S. Wallace, M. N. Coutanche, et al. 2012. "Affective-Motivational Brain Responses to Direct Gaze in Children With Autism Spectrum Disorder." *Journal of Child Psychology and Psychiatry* 53, no. 7: 790–797. https://doi.org/10.1111/j.1469-7610.2011.02522.x.

Lajiness-O'Neill, R., J. R. Brennan, J. E. Moran, et al. 2018. "Patterns of Altered Neural Synchrony in the Default Mode Network in Autism Spectrum Disorder Revealed With Magnetoencephalography (MEG): Relationship to Clinical Symptomatology." *Autism Research* 11, no. 3: 434–449. https://doi.org/10.1002/aur.1908.

Lam, J., P. Sutton, A. Kalkbrenner, et al. 2016. "A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder." *PLoS One* 11, no. 9: e0161851.

Lauttia, J., T. M. Helminen, J. M. Leppänen, et al. 2019. "Atypical Pattern of Frontal EEG Asymmetry for Direct Gaze in Young Children With Autism Spectrum Disorder." *Journal of Autism and Developmental Disorders* 49, no. 9: 3592–3601. https://doi.org/10.1007/s10803-019-04062-5.

Lawrence, K. E., L. M. Hernandez, H. C. Bowman, et al. 2020. "Sex Differences in Functional Connectivity of the Salience, Default Mode, and Central Executive Networks in Youth With ASD." *Cerebral Cortex* 30, no. 9: 5107–5120. https://doi.org/10.1093/cercor/bhaa105.

Lee, K., Y. Jung, Y. Vyas, Z. Mills, L. McNamara, and J. M. Montgomery. 2024. "Differential Effectiveness of Dietary Zinc Supplementation With Autism-Related Behaviours in Shank2 Knockout Mice." *Philosophical Transactions of the Royal Society B* 379, no. 1906: 20230230.

Lee, K., Y. Jung, Y. Vyas, et al. 2022. "Dietary Zinc Supplementation Rescues Fear-Based Learning and Synaptic Function in the Tbr1+/− Mouse Model of Autism Spectrum Disorders." *Molecular Autism* 13, no. 1: 13.

Lenroot, R. K., and J. N. Giedd. 2010. "Sex Differences in the Adolescent Brain." *Brain and Cognition* 72, no. 1: 46–55. https://doi.org/10.1016/j.bandc.2009.10.008.

Leppa, V. M., S. N. Kravitz, C. L. Martin, et al. 2016. "Rare Inherited and De Novo CNVs Reveal Complex Contributions to ASD Risk in Multiplex Families." *American Journal of Human Genetics* 99, no. 3: 540–554.

Levin, A. R., K. J. Varcin, H. M. O'Leary, H. Tager-Flusberg, and C. A. Nelson. 2017. "EEG Power at 3 Months in Infants at High Familial Risk for Autism." *Journal of Neurodevelopmental Disorders* 9, no. 1: 34. https://doi.org/10.1186/s11689-017-9214-9.

Levman, J., P. MacDonald, S. Rowley, et al. 2019. "Structural Magnetic Resonance Imaging Demonstrates Abnormal Regionally-Differential Cortical Thickness Variability in Autism: From Newborns to Adults." *Frontiers in Human Neuroscience* 13: 75. https://doi.org/10.3389/fnhum.2019.00075.

Levman, J., L. Vasung, P. MacDonald, et al. 2018. "Regional Volumetric Abnormalities in Pediatric Autism Revealed by Structural Magnetic Resonance Imaging." *International Journal of Developmental Neuroscience* 71: 34–45. https://doi.org/10.1016/j.ijdevneu.2018.08.001.

Lewis, J. D., A. C. Evans, J. R. Pruett, et al. 2014. "Network Inefficiencies in Autism Spectrum Disorder at 24 Months." *Translational Psychiatry* 4, no. 5: e388. https://doi.org/10.1038/tp.2014.24.

Lewis, J. D., A. C. Evans, J. R. Pruett Jr., et al. 2017. "The Emergence of Network Inefficiencies in Infants With Autism Spectrum Disorder." *Biological Psychiatry* 82, no. 3: 176–185. https://doi.org/10.1016/j.biopsych.2017.03.006.

Li, Y., S. Qiu, J. Shi, et al. 2020. "Association Between MTHFR C677T/A1298C and Susceptibility to Autism Spectrum Disorders: A Meta-Analysis." *BMC Pediatrics* 20: 449.

Libero, L. E., T. P. DeRamus, A. C. Lahti, G. Deshpande, and R. K. Kana. 2015. "Multimodal Neuroimaging Based Classification of Autism Spectrum Disorder Using Anatomical, Neurochemical, and White Matter Correlates." *Cortex* 66: 46–59. https://doi.org/10.1016/j.cortex.2015.02.008.

Linke, A. C., R. J. Jao Keehn, E. B. Pueschel, I. Fishman, and R. A. Müller. 2018. "Children With ASD Show Links Between Aberrant Sound Processing, Social Symptoms, and Atypical Auditory Interhemispheric and Thalamocortical Functional Connectivity." *Developmental Cognitive Neuroscience* 29: 117–126. https://doi.org/10.1016/j.dcn.2017.01.007.

Liu, J., J. B. Girault, T. Nishino, et al. 2024. "Atypical Functional Connectivity Between the Amygdala and Visual, Salience Regions in Infants With Genetic Liability for Autism." *Cerebral Cortex* 34, no. 13: 30–39. https://doi.org/10.1093/cercor/bhae092.

Liu, J., N. J. Okada, K. K. Cummings, et al. 2020. "Emerging Atypicalities in Functional Connectivity of Language-Related Networks in Young Infants at High Familial Risk for ASD." *Developmental Cognitive Neuroscience* 45: 100814. https://doi.org/10.1016/j.dcn.2020.100814.

Liu, J., T. Tsang, L. Jackson, et al. 2019. "Altered Lateralization of Dorsal Language Tracts in 6-Week-Old Infants at Risk for Autism." *Developmental Science* 22, no. 3: e12768. https://doi.org/10.1111/desc.12768.

Liu, J., T. Tsang, C. Ponting, et al. 2021. "Lack of Neural Evidence for Implicit Language Learning in 9-Month-Old Infants at High Risk for Autism." *Developmental Science* 24, no. 4: e13078. https://doi.org/10.1111/desc.13078.

Liu, X., J. Lin, H. Zhang, et al. 2022. "Oxidative Stress in Autism Spectrum Disorder—Current Progress of Mechanisms and Biomarkers." *Frontiers in Psychiatry* 13: 813304.

Lloyd-Fox, S., S. McCann, B. Milosavljevic, et al. 2024. "The Brain Imaging for Global Health (BRIGHT) Project: Longitudinal Cohort Study Protocol." *Gates Open Research* 7: 126. https://doi.org/10.12688/gatesopenres.14795.2.

Loewenfeld, I. E., and O. Lowenstein. 1993. *The Pupil: Anatomy, Physiology, and Clinical Applications*. 1st ed. Iowa State University Press, Wayne State University Press. https://cir.nii.ac.jp/crid/1130282271090099200.

Long, P., G. Wan, M. T. Roberts, and G. Corfas. 2018. "Myelin Development, Plasticity, and Pathology in the Auditory System." *Developmental Neurobiology* 78, no. 2: 80–92. https://doi.org/10.1002/dneu.22538.

Long, Z., X. Duan, D. Mantini, and H. Chen. 2016. "Alteration of Functional Connectivity in Autism Spectrum Disorder: Effect of Age and Anatomical Distance." *Scientific Reports* 6, no. 1: 26527. https://doi.org/10.1038/srep26527.

Lynch, G. T. F., S. M. James, and M. VanDam. 2018. "Pupillary Response and Phenotype in ASD: Latency to Constriction Discriminates ASD From Typically Developing Adolescents." *Autism Research* 11, no. 2: 364–375. https://doi.org/10.1002/aur.1888.

MacDuffie, K. E., A. M. Estes, L. T. Harrington, et al. 2021. "Presymptomatic Detection and Intervention for Autism Spectrum Disorder." *Pediatrics* 147, no. 5: e2020032250. https://doi.org/10.1542/peds.2020-032250.

Maenner, M. J., K. A. Shaw, J. Baio, et al. 2020. "Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years—Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2016." *MMWR Surveillance Summaries* 69, no. 4: 1–12. https://doi.org/10.15585/mmwr.ss6904a1.

Maier, S., L. Tebartz van Elst, D. Beier, et al. 2015. "Increased Hippocampal Volumes in Adults With High Functioning Autism Spectrum Disorder and an IQ>100: A Manual Morphometric Study." *Psychiatry Research* 234, no. 1: 152–155. https://doi.org/10.1016/j.pscychresns.2015.08.002.

Mamashli, F., S. Khan, H. Bharadwaj, et al. 2018. "Maturational Trajectories of Local and Long-Range Functional Connectivity in Autism During Face Processing." *Human Brain Mapping* 39, no. 10: 4094–4104. https://doi.org/10.1002/hbm.24234.

Mamashli, F., N. Kozhemiako, S. Khan, et al. 2021. "Children With Autism Spectrum Disorder Show Altered Functional Connectivity and Abnormal Maturation Trajectories in Response to Inverted Faces." *Autism Research* 14, no. 6: 1101–1114. https://doi.org/10.1002/aur.2497.

Martineau, J., N. Hernandez, L. Hiebel, L. Roché, A. Metzger, and F. Bonnet-Brilhault. 2011. "Can Pupil Size and Pupil Responses During Visual Scanning Contribute to the Diagnosis of Autism Spectrum Disorder in Children?" *Journal of Psychiatric Research* 45, no. 8: 1077–1082. https://doi.org/10.1016/j.jpsychires.2011.01.008.

Mash, L. E., B. Keehn, A. C. Linke, et al. 2020. "Atypical Relationships Between Spontaneous EEG and fMRI Activity in Autism." *Brain Connectivity* 10, no. 1: 18–28. https://doi.org/10.1089/brain.2019.0693.

Matsuzaki, J., M. Ku, M. Dipiero, et al. 2019. "Delayed Auditory Evoked Responses in Autism Spectrum Disorder Across the Life Span." *Developmental Neuroscience* 41, no. 3–4: 223–233. https://doi.org/10.1159/000504960.

McChesney, N., J. L. Barth, J. A. Rumschlag, et al. 2022. "Peripheral Auditory Nerve Impairment in a Mouse Model of Syndromic Autism." bioRxiv. https://doi.org/10.1101/2022.06.02.494499.

McKinnon, C. J., A. T. Eggebrecht, A. Todorov, et al. 2019. "Restricted and Repetitive Behavior and Brain Functional Connectivity in Infants at Risk for Developing Autism Spectrum Disorder." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 4, no. 1: 50–61. https://doi.org/10.1016/j.bpsc.2018.09.008.

McPartland, J. C., J. Wu, C. A. Bailey, L. C. Mayes, R. T. Schultz, and A. Klin. 2011. "Atypical Neural Specialization for Social Percepts in Autism Spectrum Disorder." *Social Neuroscience* 6, no. 5–6: 436–451. https://doi.org/10.1080/17470919.2011.586880.

Messina, A., V. A. Sovrano, G. Baratti, et al. 2024. "Valproic Acid Exposure Affects Social Visual Lateralization and Asymmetric Gene

Expression in Zebrafish Larvae." *Scientific Reports* 14, no. 1: 4474. https://doi.org/10.1038/s41598-024-54356-7.

Mignot, C., C. Von Stülpnagel, C. Nava, et al. 2016. "Genetic and Neurodevelopmental Spectrum of SYNGAP1-Associated Intellectual Disability and Epilepsy." *Journal of Medical Genetics* 53, no. 8: 511–522.

Moore, S. J., P. Turnpenny, A. Quinn, et al. 2000. "A Clinical Study of 57 Children With Fetal Anticonvulsant Syndromes." *Journal of Medical Genetics* 37, no. 7: 489–497.

Moyses-Oliveira, M., R. Yadav, S. Erdin, and M. E. Talkowski. 2020. "New Gene Discoveries Highlight Functional Convergence in Autism and Related Neurodevelopmental Disorders." *Current Opinion in Genetics & Development* 65: 195–206.

Mustafa, M. M. E. 2024. "Future Guides for Biomarkers for Autism Spectrum Disorders." *Hail Journal of Health Sciences* 6, no. 2: 85–91.

Nair, A., R. A. Carper, A. E. Abbott, et al. 2015. "Regional Specificity of Aberrant Thalamocortical Connectivity in Autism." *Human Brain Mapping* 36, no. 11: 4497–4511. https://doi.org/10.1002/hbm.22938.

Nair, A., R. Jalal, J. Liu, et al. 2021. "Altered Thalamocortical Connectivity in 6-Week-Old Infants at High Familial Risk for Autism Spectrum Disorder." *Cerebral Cortex* 31, no. 9: 4191–4205. https://doi.org/10.1093/cercor/bhab078.

Nair, A., J. M. Treiber, D. K. Shukla, P. Shih, and R. A. Müller. 2013. "Impaired Thalamocortical Connectivity in Autism Spectrum Disorder: A Study of Functional and Anatomical Connectivity." *Brain* 136, no. Pt 6: 1942–1955. https://doi.org/10.1093/brain/awt079.

Neuhaus, E., R. Bernier, and T. P. Beauchaine. 2014. "Brief Report: Social Skills, Internalizing and Externalizing Symptoms, and Respiratory Sinus Arrhythmia in Autism." *Journal of Autism and Developmental Disorders* 44, no. 3: 730–737. https://doi.org/10.1007/s10803-013-1923-7.

Neuhaus, E., M. Santhosh, A. Kresse, et al. 2023. "Frontal EEG Alpha Asymmetry in Youth With Autism: Sex Differences and Social-Emotional Correlates." *Autism Research* 16, no. 12: 2364–2377. https://doi.org/10.1002/aur.3032.

Nordahl, C. W., A. M. Iosif, G. S. Young, et al. 2020. "High Psychopathology Subgroup in Young Children With Autism: Associations With Biological Sex and Amygdala Volume." *Journal of the American Academy of Child and Adolescent Psychiatry* 59, no. 12: 1353–1363.e1352. https://doi.org/10.1016/j.jaac.2019.11.022.

Nordahl, C. W., A. M. Iosif, G. S. Young, et al. 2015. "Sex Differences in the Corpus Callosum in Preschool-Aged Children With Autism Spectrum Disorder." *Molecular Autism* 6: 26. https://doi.org/10.1186/s13229-015-0005-4.

Nordahl, C. W., N. Lange, D. D. Li, et al. 2011. "Brain Enlargement Is Associated With Regression in Preschool-Age Boys With Autism Spectrum Disorders." *Proceedings of the National Academy of Sciences of the United States of America* 108, no. 50: 20195–20200. https://doi.org/10.1073/pnas.1107560108.

Novelli, G., C. Ciccacci, P. Borgiani, M. P. Amati, and E. Abadie. 2008. "Genetic Tests and Genomic Biomarkers: Regulation, Qualification and Validation." *Clinical Cases in Mineral and Bone Metabolism* 5, no. 2: 149.

Nuske, H. J., G. Vivanti, and C. Dissanayake. 2014. "Brief Report: Evidence for Normative Resting-State Physiology in Autism." *Journal of Autism and Developmental Disorders* 44, no. 8: 2057–2063. https://doi.org/10.1007/s10803-014-2068-z.

Nyström, P., T. Gliga, E. Nilsson Jobs, et al. 2018. "Enhanced Pupillary Light Reflex in Infancy Is Associated With Autism Diagnosis in Toddlerhood." *Nature Communications* 9, no. 1: 1678. https://doi.org/10.1038/s41467-018-03985-4.

Nyström, P., G. Gredebäck, S. Bölte, T. Falck-Ytter, and EASE Team. 2015. "Hypersensitive Pupillary Light Reflex in Infants at Risk for Autism." *Molecular Autism* 6, no. 1: 10. https://doi.org/10.1186/s13229-015-0011-6.

Odriozola, P., L. Q. Uddin, C. J. Lynch, J. Kochalka, T. Chen, and V. Menon. 2016. "Insula Response and Connectivity During Social and Non-Social Attention in Children With Autism." *Social Cognitive and Affective Neuroscience* 11, no. 3: 433–444. https://doi.org/10.1093/scan/nsv126.

Ohta, H., C. W. Nordahl, A. M. Iosif, A. Lee, S. Rogers, and D. G. Amaral. 2016. "Increased Surface Area, but Not Cortical Thickness, in a Subset of Young Boys With Autism Spectrum Disorder." *Autism Research* 9, no. 2: 232–248. https://doi.org/10.1002/aur.1520.

Okada, N. J., J. Liu, T. Tsang, et al. 2022. "Atypical Cerebellar Functional Connectivity at 9 Months of Age Predicts Delayed Socio-Communicative Profiles in Infants at High and Low Risk for Autism." *Journal of Child Psychology and Psychiatry* 63, no. 9: 1002–1016. https://doi.org/10.1111/jcpp.13555.

Okada, Y., M. Hämäläinen, K. Pratt, et al. 2016. "BabyMEG: A Whole-Head Pediatric Magnetoencephalography System for Human Brain Development Research." *Review of Scientific Instruments* 87, no. 9: 094301. https://doi.org/10.1063/1.4962020.

Oldehinkel, M., M. Mennes, A. Marquand, et al. 2019. "Altered Connectivity Between Cerebellum, Visual, and Sensory-Motor Networks in Autism Spectrum Disorder: Results From the EU-AIMS Longitudinal European Autism Project." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 4, no. 3: 260–270. https://doi.org/10.1016/j.bpsc.2018.11.010.

Ono, Y., K. Kudoh, T. Ikeda, et al. 2020. "Auditory Steady-State Response at 20 Hz and 40 Hz in Young Typically Developing Children and Children With Autism Spectrum Disorder." *Psychiatry and Clinical Neurosciences* 74, no. 6: 354–361. https://doi.org/10.1111/pcn.12998.

Orekhova, E. V., M. Elsabbagh, E. J. Jones, G. Dawson, T. Charman, and M. H. Johnson. 2014. "EEG Hyper-Connectivity in High-Risk Infants Is Associated With Later Autism." *Journal of Neurodevelopmental Disorders* 6, no. 1: 40. https://doi.org/10.1186/1866-1955-6-40.

O'Roak, B. J., L. Vives, S. Girirajan, et al. 2012. "Sporadic Autism Exomes Reveal a Highly Interconnected Protein Network of De Novo Mutations." *Nature* 485: 246–250.

Ortug, A., Y. Guo, H. A. Feldman, et al. 2024. "Autism-Associated Brain Differences Can Be Observed In Utero Using MRI." *Cerebral Cortex* 34, no. 4: bhae117. https://doi.org/10.1093/cercor/bhae117.

Parellada, M., Á. Andreu-Bernabeu, M. Burdeus, et al. 2023. "In Search of Biomarkers to Guide Interventions in Autism Spectrum Disorder: A Systematic Review." *American Journal of Psychiatry* 180, no. 1: 23–40.

Parellada, M., L. Pina-Camacho, C. Moreno, et al. 2017. "Insular Pathology in Young People With High-Functioning Autism and First-Episode Psychosis." *Psychological Medicine* 47, no. 14: 2472–2482. https://doi.org/10.1017/s0033291717000988.

Piazza, C., C. Dondena, E. M. Riboldi, V. Riva, and C. Cantiani. 2023. "Baseline EEG in the First Year of Life: Preliminary Insights Into the Development of Autism Spectrum Disorder and Language Impairments." *iScience* 26, no. 7: 106987. https://doi.org/10.1016/j.isci.2023.106987.

Pickler, R., S. Sealschott, M. Moore, et al. 2017. "Using Functional Connectivity Magnetic Resonance Imaging to Measure Brain Connectivity in Preterm Infants." *Nursing Research* 66, no. 6: 490–495. https://doi.org/10.1097/nnr.0000000000000241.

Pierce, K., S. Marinero, R. Hazin, B. McKenna, C. C. Barnes, and A. Malige. 2016. "Eye Tracking Reveals Abnormal Visual Preference for Geometric Images as an Early Biomarker of an Autism Spectrum Disorder Subtype Associated With Increased Symptom Severity." *Biological Psychiatry* 79, no. 8: 657–666. https://doi.org/10.1016/j.biopsych.2015.03.032.

Pinto, D., E. Delaby, D. Merico, et al. 2014. "Convergence of Genes and Cellular Pathways Dysregulated in Autism Spectrum Disorders." *American Journal of Human Genetics* 94, no. 5: 677–694.

Port, R. G., J. C. Edgar, M. Ku, et al. 2016. "Maturation of Auditory Neural Processes in Autism Spectrum Disorder—A Longitudinal MEG Study." *NeuroImage: Clinical* 11: 566–577. https://doi.org/10.1016/j.nicl.2016.03.021.

Port, R. G., W. Gaetz, L. Bloy, et al. 2017. "Exploring the Relationship Between Cortical GABA Concentrations, Auditory Gamma-Band Responses and Development in ASD: Evidence for an Altered Maturational Trajectory in ASD." *Autism Research* 10, no. 4: 593–607. https://doi.org/10.1002/aur.1686.

Pote, I., S. Wang, V. Sethna, et al. 2019. "Familial Risk of Autism Alters Subcortical and Cerebellar Brain Anatomy in Infants and Predicts the Emergence of Repetitive Behaviors in Early Childhood." *Autism Research* 12, no. 4: 614–627. https://doi.org/10.1002/aur.2083.

Prigge, M. B. D., N. Lange, E. D. Bigler, et al. 2021. "A 16-Year Study of Longitudinal Volumetric Brain Development in Males With Autism." *NeuroImage* 236: 118067. https://doi.org/10.1016/j.neuroimage.2021.118067.

Pusil, S., A. Laguna, B. Chino, J. A. Zegarra, and S. Orlandi. 2025. "Early Identification of Autism Using Cry Analysis: A Systematic Review and Meta-Analysis of Retrospective and Prospective Studies." *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-025-06757-4.

Quesnel-Vallières, M., R. J. Weatheritt, S. P. Cordes, and B. J. Blencowe. 2019. "Autism Spectrum Disorder: Insights Into Convergent Mechanisms From Transcriptomics." *Nature Reviews Genetics* 20, no. 1: 51–63.

Qureshi, A. Y., S. Mueller, A. Z. Snyder, et al. 2014. "Opposing Brain Differences in 16p11.2 Deletion and Duplication Carriers." *Journal of Neuroscience* 34, no. 34: 11199–11211. https://doi.org/10.1523/jneurosci.1366-14.2014.

Regev, O., A. Hadar, G. Meiri, et al. 2022. "Association Between Ultrasonography Foetal Anomalies and Autism Spectrum Disorder." *Brain* 145, no. 12: 4519–4530. https://doi.org/10.1093/brain/awac008.

Regev, O., A. Shil, T. Bronshtein, et al. 2024. "Association Between Rare, Genetic Variants Linked to Autism and Ultrasonography Fetal Anomalies in Children With Autism Spectrum Disorder." *Journal of Neurodevelopmental Disorders* 16, no. 1: 55. https://doi.org/10.1186/s11689-024-09573-6.

Remington, A., J. Swettenham, R. Campbell, and M. Coleman. 2009. "Selective Attention and Perceptual Load in Autism Spectrum Disorder." *Psychological Science* 20, no. 11: 1388–1393. https://doi.org/10.1111/j.1467-9280.2009.02454.x.

Righi, G., A. L. Tierney, H. Tager-Flusberg, and C. A. Nelson. 2014. "Functional Connectivity in the First Year of Life in Infants at Risk for Autism Spectrum Disorder: An EEG Study." *PLoS One* 9, no. 8: e105176. https://doi.org/10.1371/journal.pone.0105176.

Roberts, T. P., D. N. Paulson, E. Hirschkoff, et al. 2014. "Artemis 123: Development of a Whole-Head Infant and Young Child MEG System." *Frontiers in Human Neuroscience* 8: 99. https://doi.org/10.3389/fnhum.2014.00099.

Roberts, T. P. L., L. Bloy, M. Ku, et al. 2020. "A Multimodal Study of the Contributions of Conduction Velocity to the Auditory Evoked Neuromagnetic Response: Anomalies in Autism Spectrum Disorder." *Autism Research* 13, no. 10: 1730–1745. https://doi.org/10.1002/aur.2369.

Roberts, T. P. L., J. Matsuzaki, L. Blaskey, et al. 2019. "Delayed M50/M100 Evoked Response Component Latency in Minimally Verbal/Nonverbal Children Who Have Autism Spectrum Disorder." *Molecular Autism* 10: 34. https://doi.org/10.1186/s13229-019-0283-3.

Safar, K., M. M. Vandewouw, and M. J. Taylor. 2021. "Atypical Development of Emotional Face Processing Networks in Autism Spectrum Disorder From Childhood Through to Adulthood." *Developmental Cognitive Neuroscience* 51: 101003. https://doi.org/10.1016/j.dcn.2021.101003.

Safar, K., S. M. Wong, R. C. Leung, B. T. Dunkley, and M. J. Taylor. 2018. "Increased Functional Connectivity During Emotional Face Processing in Children With Autism Spectrum Disorder." *Frontiers in Human Neuroscience* 12: 408. https://doi.org/10.3389/fnhum.2018.00408.

Samoylov, I., G. Arcara, I. Buyanova, et al. 2024. "Altered Neural Synchronization in Response to 2 Hz Amplitude-Modulated Tones in the Auditory Cortex of Children With Autism Spectrum Disorder: An MEG Study." *International Journal of Psychophysiology* 203: 112405. https://doi.org/10.1016/j.ijpsycho.2024.112405.

Sanders, S. J., M. T. Murtha, A. R. Gupta, et al. 2012. "De Novo Mutations Revealed by Whole-Exome Sequencing Are Strongly Associated With Autism." *Nature* 485: 237–241.

Sanders, S. J., H. Xin, A. J. Willsey, et al. 2015. "Insights Into Autism Spectrum Disorder Genomic Architecture and Biology From 71 Risk Loci." *Neuron* 87: 1215–1233.

Sandin, S., P. Lichtenstein, R. Kuja-Halkola, C. Hultman, H. Larsson, and A. J. J. Reichenberg. 2017. "The Heritability of Autism Spectrum Disorder." *JAMA* 318, no. 12: 1182–1184. https://doi.org/10.1001/jama.2017.12141.

Satterstrom, F. K., J. A. Kosmicki, J. Wang, et al. 2020. "Large-Scale Exome Sequencing Study Implicates Both Developmental and Functional Changes in the Neurobiology of Autism." *Cell* 180: 568–584.

Satterstrom, F. K., J. A. Kosmicki, J. Wang, et al. 2018. "Novel Genes for Autism Implicate Both Excitatory and Inhibitory Cell Lineages in Risk." bioRxiv. https://doi.org/10.1016/j.cell.2019.12.036.

Sauer, C., C. Montag, C. Wörner, P. Kirsch, and M. Reuter. 2012. "Effects of a Common Variant in the CD38 Gene on Social Processing in an Oxytocin Challenge Study: Possible Links to Autism." *Neuropsychopharmacology* 37: 1474–1482. https://doi.org/10.1038/npp.2011.333.

Schaefer, G. B., N. J. Mendelsohn, and P. Professional. 2013. "Clinical Genetics Evaluation in Identifying the Etiology of Autism Spectrum Disorders: 2013 Guideline Revisions." *Genetics in Medicine* 15, no. 5: 399–407. https://doi.org/10.1038/gim.2013.32.

Scheinost, D., J. Chang, C. Lacadie, et al. 2022. "Hypoconnectivity Between Anterior Insula and Amygdala Associates With Future Vulnerabilities in Social Development in a Neurodiverse Sample of Neonates." *Scientific Reports* 12, no. 1: 16230. https://doi.org/10.1038/s41598-022-20617-6.

Schielen, S. J. C., J. Pilmeyer, A. P. Aldenkamp, and S. Zinger. 2024. "The Diagnosis of ASD With MRI: A Systematic Review and Meta-Analysis." *Translational Psychiatry* 14, no. 1: 318. https://doi.org/10.1038/s41398-024-03024-5.

Sestan, N., and M. W. State. 2018. "Lost in Translation: Traversing the Complex Path From Genomics to Therapeutics in Autism Spectrum Disorder." *Neuron* 100: 406–423.

Seymour, R. A., G. Rippon, G. Gooding-Williams, P. F. Sowman, and K. Kessler. 2020. "Reduced Auditory Steady State Responses in Autism Spectrum Disorder." *Molecular Autism* 11, no. 1: 56. https://doi.org/10.1186/s13229-020-00357-y.

Shen, G., H. L. Green, R. E. Franzen, et al. 2024. "Resting-State Activity in Children: Replicating and Extending Findings of Early Maturation of Alpha Rhythms in Autism Spectrum Disorder." *Journal of Autism and Developmental Disorders* 54, no. 5: 1961–1976. https://doi.org/10.1007/s10803-023-05926-7.

Shen, L., X. Liu, H. Zhang, J. Lin, C. Feng, and J. Iqbal. 2020. "Biomarkers in Autism Spectrum Disorders: Current Progress." *Clinica Chimica Acta* 502: 41–54. https://doi.org/10.1016/j.cca.2019.12.009.

Shen, M. D., S. H. Kim, R. C. McKinstry, et al. 2017. "Increased Extra-Axial Cerebrospinal Fluid in High-Risk Infants Who Later Develop Autism." *Biological Psychiatry* 82, no. 3: 186–193. https://doi.org/10.1016/j.biopsych.2017.02.1095.

Shen, M. D., D. D. Li, C. L. Keown, et al. 2016. "Functional Connectivity of the Amygdala Is Disrupted in Preschool-Aged Children With Autism Spectrum Disorder." *Journal of the American Academy of Child and Adolescent Psychiatry* 55, no. 9: 817–824. https://doi.org/10.1016/j.jaac.2016.05.020.

Shen, M. D., C. W. Nordahl, D. D. Li, et al. 2018. "Extra-Axial Cerebrospinal Fluid in High-Risk and Normal-Risk Children With Autism Aged 2–4 Years: A Case-Control Study." *Lancet Psychiatry* 5, no. 11: 895–904. https://doi.org/10.1016/s2215-0366(18)30294-3.

Shen, M. D., C. W. Nordahl, G. S. Young, et al. 2013. "Early Brain Enlargement and Elevated Extra-Axial Fluid in Infants Who Develop Autism Spectrum Disorder." *Brain* 136, no. Pt 9: 2825–2835. https://doi.org/10.1093/brain/awt166.

Shen, M. D., M. R. Swanson, J. J. Wolff, et al. 2022. "Subcortical Brain Development in Autism and Fragile X Syndrome: Evidence for Dynamic, Age- and Disorder-Specific Trajectories in Infancy." *American Journal of Psychiatry* 179, no. 8: 562–572. https://doi.org/10.1176/appi.ajp.21090896.

Shiohama, T., A. Ortug, J. L. A. Warren, et al. 2022. "Small Nucleus Accumbens and Large Cerebral Ventricles in Infants and Toddlers Prior to Receiving Diagnoses of Autism Spectrum Disorder." *Cerebral Cortex* 32, no. 6: 1200–1211. https://doi.org/10.1093/cercor/bhab283.

Shiota, Y., D. Soma, T. Hirosawa, et al. 2022. "Alterations in Brain Networks in Children With Sub-Threshold Autism Spectrum Disorder: A Magnetoencephalography Study." *Frontiers in Psychiatry* 13: 959763. https://doi.org/10.3389/fpsyt.2022.959763.

Skalny, A. V., A. L. Mazaletskaya, O. P. Ajsuvakova, et al. 2020. "Magnesium Status in Children With Attention-Deficit/Hyperactivity Disorder and/or Autism Spectrum Disorder." *Journal of the Korean Academy of Child and Adolescent Psychiatry* 31, no. 1: 41–45.

Skalny, A. V., M. G. Skalnaya, G. Bjørklund, V. A. Gritsenko, J. Aaseth, and A. A. Tinkov. 2018. "Selenium and Autism Spectrum Disorder." In *Selenium*, 193–210. Academic Press.

Smith, R. E. W., J. A. Avery, G. L. Wallace, L. Kenworthy, S. J. Gotts, and A. Martin. 2019. "Sex Differences in Resting-State Functional Connectivity of the Cerebellum in Autism Spectrum Disorder." *Frontiers in Human Neuroscience* 13: 104. https://doi.org/10.3389/fnhum.2019.00104.

Solomon, M., J. H. Yoon, J. D. Ragland, et al. 2014. "The Development of the Neural Substrates of Cognitive Control in Adolescents With Autism Spectrum Disorders." *Biological Psychiatry* 76, no. 5: 412–421. https://doi.org/10.1016/j.biopsych.2013.08.036.

Solso, S., R. Xu, J. Proudfoot, et al. 2016. "Diffusion Tensor Imaging Provides Evidence of Possible Axonal Overconnectivity in Frontal Lobes in Autism Spectrum Disorder Toddlers." *Biological Psychiatry* 79, no. 8: 676–684. https://doi.org/10.1016/j.biopsych.2015.06.029.

Song, S. K., S. W. Sun, M. J. Ramsbottom, C. Chang, J. Russell, and A. H. Cross. 2002. "Dysmyelination Revealed Through MRI as Increased Radial (But Unchanged Axial) Diffusion of Water." *NeuroImage* 17, no. 3: 1429–1436. https://doi.org/10.1006/nimg.2002.1267.

Song, S. K., J. Yoshino, T. Q. Le, et al. 2005. "Demyelination Increases Radial Diffusivity in Corpus Callosum of Mouse Brain." *NeuroImage* 26, no. 1: 132–140. https://doi.org/10.1016/j.neuroimage.2005.01.028.

State, M. W., and N. Sestan. 2012. "The Emerging Biology of Autism Spectrum Disorders." *Science* 337: 1301–1303.

Stoodley, C. J., A. M. D'Mello, J. Ellegood, et al. 2017. "Altered Cerebellar Connectivity in Autism and Cerebellar-Mediated Rescue of Autism-Related Behaviors in Mice." *Nature Neuroscience* 20, no. 12: 1744–1751. https://doi.org/10.1038/s41593-017-0004-1.

Stroganova, T. A., K. S. Komarov, O. V. Sysoeva, et al. 2020. "Left Hemispheric Deficit in the Sustained Neuromagnetic Response to Periodic Click Trains in Children With ASD." *Molecular Autism* 11, no. 1: 100. https://doi.org/10.1186/s13229-020-00408-4.

Studholme, C., C. D. Kroenke, and M. Dighe. 2020. "Motion Corrected MRI Differentiates Male and Female Human Brain Growth Trajectories From Mid-Gestation." *Nature Communications* 11, no. 1: 3038. https://doi.org/10.1038/s41467-020-16763-y.

Sullivan, J. M., S. De Rubeis, and A. Schaefer. 2019. "Convergence of Spectrums: Neuronal Gene Network States in Autism Spectrum Disorder." *Current Opinion in Neurobiology* 59: 102–111.

Supekar, K., S. Ryali, P. Mistry, and V. Menon. 2021. "Aberrant Dynamics of Cognitive Control and Motor Circuits Predict Distinct Restricted and Repetitive Behaviors in Children With Autism." *Nature Communications* 12, no. 1: 3537. https://doi.org/10.1038/s41467-021-23822-5.

Supekar, K., L. Q. Uddin, A. Khouzam, et al. 2013. "Brain Hyperconnectivity in Children With Autism and Its Links to Social Deficits." *Cell Reports* 5, no. 3: 738–747. https://doi.org/10.1016/j.celrep.2013.10.001.

Taddei, M., P. Cuesta, S. Annunziata, et al. 2024. "Correlation Between Autistic Traits and Brain Functional Connectivity in Preschoolers With Autism Spectrum Disorder: A Resting State MEG Study." *Neurological Sciences* 45, no. 9: 4549–4561. https://doi.org/10.1007/s10072-024-07528-2.

Tammimies, K., C. R. Marshall, and S. Walker. 2015. "Molecular Diagnostic Yield of Chromosomal Microarray Analysis and Whole-Exome Sequencing in Children With Autism Spectrum Disorder." *JAMA* 314, no. 9: 895–903. https://doi.org/10.1001/jama.2015.10078.

Thomas, R. H., L. M. Zhang, G. L. Carvill, et al. 2015. "CHD2 Myoclonic Encephalopathy Is Frequently Associated With Self-Induced Seizures." *Neurology* 84, no. 9: 951–958.

Thomason, M., A. Austin, and C. Hendrix. 2021. "Fetal Amygdala Functional Connectivity Relates to Autism Spectrum Disorder Traits at Age 3." *Biological Psychiatry* 89, no. 9: S29. https://doi.org/10.1016/j.biopsych.2021.02.091.

Tick, B., P. Bolton, F. Happe, M. Rutter, and F. Rijsdijk. 2016. "Heritability of Autism Spectrum Disorders: A Meta-Analysis of Twin Studies." *Journal of Child Psychology and Psychiatry* 57: 585–595.

Tierney, A. L., L. Gabard-Durnam, V. Vogel-Farley, H. Tager-Flusberg, and C. A. Nelson. 2012. "Developmental Trajectories of Resting EEG Power: An Endophenotype of Autism Spectrum Disorder." *PLoS One* 7, no. 6: e39127. https://doi.org/10.1371/journal.pone.0039127.

Tilwani, D., J. Bradshaw, A. Sheth, and C. O'Reilly. 2023. "ECG Recordings as Predictors of Very Early Autism Likelihood: A Machine Learning Approach." *Bioengineering* 10, no. 7: 827. https://doi.org/10.3390/bioengineering10070827.

Tioleco, N., A. E. Silberman, K. Stratigos, et al. 2021. "Prenatal Maternal Infection and Risk for Autism in Offspring: A Meta-Analysis." *Autism Research* 14, no. 6: 1296–1316.

Tomasi, D., and N. D. Volkow. 2019. "Reduced Local and Increased Long-Range Functional Connectivity of the Thalamus in Autism Spectrum Disorder." *Cerebral Cortex* 29, no. 2: 573–585. https://doi.org/10.1093/cercor/bhx340.

Tomescu, M. I., T. A. Rihs, V. Rochas, et al. 2018. "From Swing to Cane: Sex Differences of EEG Resting-State Temporal Patterns During Maturation and Aging." *Developmental Cognitive Neuroscience* 31: 58–66. https://doi.org/10.1016/j.dcn.2018.04.011.

Tordjman, S., E. Somogyi, N. Coulon, et al. 2014. "Gene × Environment Interactions in Autism Spectrum Disorders: Role of Epigenetic Mechanisms." *Frontiers in Psychiatry* 5: 53.

Tran, X. A., N. McDonald, A. Dickinson, et al. 2021. "Functional Connectivity During Language Processing in 3-Month-Old Infants

at Familial Risk for Autism Spectrum Disorder." *European Journal of Neuroscience* 53, no. 5: 1621–1637. https://doi.org/10.1111/ejn.15005.

Tsai, P. T., S. Rudolph, C. Guo, et al. 2018. "Sensitive Periods for Cerebellar-Mediated Autistic-Like Behaviors." *Cell Reports* 25, no. 2: 357–367.e354. https://doi.org/10.1016/j.celrep.2018.09.039.

Tsang, T., S. A. Green, J. Liu, et al. 2024. "Salience Network Connectivity Is Altered in 6-Week-Old Infants at Heightened Likelihood for Developing Autism." *Communications Biology* 7, no. 1: 485. https://doi.org/10.1038/s42003-024-06016-9.

Uddin, L. Q., K. Supekar, C. J. Lynch, et al. 2015. "Brain State Differentiation and Behavioral Inflexibility in Autism." *Cerebral Cortex* 25, no. 12: 4740–4747. https://doi.org/10.1093/cercor/bhu161.

Uddin, L. Q., K. Supekar, C. J. Lynch, et al. 2013. "Salience Network-Based Classification and Prediction of Symptom Severity in Children With Autism." *JAMA Psychiatry* 70, no. 8: 869–879. https://doi.org/10.1001/jamapsychiatry.2013.104.

Urraca, N., J. Cleary, V. Brewer, et al. 2013. "The Interstitial Duplication 15q11.2-q13 Syndrome Includes Autism, Mild Facial Anomalies and a Characteristic EEG Signature." *Autism Research* 6, no. 4: 268–279. https://doi.org/10.1002/aur.1284.

Van Dijck, A., A. T. V. V. Silfhout, E. Cappuyns, et al. 2019. "Clinical Presentation of a Complex Neurodevelopmental Disorder Caused by Mutations in ADNP." *Biological Psychiatry* 85: 287–297. https://doi.org/10.1016/j.biopsych.2018.02.1173.

Vanaken, G.-J., I. Noens, J. Steyaert, L. van Esch, P. Warreyn, and K. Hens. 2023. "The Earlier, the Better? An In-Depth Interview Study on the Ethics of Early Detection With Parents of Children at an Elevated Likelihood for Autism." *Journal of Autism and Developmental Disorders* 54, no. 11: 4130–4144. https://doi.org/10.1007/s10803-023-06139-8.

Vasconcelos, C., I. S. Perry, C. Gottfried, R. Riesgo, and K. Castro. 2025. "Folic Acid and Autism: Updated Evidence." *Nutritional Neuroscience* 28, no. 3: 273–307.

Vasko, A., and S. A. Schrier Vergano. 2022. "Language Impairments in Individuals With Coffin-Siris Syndrome." *Frontiers in Neuroscience* 15: 802583.

Virues-Ortega, J., N. S. McKay, J. C. McCormack, N. Lopez, R. Liu, and I. Kirk. 2022. "A Callosal Biomarker of Behavioral Intervention Outcomes for Autism Spectrum Disorder? A Case-Control Feasibility Study With Diffusion Tensor Imaging." *PLoS One* 17, no. 2: e0262563. https://doi.org/10.1371/journal.pone.0262563.

Vogel Ciernia, A., and J. LaSalle. 2016. "The Landscape of DNA Methylation Amid a Perfect Storm of Autism Aetiologies." *Nature Reviews Neuroscience* 17, no. 7: 411–423.

Vyas, Y., K. Lee, Y. Jung, and J. M. Montgomery. 2020. "Influence of Maternal Zinc Supplementation on the Development of Autism-Associated Behavioural and Synaptic Deficits in Offspring Shank3-Knockout Mice." *Molecular Brain* 13: 1–18.

Wagner, L., M. Banchik, N. J. Okada, et al. 2023. "Associations Between Thalamocortical Functional Connectivity and Sensory Over-Responsivity in Infants at High Likelihood for ASD." *Cerebral Cortex* 33, no. 12: 8075–8086. https://doi.org/10.1093/cercor/bhad100.

Walker, C. K., P. Krakowiak, A. Baker, R. L. Hansen, S. Ozonoff, and I. Hertz-Picciotto. 2015. "Preeclampsia, Placental Insufficiency, and Autism Spectrum Disorder or Developmental Delay." *JAMA Pediatrics* 169, no. 2: 154–162.

Walsh, J. J., D. J. Christoffel, B. D. Heifets, et al. 2018. "5-HT Release in Nucleus Accumbens Rescues Social Deficits in Mouse Autism Model." *Nature* 560, no. 7720: 589–594. https://doi.org/10.1038/s41586-018-0416-4.

Wang, Z., R. Ding, and J. Wang. 2020. "The Association Between Vitamin D Status and Autism Spectrum Disorder (ASD): A Systematic Review and Meta-Analysis." *Nutrients* 13, no. 1: 86.

Washington, A. M., A. H. Mercer, C. A. Burrows, et al. 2024. "Parent Attitudes Towards Predictive Testing for Autism in the First Year of Life." *Journal of Neurodevelopmental Disorders* 16, no. 1: 47. https://doi.org/10.1186/s11689-024-09561-w.

Weiner, D., E. Wigdor, and S. Ripke. 2017. "Polygenic Transmission Disequilibrium Confirms That Common and Rare Variation Act Additively to Create Risk for Autism Spectrum Disorders." *Nature Genetics* 49, no. 7: 978–985. https://doi.org/10.1038/ng.3863.

Weinstein, M., L. Ben-Sira, Y. Levy, et al. 2011. "Abnormal White Matter Integrity in Young Children With Autism." *Human Brain Mapping* 32, no. 4: 534–543. https://doi.org/10.1002/hbm.21042.

Wen, T. H., A. Cheng, C. Andreason, et al. 2022. "Large Scale Validation of an Early-Age Eye-Tracking Biomarker of an Autism Spectrum Disorder Subtype." *Scientific Reports* 12, no. 1: 4253. https://doi.org/10.1038/s41598-022-08102-6.

Williamson, I. O., J. T. Elison, J. J. Wolff, and C. F. Runge. 2020. "Cost-Effectiveness of MRI-Based Identification of Presymptomatic Autism in a High-Risk Population." *Frontiers in Psychiatry* 11: 60. https://doi.org/10.3389/fpsyt.2020.00060.

Willsey, H. R., A. J. Willsey, B. Wang, and M. W. State. 2022. "Genomics, Convergent Neuroscience and Progress in Understanding Autism Spectrum Disorder." *Nature Reviews Neuroscience* 23, no. 6: 323–341.

Wiltrout, K., E. Brimble, and A. Poduri. 2024. "Comprehensive Phenotypes of Patients With SYNGAP1-Related Disorder Reveals High Rates of Epilepsy and Autism." *Epilepsia* 65, no. 5: 1428–1438.

Wolff, J. J., G. Gerig, J. D. Lewis, et al. 2015. "Altered Corpus Callosum Morphology Associated With Autism Over the First 2 Years of Life." *Brain* 138, no. Pt 7: 2046–2058. https://doi.org/10.1093/brain/awv118.

Wolff, J. J., H. Gu, G. Gerig, et al. 2012. "Differences in White Matter Fiber Tract Development Present From 6 to 24 Months in Infants With Autism." *American Journal of Psychiatry* 169, no. 6: 589–600. https://doi.org/10.1176/appi.ajp.2011.11091447.

Wolff, J. J., and J. Piven. 2021. "Predicting Autism in Infancy." *Journal of the American Academy of Child & Adolescent Psychiatry* 60, no. 8: 958–967. https://doi.org/10.1016/j.jaac.2020.07.910.

Wolff, J. J., M. R. Swanson, J. T. Elison, et al. 2017. "Neural Circuitry at Age 6 Months Associated With Later Repetitive Behavior and Sensory Responsiveness in Autism." *Molecular Autism* 8, no. 1: 8. https://doi.org/10.1186/s13229-017-0126-z.

Wood, E. T., K. K. Cummings, J. Jung, et al. 2021. "Sensory Over-Responsivity Is Related to GABAergic Inhibition in Thalamocortical Circuits." *Translational Psychiatry* 11, no. 1: 39. https://doi.org/10.1038/s41398-020-01154-0.

Woodward, N. D., M. Giraldo-Chica, B. Rogers, and C. J. Cascio. 2017. "Thalamocortical Dysconnectivity in Autism Spectrum Disorder: An Analysis of the Autism Brain Imaging Data Exchange." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 2, no. 1: 76–84. https://doi.org/10.1016/j.bpsc.2016.09.002.

Wright, B., B. Alderson-Day, G. Prendergast, et al. 2012. "Gamma Activation in Young People With Autism Spectrum Disorders and Typically-Developing Controls When Viewing Emotions on Faces." *PLoS One* 7, no. 7: e41326. https://doi.org/10.1371/journal.pone.0041326.

Wu, H., C. M. Eckhardt, and A. A. Baccarelli. 2023. "Molecular Mechanisms of Environmental Exposures and Human Disease." *Nature Reviews Genetics* 24, no. 5: 332–344.

Wulffaert, J., I. A. Van Berckelaer-Onnes, and E. M. Scholte. 2009. "Autistic Disorder Symptoms in Rett Syndrome." *Autism* 13, no. 6: 567–581. https://doi.org/10.1177/1362361309338184.

Xiao, Z., T. Qiu, X. Ke, et al. 2014. "Autism Spectrum Disorder as Early Neurodevelopmental Disorder: Evidence From the Brain Imaging Abnormalities in 2-3 Years Old Toddlers." *Journal of Autism and*

Developmental Disorders 44, no. 7: 1633–1640. https://doi.org/10.1007/s10803-014-2033-x.

Xie, L., H. Kang, Q. Xu, et al. 2013. "Sleep Drives Metabolite Clearance From the Adult Brain." *Science* 342, no. 6156: 373–377. https://doi.org/10.1126/science.1241224.

Xu, N., X. Li, and Y. Zhong. 2015. "Inflammatory Cytokines: Potential Biomarkers of Immunologic Dysfunction in Autism Spectrum Disorders." *Mediators of Inflammation* 2015, no. 1: 531518.

Yamasue, H., T. Okada, T. Munesue, et al. 2020. "Effect of Intranasal Oxytocin on the Core Social Symptoms of Autism Spectrum Disorder: A Randomized Clinical Trial." *Molecular Psychiatry* 25, no. 8: 1849–1858. https://doi.org/10.1038/s41380-018-0097-2.

Yenkoyan, K., M. Mkhitaryan, and G. Bjørklund. 2024. "Environmental Risk Factors in Autism Spectrum Disorder: A Narrative Review." *Current Medicinal Chemistry* 31, no. 17: 2345–2360.

Ypma, R. J., R. L. Moseley, R. J. Holt, et al. 2016. "Default Mode Hypoconnectivity Underlies a Sex-Related Autism Spectrum." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* 1, no. 4: 364–371. https://doi.org/10.1016/j.bpsc.2016.04.006.

Zeidan, J., E. Fombonne, J. Scorah, et al. 2022. "Global Prevalence of Autism: A Systematic Review Update." *Autism Research* 15, no. 5: 778–790. https://doi.org/10.1002/aur.2696.

Zerbo, O., C. Yoshida, E. P. Gunderson, K. Dorward, and L. A. Croen. 2015. "Interpregnancy Interval and Risk of Autism Spectrum Disorders." *Pediatrics* 136, no. 4: 651–657.

Zhang, X., M. Liang, W. Qin, B. Wan, C. Yu, and D. Ming. 2020. "Gender Differences Are Encoded Differently in the Structure and Function of the Human Brain Revealed by Multimodal MRI." *Frontiers in Human Neuroscience* 14: 244. https://doi.org/10.3389/fnhum.2020.00244.

Zhang, Y., B. Qin, L. Wang, et al. 2023. "Corpus Callosum Volumes in Children With Autism Spectrum Disorders: Sex-Associated Differences." *Journal of Autism and Developmental Disorders* 53, no. 6: 2421–2429. https://doi.org/10.1007/s10803-022-05538-7.

Zhao, H., H. Zhang, W. Luo, Y. Jiang, and J. Gao. 2021. "Association of Peripheral Blood Levels of Cytokines With Autism Spectrum Disorder: A Meta-Analysis." *Frontiers in Psychiatry* 12: 670200.

Zhao, S., Y. Liu, and K. Wei. 2022. "Pupil-Linked Arousal Response Reveals Aberrant Attention Regulation Among Children With Autism Spectrum Disorder." *Journal of Neuroscience* 42, no. 27: 5427–5437. https://doi.org/10.1523/jneurosci.0223-22.2022.

Zhong, C., J. Tessing, B. K. Lee, and K. Lyall. 2020. "Maternal Dietary Factors and the Risk of Autism Spectrum Disorders: A Systematic Review of Existing Evidence." *Autism Research* 13, no. 10: 1634–1658.

Zhou, C., S. Yan, S. Qian, et al. 2019. "Atypical Response Properties of the Auditory Cortex of Awake MECP2-Overexpressing Mice." *Frontiers in Neuroscience* 13: 439. https://doi.org/10.3389/fnins.2019.00439.

Zhou, X., J. Y. Lu, R. D. Darling, et al. 2015. "Behavioral Training Reverses Global Cortical Network Dysfunction Induced by Perinatal Antidepressant Exposure." *Proceedings of the National Academy of Sciences of the United States of America* 112, no. 7: 2233–2238. https://doi.org/10.1073/pnas.1416582111.

Zielinski, B. A., D. S. Andrews, J. K. Lee, et al. 2022. "Sex-Dependent Structure of Socioemotional Salience, Executive Control, and Default Mode Networks in Preschool-Aged Children With Autism." *NeuroImage* 257: 119252. https://doi.org/10.1016/j.neuroimage.2022.119252.

Zöllei, L., J. E. Iglesias, Y. Ou, P. E. Grant, and B. Fischl. 2020. "Infant FreeSurfer: An Automated Segmentation and Surface Extraction Pipeline for T1-Weighted Neuroimaging Data of Infants 0–2 Years." *NeuroImage* 218: 116946. https://doi.org/10.1016/j.neuroimage.2020.116946.

Zuo, C., D. Wang, F. Tao, and Y. Wang. 2019. "Changes in the Development of Subcortical Structures in Autism Spectrum Disorder." *Neuroreport* 30, no. 16: 1062–1067. https://doi.org/10.1097/wnr.0000000000001300.