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Comparing the autism phenotype in children born extremely preterm and children born at term

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Thesis

**COMPARING THE AUTISM PHENOTYPE IN CHILDREN BORN
EXTREMELY PRETERM AND CHILDREN BORN AT TERM**

by

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ABSTRACT

Background and Objective: It has been well established that children born preterm are at an increased risk of developing Autism Spectrum Disorder (ASD), and that risk increases as gestational age decreases. However, there is limited knowledge on how the ASD phenotype in preterm-born children compares to ASD presentation in children born at term. The objective of this study is to compare ASD core symptoms and characteristics commonly associated with ASD in children born extremely preterm (EP) and children born at term.

Methods: Extremely preterm (EP) participants (n=59) from the Extremely Low Gestational Age Newborn (ELGAN) Study who met diagnostic criteria for ASD at approximately 10 years of age were matched with term participants (n=59) from the Simons Simplex Collection (SSC) on age, sex, and nonverbal IQ. Differences in core ASD symptomatology were evaluated using the Autism Diagnostic Interview-Revised (ADI-R), an in-depth parent interview, and the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2), a semi-structured clinical observation assessment. Developmental milestones, anthropometrics, seizure disorder, and psychiatric symptoms were also investigated as associated characteristics of ASD. Analyses excluding multiplex EP individuals and their term matches, as well female-only analyses, were also conducted.

Results: On the ADI-R, the EP group had lower scores (decreased symptom severity) on verbal communication, specifically stereotypic language, and restricted and repetitive behaviors (RRBs). However, no between-group differences were observed with direct observation based on the ADOS-2 assessment. The EP group was more likely to have delayed speech milestones, lower height, weight, and head circumference, and lower rates of depression and anxiety symptoms. When 7 multiplex EP participants and their term control matches were eliminated from the sample, there were no differences from the primary analyses. Female-only analyses were similar to primary analyses on core ASD symptomatology findings. Regarding associated characteristics, females only differed on height, head circumference, and anxiety symptoms.

Conclusions: Accounting for age, sex, nonverbal IQ, and prior ASD diagnosis status, EP children had less severe stereotypic language and RRB symptoms compared to term children based on ADI-R parent report, but exhibited no differences on parent-reported nonverbal communication or reciprocal social interaction symptoms, or with direct observation of social affective and repetitive and restricted ASD symptoms on the ADOS-2. EP children with ASD also showed decreased physical growth and delayed language relative to those born at term, possibly reflecting the developmental effects of being born EP. In sum, the ASD phenotype was generally similar between EP and term born children, with the exception of less severity of retrospectively parent-reported stereotypic behaviors, lower physical growth parameters, and increased delays in language milestones among EP born children with ASD.

TABLE OF CONTENTS

ACKNOWLEDGMENTS	iv
ABSTRACT	v
TABLE OF CONTENTS	vii
LIST OF TABLES	ix
INTRODUCTION	1
Study Rationale	1
Preterm Birth	1
Autism Spectrum Disorder	2
ASD Sex Differences in Prevalence and Phenotype	3
Characteristics Commonly Associated with ASD	4
ASD and Preterm Birth	8
METHODS	10
Participants	10
Extremely Low Gestational Newborn (ELGAN) Study	10
Simons Simplex Collection (SSC)	10
Sample Selection	10
ASD Phenotype Assessments	12
Autism Diagnostic Interview-Revised (ADI-R)	12
Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2)	13
Intellectual Ability Assessments	14

Measures of Associated Characteristics	15
Demographic and Newborn Characteristics	15
Gross Motor Delay/Impairment	15
Anthropometrics	16
Seizure Disorder	16
Psychiatric Measures	16
Statistical Analysis	17
RESULTS	18
Maternal, Demographic, and Neonatal Characteristics	18
ASD Symptomatology	20
Associated Characteristics	26
Secondary Analyses	29
Female-Only Analyses	29
DISCUSSION	32
Study Strengths and Limitations	37
Clinical Implications	38
Conclusions	39
REFERENCES	40
CURRICULUM VITAE	52

LIST OF TABLES

Table 1. Maternal demographics and age 10 child characteristics of extremely preterm (EP) and term born children study samples	19
Table 2. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born children with ASD.....	21
Table 3. Descriptive statistics for IQ and parent-report autism symptom measures for extremely preterm (EP) children without and with prior ASD diagnosis.....	22
Table 4. Descriptive statistics for IQ and parent-report autism symptom measures for extremely preterm (EP) and term born children with prior ASD diagnosis	23
Table 5. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born children with ASD.....	25
Table 6. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born children with ASD excluding multiplex ELGAN individuals (n=7) and SSC matches (n=7).....	27
Table 7. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born children with ASD excluding multiplex ELGAN individuals (n=7) and SSC matches (n=7).....	28
Table 8. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born female with ASD.....	30
Table 9. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born females with ASD.....	31

INTRODUCTION

Study Rationale

Previous studies have established that preterm birth is associated with an increased risk of developing Autism Spectrum Disorder (ASD), with a prevalence rate of approximately 6-7% (Agrawal et al., 2018; Crump et al., 2021; Joseph, O'Shea, et al., 2017). The prevalence of ASD in the preterm population is several times greater than the 1-2% ASD prevalence within the general population (Crump et al., 2021; Christensen et al., 2019). However, less is known about whether ASD symptoms present differently in preterm-born children compared to term-born children. One reason for this is that preterm birth is a risk factor for developmental and behavioral difficulties in general (Fitzallen et al., 2020; Peralta-Carcelen et al., 2018), which may obscure or overshadow the ASD phenotype in children with co-occurring conditions (Antshel et al., 2016; Rosen et al., 2018). Additionally, because preterm birth is associated with decreased IQ (Joseph et al., 2016; Kerr-Wilson et al., 2012), and decreased IQ is associated with increased ASD symptom severity (Mayes et al., 2011), IQ differences or different prevalences of intellectual disability may confound comparisons between ASD samples with different gestational ages. Thus, the aim of this study is to identify phenotypic similarities and differences in ASD phenotype between an extremely preterm-born sample and a matched term-born sample.

Preterm Birth

Preterm birth, defined as birth before 37 weeks of gestational age, accounts for about 10% of live births in the United States, which is similar to current worldwide

estimates (Martin et al., 2019; Walani, 2020). Preterm birth can be further categorized as extremely preterm (<28 weeks), very preterm (28 to <32 weeks), moderate preterm (32 to <34 weeks), and late preterm (34 to <37 weeks) (WHO, 2018). Premature newborns are at high risk for neurological damage and developmental dysfunctions, with those born extremely preterm having the greatest vulnerability (O'Shea et al., 2009).

While survival rates for children born preterm have improved considerably, there has been relatively little change in neurodevelopmental outcomes (Anderson, 2014). Children born preterm have a mean IQ difference of 11-12 points compared to term-born peers (Kerr-Wilson et al., 2012). There is a linear relationship between gestational age and decreased IQ, such that lower gestational age is associated with a greater IQ difference compared to term-born children (Joseph et al., 2016; Kerr-Wilson et al., 2012). Children born preterm are also at increased risk for behavioral and socioemotional difficulties, with increased rates of Attention-Deficit/Hyperactivity Disorder (ADHD), Anxiety Disorder, and Autism Spectrum Disorder (ASD) (Fitzallen et al., 2020; Peralta-Carcelen et al., 2018).

Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder with a prevalence of 1.3-1.7% in the United States (Christensen et al., 2019). ASD is characterized by two core symptom domains: deficits in social communication and interaction and the presence of restricted, repetitive behaviors (American Psychiatric Association, 2013). ASD is notably heterogeneous in its presentation, encompassing a wide range of core symptoms, language and cognitive ability, and other associated

features (Masi et al., 2017). Although ASD can be reliably diagnosed by the age of 2 years, the median age of ASD diagnosis in the US is 4 years 3 months, and a recent meta-analysis estimates the worldwide mean age of diagnosis at 5 years (Corsello et al., 2013; Maenner et al., 2020; Van 't Hof et al., 2021). This delay in diagnosis is of particular concern because ASD prognosis is markedly improved with early detection and intervention (Zwaigenbaum et al., 2015). Previous studies have reported delayed diagnosis in females, African American and Hispanic children, and children of lower socioeconomic status, but findings on these associated factors have been mixed (Hyman et al., 2020; Lai et al., 2015; Van 't Hof et al., 2021).

ASD Sex Differences in Prevalence and Phenotype

ASD disproportionately affects males (Ferri et al., 2018). The male-to-female ratio within the general ASD population has been reported most recently to be 3.5-4.5:1 (Loomes et al., 2017; Maenner et al., 2014). However, this ratio varies by ASD severity. Among individuals with higher cognitive ability, the male-to-female ratio is estimated at 6-9:1, while in cases with moderate to severe cognitive impairment, the male-to-female ratio is about 2:1 (Frazier et al., 2014; Werling & Geschwind, 2013). Various explanations have been proposed to explain these sex differences in ASD. It has been suggested that females may have protective factors that lower their ASD risk (Werling & Geschwind, 2013). However, it may also be possible that females have been historically underdiagnosed, especially those with milder symptoms (Lai et al., 2015).

Given the well-established sex differences in prevalence, a recent area of research has focused on the potential phenotypic differences between males and females with

ASD. Findings have been mixed, likely due to the substantial heterogeneity of ASD symptoms overall (Ferri et al., 2018). Generally, studies have reported that females exhibit lower frequencies of restricted, repetitive behaviors (RRBs), although this finding is predominantly based on parent-report measures (Frazier et al., 2014; Kaat et al., 2021; Knutsen et al., 2019; Tillmann et al., 2018). Findings on social and communication deficits have been equivocal (Frazier et al., 2014; Lai et al., 2015; Tillmann et al., 2018).

Characteristics Commonly Associated with ASD

Various phenotypic features and co-occurring conditions have been associated with ASD, despite falling outside of DSM-5 diagnostic criteria. Intellectual disability (ID), conventionally defined as $IQ \leq 70$ (2 or more standard deviations below the normative mean), is relatively common within the ASD population. Although the prevalence of co-occurring ID has historically been estimated to be as high as 75%, most current estimates range from 30-35% (Maenner et al., 2014; Russell et al., 2019). Similarly, the prevalence of minimally verbal ASD has been estimated most recently to be between 25-35%, declining from historical estimates of up to 50% (Eigsti et al., 2011; Norrelgen et al., 2015; Rose et al., 2016). These decreases in prevalence are likely due to changes in diagnostic criteria, leading to increased diagnosis of milder cases of ASD (Tager-Flusberg & Kasari, 2013).

Many individuals with ASD may have one or more co-occurring psychiatric conditions. Attention-Deficit/Hyperactivity Disorder (ADHD) shares some symptomatology with ASD. In previous DSM editions, these two conditions could not be diagnosed within the same individual, but this was amended in DSM-5 (Antshel et al.,

2016). Previous studies have estimated that between 40-70% of children and adolescents with ASD have co-occurring ADHD, while population-based prevalence estimates range from 20-40% (Antshel & Russo, 2019; Levy et al., 2010; Supekar et al., 2017). Although ASD and ADHD are both characterized by social deficits and executive function impairment, the presentation of these deficits is distinctive to each condition (Antshel & Russo, 2019; Rosen et al., 2018). Abnormalities in eye contact, facial expressions, and reciprocal social communication are distinctive ASD social deficits, whereas ADHD social deficits are characterized by disruptive patterns of social interaction (Antshel & Russo, 2019; Grzadzinski et al., 2016). Moreover, executive function impairment in ASD is characterized by cognitive inflexibility, whereas executive function impairment in ADHD tends to present as behavioral disinhibition (Antshel & Russo, 2019; Craig et al., 2016). In children with co-occurring ASD and ADHD, ASD diagnosis can be delayed by several years (Stevens et al., 2016). Prevalence rates of anxiety and depression are also greater in individuals with ASD compared to the general population (Gotham et al., 2015; Rosen et al., 2018). Anxiety and depression may present with typical symptoms, or the presentation may be influenced by ASD symptoms (Kerns et al., 2014; Pezzimenti et al., 2019). Unlike ADHD, which decreases in prevalence with age, anxiety and depression in ASD are associated with increased age and higher IQ; this may be due to older, higher-IQ individuals with ASD having greater awareness of their difficulties with social interactions (Gotham et al., 2015; Rosen et al., 2018; Vasa et al., 2013).

Children and adolescents with ASD are known to be at increased risk for seizure disorders. Compared to a prevalence of 0.6-1% within the general population, between 2-

26% of individuals with ASD have a co-occurring seizure disorder (El Achkar & Spence, 2015; Robertson et al., 2015). In particular, individuals with co-occurring ASD and ID are at greater risk for seizure disorder, although it should be noted that ID alone is also a risk factor for seizure disorder (El Achkar & Spence, 2015; Jokiranta et al., 2014). For individuals with ASD without ID, findings of epilepsy risk have been mixed (Hyman et al., 2020; Jokiranta et al., 2014). The onset of seizure disorders among those with ASD may follow a bimodal distribution, with one peak in early childhood and a second peak occurring approximately between 10-13 years of age (Bolton et al., 2011; Takano et al., 2014). ASD with co-occurring seizure disorder is associated with increased ASD severity, but this tends to be associated with lower IQ. After controlling for IQ, only hyperactivity symptoms remain elevated in individuals with ASD and co-occurring seizure disorder compared to those with only ASD (Viscidi et al., 2014).

Although not included in the DSM-5 criteria for ASD, motor deficits are common in individuals with ASD (up to 87% prevalence), such that recent literature has advocated for adding motor deficits as a third symptom domain of ASD (Bhat, 2020; Kaur et al., 2018; Licari et al., 2020). A wide range of motor deficits has been observed in individuals with ASD, including low muscle tone and deficits in motor planning (praxis) involving both upper and lower extremities, and in both gross and fine motor skills (Bhat et al., 2011; Fournier et al., 2010). While motor deficits are present in other developmental disorders, such as ADHD, motor skills involving dynamic processing of visual-motor feedback may be specifically impaired in ASD (Ament et al., 2014; Zampella et al., 2021). Motor deficits during infancy may also be an early indicator of

ASD risk, which may be identifiable before other symptoms emerge (LeBarton & Landa, 2019; Zampella et al., 2021). For example, in a sample of term-born infants at high risk for ASD (siblings of children with ASD), there was an association between head lag during a pull-to-sit task at 6 months of age and ASD diagnosis at 36 months of age (Flanagan et al., 2012).

Increased head circumference (HC) and increased cerebral volume have been consistently associated with ASD. The prevalence of macrocephaly (defined as HC greater than the 97th percentile of normative data) has been reported at 15.7% (Pan et al., 2021; Sacco et al., 2015). Previous studies have established that individuals with ASD are born with normal HC, followed by an above average increase in brain and head growth between one to four years of age. This overgrowth is later followed by a decline in growth rate such that HC measurements in adolescence match those of controls (Hyman et al., 2020; Sacco et al., 2015). Increased HC in ASD may be associated with generalized overgrowth, as indicated by above-average height and weight measurements (Chawarska et al., 2011). Additionally, simplex individuals with ASD (no first-degree relatives with ASD) have similar HC percentiles to their non-ASD relatives, suggesting that using normative data alone may overestimate the association between enlarged HC and ASD (Chaste et al., 2013). In simplex ASD, increased HC is associated with greater ASD symptom severity and lower nonverbal IQ (Chaste et al., 2013). However, in multiplex ASD (families having 2 or more children with ASD), increased HC is not associated with ASD symptom severity, and is associated with above-average nonverbal IQ (Davis et al., 2013).

ASD and Preterm Birth

Although ASD has a large genetic component, with an estimated heritability of 73-85% (Bai et al., 2019), many environmental risk factors have been identified, including preterm birth (Muhle et al., 2018). Among individuals born preterm, ASD prevalence has been estimated at 6-7% (Agrawal et al., 2018; Crump et al., 2021; Joseph, O'Shea, et al., 2017). Furthermore, a recent large national cohort study found that ASD prevalence increases as gestational age decreases, ranging from 6.1% for extremely preterm births to 1.4% for term births (Crump et al., 2021). Prenatal environmental exposures, such as maternal infection and inflammation, which are associated with both preterm birth (Cappelletti et al., 2016) and increased ASD prevalence, are possible moderators of the relationship between preterm birth and ASD risk (Meltzer & Van De Water, 2017). Placental abnormalities during preterm birth may also increase the risk of ASD (Kratimenos & Penn, 2019).

Previous studies have investigated the ASD phenotype in term-born children compared to those born preterm, but these studies have generally examined preterm individuals without distinguishing between gestational age (i.e., the degree of prematurity), or have focused on late preterm individuals (Bowers et al., 2015; Brayette et al., 2019; Chen et al., 2019; Luu et al., 2020). Because late preterm birth confers less developmental vulnerability than extremely preterm birth, potential phenotypic differences between term-born and preterm-born children may be most apparent with an extremely preterm-born sample. To date, no study has compared both ASD core symptoms and associated characteristics within children diagnosed with gold-standard

assessments in a relatively large sample of EP children. In this study, we compare core ASD features and associated characteristics between 10-year-old children born extremely preterm versus at term, matched for sex, general language ability, and nonverbal IQ. The objective of this study is to characterize the ASD phenotype in children born extremely preterm and to identify phenotypic similarities and differences in comparison with term born children with ASD.

METHODS

Participants

Extremely Low Gestational Newborn (ELGAN) Study

The ELGAN Study is a multicenter observational study of the risk of structural and functional neurologic disorders in extremely preterm (EP) infants (O'Shea et al., 2009). From 2002-2004, a total of 1,506 infants born before 28 weeks of gestation were enrolled in the study. Of the 1,200 individuals who survived to the age of 2 years, 1,102 participated in the two-year follow-up. Of the 1,198 children who survived to 10 years, 889 individuals participated in the 10-year follow-up. Study procedures were approved by the institutional review boards of the participating institutions.

Simons Simplex Collection (SSC)

The SSC is a cohort of simplex families of children with ASD, recruited from across the United States (Fischbach & Lord, 2010). Families were included in the study if they had only one child who met diagnostic criteria for ASD. Demographic and phenotypic data on probands and their families were extracted from the SSC database, version 15.3 (released 8/6/2013). SSC exclusion criteria included a gestational age of less than 36 weeks and a birth weight of less than 2,000 grams (Simons Foundation Autism Research Initiative, 2014).

Sample Selection

During the ELGAN 10-year follow-up, 857 children were assessed for ASD. Children with severe gross motor impairment or uncorrectable blindness were excluded, as an ASD diagnosis would not be valid based on DSM-5 criteria. Study participants

were first screened with the Social Communication Questionnaire (SCQ), a parent-report questionnaire that assesses ASD symptoms. Children who met SCQ screening criteria (score ≥ 11) were then administered the Autism Diagnostic Interview-Revised (ADI-R), an in-depth parent interview that assesses core ASD symptoms. Children who met ADI-R criteria for ASD were administered the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2), which was the criterion measure for inclusion in the ELGAN ASD sample. Two children who met ADOS-2 diagnostic criteria did not have ADI-R interview results. Nine children did not meet ADI-R criteria but were assessed with the ADOS-2 because of a parent-reported prior clinical diagnosis of ASD or because the on-site psychologist observed ASD symptoms during the study visit. Four of these children met ADOS-2 criteria for ASD. Of the children assessed for ASD during the ELGAN 10-year follow-up, 61 children met diagnostic criteria for ASD based on the ADOS-2 evaluation (Joseph, O'Shea, et al., 2017).

The 61 ELGAN participants who met study criteria for ASD included two twin pairs. To reduce potential bias from familial overrepresentation, one member from each twin pair was excluded from study analyses, resulting in a final EP sample of $n = 59$. Whereas the SSC term sample was selected based on having a prior clinical diagnosis of ASD, the ELGAN EP sample was selected for having extremely low gestational age. Approximately one-third (36%) of the ELGAN sample did not have a prior clinical diagnosis of ASD.

Case-control matching was performed using SPSS version 27. ELGAN participants were matched one-to-one to SSC probands based on age, sex, ADOS-2

module (reflecting spoken language level), and nonverbal IQ. For ADOS-2 module matching, participants who received Module 1 or Module 2 (single words to phrase speech) were matched together, due to the low number of participants who had received Module 2. Participants who received Module 3 (fluent speech) were matched with each other.

ASD Phenotype Assessments

Autism Diagnostic Interview-Revised (ADI-R)

The ADI-R is a semi-structured diagnostic interview, in which the primary caregiver is asked about a child's symptoms, both currently and during early development (Le Couteur et al., 2003). Diagnostic algorithms were used to calculate scores, based on "most abnormal" age 4 to 5 years or "ever," in three domains: reciprocal social interaction, verbal and/or nonverbal communication, and restricted and repetitive behavior (RRB). Individual RRB items were also categorized using Repetitive Sensory Motor and Insistence on Sameness subscales (Bishop et al., 2013). Because only ADI-R diagnostic algorithm scores ("most abnormal" or "ever") were available for the ELGAN cohort, the subscales delineated by Bishop et al. were modified. In this study, ADI-R Items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms, and Items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess Insistence on Sameness symptoms. ADI-R

Items 9 and 10 were used to assess delays in single word speech and phrase speech, respectively.

ADI-R cutoffs for both the ELGAN and SSC cohorts were based on Collaborative Programs for Excellence in Autism (CPEA) classification criteria (Lord et al., 2012; Risi et al., 2006). These criteria require that the participant meets autism cutoff for reciprocal social interaction and meets cutoff for either communication or repetitive behavior; meets cutoffs for reciprocal social interaction and communication or meets cutoff for social and within 2 points of communication cutoff; or meets cutoff for communication and within 2 points of reciprocal social interaction cutoff or within 1 point of both reciprocal social interaction and communication cutoffs.

Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2)

The ADOS-2 is a validated semi-structured observational assessment, in which a trained clinician interacts with the child with developmentally appropriate play-based activities (Lord et al., 2012). For the present study, one of Modules 1, 2, or 3 was administered based on the child's language ability. Module 1 was administered to children with no expressive language or only single words. Module 2 was administered to children with phrase speech. Module 3 was administered to children with fluent speech. Using module-specific algorithms, behavioral items were converted to separate diagnostic scores for Social Affect (SA, which is generally consistent with the DSM-5 social communication and interaction symptom domain) and Restricted and Repetitive Behaviors (RRBs), which were added together to yield Total Severity scores. Calibrated

Severity Scores were also calculated to allow for cross-module comparisons of overall symptom severity (Gotham et al., 2009).

Intellectual Ability Assessments

Intellectual ability was assessed with the Preschool or the School-Age Differential Ability Scales-II (DAS-II) Verbal (VIQ) and Nonverbal Reasoning (NVIQ) scales (Elliot, 2007). SSC participants included in the current study who received Module 1 or 2 of ADOS-2 were tested “out of level” with the Preschool version of the DAS-II, yielding age-equivalent but not standard IQ scores. For these individuals, an age-adjusted ratio IQ was calculated. Nonverbal ratio IQ was calculated by averaging the Preschool DAS-II age-equivalent Matrices and Picture Similarities subtest scores, dividing by the age of the child in months and multiplying by 100. Verbal ratio IQ scores were calculated by averaging the Preschool DAS-II Verbal Comprehension and Naming Vocabulary subtest scores, dividing by the age of the child in months, and multiplying by 100. For primary analyses, verbal IQ scores were available for 57 ELGAN participants and 52 SSC participants. SSC participants who were administered ADOS Module 3 were administered the School-Age version of the DAS-II. All ELGAN participants were administered the School-Age version of the DAS-II regardless of the ADOS-2 module (1, 2, or 3) they received.

Measures of Associated Characteristics

Demographic and Newborn Characteristics

Data on maternal age at birth, parental marital status, maternal education, and race/ethnicity were obtained from parent report. Maternal education data was missing for 2 ELGAN participants and 1 SSC participant.

For the ELGAN participants, gestational age, birth weight, and birthweight z-score for gestational age were examined. Birthweight z-scores for gestational age were calculated as the number of standard deviations above or below the median birthweight in a reference birthweight distribution (Yudkin et al., 1987). Being small for gestational age (or fetal growth restriction) was defined as having a birthweight z-score < -2 (Joseph et al., 2017).

Gross Motor Delay/Impairment

For the ELGAN cohort, gross motor function at the age 2 follow-up was examined. Gross motor delay/impairment was defined as having a score greater than 0 on the Gross Motor Function Classification System (GMFCS). The GMFCS is a classification system based on functional gross motor skills, most commonly used to classify children with cerebral palsy (Palisano et al., 2000). A score of 0 on the GMFCS refers to no limitations in walking or other lower extremity movements. GMFCS data were missing for 3 ELGAN participants. For the SSC cohort, gross motor delay/impairment was defined as walking unaided later than 24 months, based on ADI-R data.

Anthropometrics

Head circumference, height, and weight measurements were extracted from the ELGAN and SSC databases. Head circumferences were taken as the widest occipital-frontal circumference, to the closest millimeter (Chaste et al., 2013; McElrath et al., 2010). BMI values were calculated as weight (in kilograms) divided by the square of height (in meters). Age- and sex-adjusted Z-scores for height, weight, and BMI with respect to CDC reference norms were calculated using the CDC LMS method in Microsoft Excel (Centers for Disease Control and Prevention, 2009; Flegal & Cole, 2013). Anthropometric data was missing for 1 ELGAN participant.

Seizure Disorder

For the ELGAN cohort, seizure disorder was identified with a validated seizure screen followed by a structured interview with a study coordinator, then an open-ended interview with a pediatric epilepsy specialist (Douglass et al., 2017). For the SSC cohort, seizure disorder data were obtained via parent report on the medical history interview. Parents reported whether the participant had a history of afebrile seizures: the code “2” was used to indicate likely seizure disorder, and the code “3” was used to indicate a clinical epilepsy diagnosis. Individuals with a code of “2” or “3” were considered to have seizure disorder.

Psychiatric Measures

The Child Symptom Inventory-4 (CSI-4, Gadow & Sprafkin, 2002; Sprafkin et al., 2002) was used to assess parent-reported psychiatric symptoms in the ELGAN EP sample at age 10 years. The CSI-4 Combined ADHD T-score, including symptoms of

both inattention and hyperactivity/impulsivity, was used to screen for ADHD. To assess anxiety symptoms, the average of T-scores on anxiety disorder, social phobia, and separation anxiety was used. To assess depression symptoms, the average of T-scores on major depressive disorder and dysthymic disorder was used (Moore et al., 2021). CSI-4 data were missing for 3 ELGAN participants. For the SSC term sample, parent-reported age 10 symptoms on the Child Behavior Checklist (CBCL, Achenbach & Rescorla, 2001) yielded CBCL T-scores on the DSM-oriented attention problems, anxiety problems, and affective problems scales, which were used to assess ADHD, anxiety, and depression symptoms, respectively. Higher scores on the CSI-4 and CBCL norm-referenced scales represent higher levels of symptomatology (Achenbach & Rescorla, 2001). T-scores from the CBCL and CSI-4 were dichotomized as less than 65, indicating non-clinical or subclinical symptoms, and 65 or greater, indicating clinically significant symptoms.

Statistical Analysis

All statistical analyses were performed using SPSS version 27. T-tests and Pearson's chi-square tests were used to evaluate group differences for continuous variables and categorical outcome variables, respectively. In secondary analyses, ELGAN participants ($n = 7$) who were multiplex (known to have a sibling who also met diagnostic criteria for ASD) were excluded, and their SSC matches were also removed from the sample. Analyses including only female participants (20 ELGAN cases and 20 SSC controls) were also conducted. Alpha was set at 0.05. Corrections for multiple comparisons were not made. Cohen's effect size (d) is reported for all t-tests.

RESULTS

Maternal, Demographic, and Neonatal Characteristics

Among the 61 ELGAN individuals who met study criteria for ASD, there were two twin pairs. After removing one member from each twin pair, 9 participants (15.3%) were born at 27 weeks gestational age, 25 participants (42.4%) were born at 25-26 weeks, and 25 participants (42.4%) were born at 23-24 weeks. Z-scores were calculated based on birth weight adjusted for gestational age. Eight participants (13.6%) had a birth weight z-score < -2 , 6 participants (10.2%) had a birth weight z-score between -2 and -1 , and 45 participants (76.3%) had a birth weight z-score of -1 or higher.

Table 1 compares maternal and child characteristics at age 10 years between the EP and term groups. Mothers of children in the SSC cohort had received more education and were more likely to be married/partnered than mothers of children in the ELGAN cohort. There were no group differences in maternal age at delivery. As expected, because of case-control matching procedures, age and nonverbal IQ did not differ between groups. However, verbal IQ was significantly lower among the ELGAN EP sample relative to the SSC term sample.

Table 1. Maternal demographics and age 10 child characteristics of extremely preterm (EP) and term born children study samples

	ELGAN EP ASD (n = 59)	SSC Term ASD (n = 59)	t or X ² , p
Maternal demographics			
Maternal age, years at birth	30.4 (5.9)	30.7 (5.0)	t = 0.3 (p = .79)
Maternal education at age 10			
≤ 12 (high school)	28 (49.1%)	12 (20.7%)	X ² = 10.7 (p = .005)
> 12, < 16	8 (14.0%)	16 (27.6%)	
≥ 16 (≥ college)	21 (36.8%)	30 (51.7%)	
Marital status at age 10			
Single	22 (37.3%)	8 (13.6%)	X ² = 8.8 (p = .003)
Married/partnered	37 (62.7%)	51 (86.4%)	
Racial identity			
White	36 (61.0%)	46 (78.0%)	
Black	18 (30.5%)	3 (5.1%)	
Asian	2 (3.4%)	4 (6.8%)	
Native American	0 (0%)	0 (0%)	
Mixed	2 (3.4%)	3 (5.1%)	
Not identified (other)	1 (1.7%)	3 (5.1%)	
Hispanic			
Yes	4 (6.8%)	9 (15.3%)	
No	55 (93.2%)	50 (84.8%)	
Child characteristics at age of ASD assessment			
Age	10.0 (0.7)	10.0 (0.6)	t = 0.3 (p = .81)
Nonverbal IQ	70.4 (25.9)	72.3 (23.5)	t = 0.4 (p = .68)
Verbal IQ	62.6 (28.5)	74.8 (25.8)	t = 2.4 (p = .021)
Prior clinical diagnosis of ASD			
Yes	38	59	X ² = 25.5 (p < .001)
No	21	0	

ASD Symptomatology

On the ADI-R (Table 2), the ELGAN group had significantly lower mean scores, reflecting decreased symptom severity, on verbal communication relative to the SSC group. The ADI-R verbal communication subdomain is comprised of items indicating relative failure to initiate or sustain conversational interchange and items indicating stereotypic, repetitive, or idiosyncratic speech. When these two sub-scores were analyzed separately, only stereotypic language showed significant group differences. The ELGAN group also had significantly lower mean scores in the ADI-R RRB domain, and lower mean scores on both the Repetitive Sensory Motor and Insistence on Sameness subcomponents of the ADI-R RRB scores. In contrast, there were no group differences in the ADI-R reciprocal social interaction or nonverbal communication symptom domains. In addition, there were no group differences on the ADOS-2 social affect or repetitive and restricted domain scores or calibrated severity scores.

We conducted analyses to examine whether a prior clinical diagnosis was associated with differences in ADI-R scores within the ELGAN EP group (Table 3). The EP subset without a prior ASD diagnosis had lower nonverbal IQ. The EP group without prior diagnosis had lower scores on the ADI-R in the reciprocal social interaction domain, verbal communication subdomain, and RRB domain. When the verbal communication subdomains were analyzed separately, only stereotypic language showed significant differences. Within the RRB domain, the group without prior ASD diagnosis had lower scores on both the Repetitive Sensory Motor and Insistence on Sameness subcomponents.

Table 2. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born children with ASD

	ELGAN EP			SSC Term			t	p	d
	n	Mean	SD	n	Mean	SD			
Social Communication									
ADI-R reciprocal social interaction	57	20.2	7.2	59	21.7	5.3	1.3	.21	0.2
ADI-R nonverbal communication	57	9.1	4.1	59	10.0	3.0	1.4	.18	0.3
ADI-R verbal communication	46	6.4	2.5	51	8.1	2.0	3.9	<.001	0.8
ADI-R social initiation	46	3.3	1.2	51	3.7	0.7	2.0	.055	0.4
ADI-R stereotyped language	46	3.0	1.8	51	4.4	1.7	4.0	<.001	0.8
ADOS-2 module 1/2 social affect	18	14.0	3.9	18	13.8	3.9	0.2	.83	0.1
ADOS-2 module 3 social affect	41	10.9	4.6	41	9.7	3.1	1.4	.16	0.3
ADOS-2 social affect calibrated severity	59	7.5	2.1	59	7.4	1.6	0.3	.77	0.1
Restricted and repetitive behaviors (RRB)									
ADI-R RRB total	57	4.8	2.9	59	6.9	2.3	4.2	<.001	0.8
ADI-R repetitive sensorimotor (RSM) ¹	57	4.1	2.8	59	5.7	2.4	3.3	.001	0.6
ADI-R insistence on sameness (IS) ²	57	1.3	1.3	59	2.8	1.6	5.6	<.001	1.0
ADOS-2 module 1/2 RRB total	18	5.1	2.1	18	5.1	1.9	0.1	.93	0.03
ADOS-2 module 3 RRB total	41	3.4	1.9	41	3.5	1.6	0.4	.70	0.1
ADOS-2 RRB calibrated severity	59	7.8	2.0	59	8.0	1.7	0.7	.52	0.1

¹ ADI-R items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms. The score of this Repetitive Sensorimotor subscale has a range of 0-10.

² ADI-R items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess insistence on sameness symptoms. The score of this Insistence on Sameness subscale has a range of 0-4.

Table 3. Descriptive statistics for IQ and parent-report autism symptom measures for extremely preterm (EP) children without and with prior ASD diagnosis

	EP, no prior diagnosis			EP, prior diagnosis			t	p	d
	n	Mean	SD	n	Mean	SD			
IQ									
Nonverbal IQ	21	61.5	21.7	38	75.3	26.9	2.0	.049	0.5
Verbal IQ	21	56.9	23.9	36	65.9	30.6	1.2	.25	0.3
Social Communication									
ADI-R reciprocal social interaction	21	16.9	7.3	36	22.1	6.5	2.8	.007	0.8
ADI-R nonverbal communication	21	8.2	4.0	36	9.6	4.1	1.3	.22	0.3
ADI-R verbal communication	16	5.1	2.5	30	7.0	2.2	2.7	.009	0.8
ADI-R B2 social initiation	16	2.9	1.3	30	3.5	1.0	1.7	.13	0.5
ADI-R B3 stereotyped language	16	2.1	1.6	30	3.5	1.7	2.7	.010	0.8
Restricted and repetitive behaviors (RRB)									
ADI-R RRB total	21	3.5	2.8	36	5.6	2.7	2.7	.009	0.7
ADI-R repetitive sensorimotor (RSM) ¹	21	2.8	2.3	36	4.9	2.8	2.9	.005	0.8
ADI-R insistence on sameness (IS) ²	21	0.8	1.0	36	1.6	1.3	2.5	.014	0.7

¹ ADI-R items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms. The score of this Repetitive Sensorimotor subscale has a range of 0-10.

² ADI-R items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess insistence on sameness symptoms. The score of this Insistence on Sameness subscale has a range of 0-4.

Table 4. Descriptive statistics for IQ and parent-report autism symptom measures for extremely preterm (EP) and term born children with prior ASD diagnosis

	EP, prior diagnosis			SSC			t	p	d
	n	Mean	SD	n	Mean	SD			
IQ									
Nonverbal IQ	38	75.3	26.9	38	77.1	24.5	0.3	.76	0.07
Verbal IQ	36	65.9	30.6	35	74.4	27.5	1.2	.22	0.3
Social Communication									
ADI-R reciprocal social interaction	36	22.1	6.5	38	21.5	5.6	0.4	.67	0.1
ADI-R nonverbal communication	36	9.6	4.1	38	9.7	2.8	0.2	.88	0.04
ADI-R verbal communication	30	7.0	2.2	35	8.3	2.0	2.4	.022	0.6
ADI-R B2 social initiation	30	3.5	1.0	35	3.7	0.7	0.7	.48	0.2
ADI-R B3 stereotyped language	30	3.5	1.7	35	4.6	1.7	2.6	.012	0.6
Restricted and repetitive behaviors (RRB)									
ADI-R RRB total	36	5.6	2.7	38	6.8	2.2	2.1	.038	0.5
ADI-R repetitive sensorimotor (RSM) ¹	36	4.9	2.8	38	5.8	2.4	1.5	.13	0.4
ADI-R insistence on sameness (IS) ²	36	1.6	1.3	38	2.5	1.4	2.6	.011	0.6

¹ ADI-R items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms. The score of this Repetitive Sensorimotor subscale has a range of 0-10.

² ADI-R items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess insistence on sameness symptoms. The score of this Insistence on Sameness subscale has a range of 0-4.

We then conducted analyses comparing only EP individuals with a prior diagnosis to their matched term controls, as all term individuals had a prior ASD diagnosis (Table 4). When only individuals with a prior diagnosis were included, verbal IQ was no longer different between the term and EP groups. The EP group with a prior ASD diagnosis had lower ADI-R scores in the verbal communication subdomain, which was driven by a lower stereotypic language subscore. The EP group also had a lower RRB domain score. The Insistence on Sameness subcomponent score was also lower in the EP group, but there was no difference on the Repetitive Sensory Motor subcomponent. Effect sizes of between-group differences were attenuated when analyses were restricted to participants with a prior clinical ASD diagnosis. Cohen's effect sizes in the primary analyses were large for between-group differences in the ADI-R verbal communication stereotypic language sub-score ($d = 0.8$), RRB domain ($d = 0.8$), and Insistence on Sameness subcomponent ($d = 1.0$). When only individuals with a prior diagnosis were included, Cohen's effect sizes were medium in magnitude (ADI-R verbal communication: $d = 0.6$; ADI-R stereotypic language: $d = 0.6$; ADI-R RRB: $d = 0.5$; ADI-R Insistence on Sameness: $d = 0.6$).

Table 5. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born children with ASD

	ELGAN EP ASD (n = 59)	SSC Term ASD (n = 59)	t or X ² , p
Single words > 24 months			
Yes	39 (67.4%)	25 (42.4%)	X ² = 8.0 (p=.005)
No	18 (31.6%)	34 (57.6%)	
Phrase speech > 33 months			
Yes	49 (86.0%)	40 (67.8%)	X ² = 5.4 (p=.021)
No	8 (14.0%)	19 (32.2%)	
Gross motor delay/impairment at age 2¹			
Yes	11 (19.6%)	6 (10.3%)	X ² = 1.9 (p=.16)
No	45 (80.4%)	52 (89.7%)	
Anthropometrics/physical growth measures at age 10			
Head circumference, raw	52.4 (SD=3.0)	54.4 (SD=2.2)	t=4.0 (p<.001)
Height z-score ²	-0.5 (SD=1.1)	0.3 (SD=1.1)	t=3.7 (p<.001)
Weight z-score	-0.1 (SD=1.6)	0.5 (SD=1.2)	t=2.4 (p=.020)
Body mass index z-score	0.1 (SD=1.6)	0.4 (SD=1.3)	t=1.2 (p=.23)
Seizure disorder at age 10			
Yes	8 (13.6%)	4 (6.8%)	X ² = 1.5 (p=.22)
No	51 (86.4%)	55 (93.2%)	
Psychiatric symptoms at age 10³			
ADHD			
T ≥ 65	20 (35.7%)	23 (39.0%)	X ² = 0.1 (p=.72)
T < 65	36 (64.3%)	36 (61.0%)	
Anxiety			
T ≥ 65	9 (16.1%)	28 (47.5%)	X ² = 13.0 (p<.001)
T < 65	47 (83.9%)	31 (52.5%)	
Depression			
T ≥ 65	10 (17.9%)	21 (35.6%)	X ² = 4.6 (p=.032)
T < 65	46 (82.1%)	38 (64.4%)	

¹The Gross Motor Function Classification System (GMFCS) was used to assess gross motor delay/impairment in the ELGAN sample. A score of 0 on the GMFCS indicates no limitations in lower extremity movement. Item 5 of the Autism Diagnostic Interview-Revised (ADI-R) was used to assess gross motor delay in the SSC cohort. On item 5, parents were asked at what age (in months) their child started walking unaided. Children who began walking at 24 months or later were designated as having gross motor delay/impairment. One SSC individual was missing data on ADI-R Item 5.

²Anthropometric z-scores are relative to CDC normative data, which are sex-adjusted and age-adjusted (to the nearest month). One ELGAN participant was missing anthropometric data.

³Three ELGAN participants were missing data on the CSI-4 screener for psychiatric symptoms.

Associated Characteristics

Developmental milestones, anthropometrics, prevalence of seizure disorder, and psychiatric symptoms were compared between the SSC and ELGAN cohorts (Table 5). A greater proportion of the ELGAN cohort had the development of single-word speech after 24 months and phrase speech development after 36 months, although a considerable proportion of the SSC cohort also had delayed speech milestones. There were no group differences in delay of gross motor milestones at the age of 2 years.

At the age of 10 years, the ELGAN cohort had significantly lower mean height and weight z-scores, calculated relative to CDC normative data, sex-adjusted and age-adjusted to the nearest month. There were no group differences in CDC-adjusted BMI z-scores. The ELGAN group had significantly smaller mean head circumference. (Head circumference could not be converted to an age-adjusted z-score due to lack of CDC reference data on head circumference after 36 months of age.)

There were no group differences in the frequency of seizure disorders at the age of 10 years. Based on CSI-4 and CBCL parent-report data, 16.1% of ELGAN participants exhibited clinical levels of anxiety, compared to 47.5% of the SSC sample. The ELGAN group also had a lower percentage of individuals who met the clinical threshold for depression symptoms. There were no group differences in the prevalence of ADHD symptoms.

Table 6. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born children with ASD excluding multiplex ELGAN individuals (n=7) and SSC matches (n=7).

	ELGAN EP			SSC Term			t	p	d
	n	Mean	SD	n	Mean	SD			
Age	52	10.0	0.7	52	10.0	0.6	0.2	.87	0.03
IQ									
Nonverbal IQ	52	70.5	25.8	52	23.6	3.3	0.3	.73	0.07
Verbal IQ	50	62.4	28.8	46	26.1	3.9	2.1	.035	0.4
Social Communication									
ADI-R reciprocal social interaction	50	19.9	7.1	52	21.8	5.5	1.5	.15	0.3
ADI-R nonverbal communication	50	9.1	4.0	52	10.2	3.1	1.5	.13	0.3
ADI-R verbal communication	40	6.2	2.6	44	8.0	2.1	3.5	<.001	0.8
ADI-R B2 social initiation	40	3.3	1.2	44	3.7	0.7	1.9	.066	0.4
ADI-R B3 stereotyped language	40	2.9	1.9	44	4.3	1.7	3.6	<.001	0.8
ADOS-2 module 1/2 social affect	17	14.2	4.0	17	14.2	3.6	0.0	1.00	0.00
ADOS-2 module 3 social affect	35	10.9	4.8	35	9.6	3.1	1.3	.19	0.3
ADOS-2 social affect calibrated severity	52	7.4	2.2	52	7.4	1.7	0.2	.84	0.04
Restricted and repetitive behaviors (RRB)									
ADI-R RRB total	50	4.6	2.8	52	6.9	2.4	4.4	<.001	0.9
ADI-R repetitive sensorimotor (RSM) ¹	50	4.0	2.8	52	5.9	2.5	3.5	<.001	0.7
ADI-R insistence on sameness (IS) ²	50	1.2	1.2	52	2.7	1.6	5.5	<.001	1.1
ADOS-2 module 1/2 RRB total	17	5.0	2.1	17	5.1	2.0	0.2	.87	0.06
ADOS-2 module 3 RRB total	35	3.4	1.9	35	3.5	1.6	0.2	.84	0.05
ADOS-2 RRB calibrated severity	52	7.8	1.9	52	8.0	1.7	0.4	.70	0.08

¹ADI-R items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms. The score of this Repetitive Sensory Motor subscale has a range of 0-10.

²ADI-R items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess insistence on sameness symptoms. The score of this Insistence on Sameness subscale has a range of 0-4.

Table 7. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born children with ASD excluding multiplex ELGAN individuals (n=7) and SSC matches (n=7)

	ELGAN EP ASD	SSC Term ASD	t or X ² , p
Single words > 24 months			
Yes	34 (68.0%)	21 (40.4%)	X ² = 7.82 (p=.005)
No	16 (32.0%)	31 (59.6%)	
Phrase speech > 33 months			
Yes	43 (86.0%)	34 (65.4%)	X ² = 5.9 (p=.016)
No	7 (14.0%)	18 (34.6%)	
Gross motor delay/impairment at age 2¹			
Yes	10 (20.4%)	5 (9.6%)	X ² = 2.3 (p=.13)
No	39 (79.6%)	47 (90.4%)	
Anthropometrics/physical growth measures at age 10			
Head circumference, raw	52.4 (SD=3.0)	54.5 (SD=2.3)	t=4.0 (p<.001)
Height z-score ²	-0.5 (SD=1.1)	0.3 (SD=1.1)	t=3.6 (p<.001)
Weight z-score	-0.2 (SD=1.6)	0.6 (SD=1.2)	t=2.6 (p=.010)
Body mass index z-score	0.02 (SD=1.7)	0.5 (SD=1.4)	t=1.6 (p=.12)
Seizure disorder at age 10			
Yes	7 (13.5%)	4 (7.7%)	X ² = 0.9 (p=.34)
No	45 (86.5%)	48 (92.3%)	
Psychiatric symptoms at age 10³			
ADHD			
T ≥ 65	19 (38.8%)	21 (40.4%)	X ² = 0.03 (p=.87)
T < 65	30 (61.2%)	31 (59.6%)	
Anxiety			
T ≥ 65	8 (16.3%)	25 (48.1%)	X ² = 11.6 (p<.001)
T < 65	41 (83.7%)	27 (51.9%)	
Depression			
T ≥ 65	10 (20.4%)	20 (38.5%)	X ² = 3.9 (p=.047)
T < 65	39 (79.6%)	32 (61.5%)	

¹The Gross Motor Function Classification System (GMFCS) was used to assess gross motor delay/impairment in the ELGAN sample. A score of 0 on the GMFCS indicates no limitations in lower extremity movement. Item 5 of the Autism Diagnostic Interview-Revised (ADI-R) was used to assess gross motor delay in the SSC cohort. On item 5, parents were asked at what age (in months) their child started walking unaided. Children who began walking at 24 months or later were designated as having gross motor delay/impairment. One SSC individual was missing data on ADI-R Item 5.

²Anthropometric z-scores are relative to CDC normative data, which are sex-adjusted and age-adjusted (to the nearest month). One ELGAN participant was missing anthropometric data.

³Three ELGAN participants were missing data on the CSI-4 screener for psychiatric symptoms.

Secondary Analyses

Secondary analyses were performed by removing all multiplex individuals (having a first-degree relative with ASD) from the ELGAN sample, as well as their SSC matches (Tables 6 and 7). All significant group differences observed in primary analyses were maintained in the secondary analyses. No additional significant group differences emerged.

Female-Only Analyses

ELGAN females had significantly lower ADI-R verbal communication scores (Table 8). This group difference was primarily driven by a lower score in stereotypic language. ELGAN females also had significantly lower ADI-R RRB domain scores and significantly lower scores on both Repetitive Sensory Motor and Insistence on Sameness subscales. There were no significant differences between ELGAN females and SSC females on any of the ADOS-2 scores.

ELGAN females demonstrated a significantly smaller average head circumference and shorter height than SSC females (Table 9). They were also more likely to have anxiety symptoms than SSC females. All other comparisons between ELGAN females and SSC females showed no significant group differences.

Table 8. Descriptive statistics for autism symptom measures for extremely preterm (EP) and term born female with ASD

	ELGAN EP			SSC Term			t	p	d
	n	Mean	SD	n	Mean	SD			
Age	20	10.0	0.9	20	10.1	0.6	0.4	.70	0.1
IQ									
Nonverbal IQ	20	72.1	24.7	20	74.1	21.5	0.3	.79	0.09
Verbal IQ	19	65.7	31.2	19	74.3	25.1	0.9	.36	0.3
Social Communication									
ADI-R reciprocal social interaction	19	18.5	8.0	20	20.6	5.6	1.0	.34	0.3
ADI-R nonverbal communication	19	7.7	4.4	20	9.7	3.1	1.6	.12	0.5
ADI-R verbal communication	15	5.3	2.6	19	8.7	2.1	4.2	<.001	1.5
ADI-R B2 social initiation	15	3.2	1.3	19	3.8	0.4	1.7	.12	0.6
ADI-R B3 stereotyped language	15	2.1	1.8	19	4.9	1.9	4.3	<.001	1.5
ADOS-2 module 1/2 social affect	4	11.5	5.5	4	11.0	4.8	0.1	.90	0.1
ADOS-2 module 3 social affect	16	10.4	4.5	16	10.6	3.6	0.2	.86	0.06
ADOS-2 social affect calibrated severity	20	7.1	2.4	20	7.4	1.8	0.5	.61	0.2
Restricted and repetitive behaviors (RRB)									
ADI-R RRB total	19	3.5	2.5	20	6.5	2.2	3.9	<.001	1.3
ADI-R repetitive sensorimotor (RSM) ¹	19	3.4	2.5	20	5.5	2.6	2.6	.012	0.8
ADI-R insistence on sameness (IS) ²	19	0.7	0.9	20	2.8	1.6	4.7	<.001	1.5
ADOS-2 module 1/2 RRB total	4	6.5	1.0	4	4.0	2.0	2.2	.067	1.6
ADOS-2 module 3 RRB total	16	3.1	2.1	16	3.3	1.8	0.4	.72	0.1
ADOS-2 RRB calibrated severity	20	7.5	2.7	20	7.7	1.6	0.4	.73	0.1

¹ADI-R items 67 (unusual preoccupations), 69 (repetitive use of objects or interest in parts of objects), 71 (unusual sensory interests), 77 (hand and finger mannerisms), and 78 (other complex mannerisms or stereotyped body movements) were used to assess Repetitive Sensory Motor symptoms. The score of this Repetitive Sensory Motor subscale has a range of 0-10.

²ADI-R items 68 (circumscribed interests) and 70 (compulsions/rituals) were used to assess insistence on sameness symptoms. The score of this Insistence on Sameness subscale has a range of 0-4.

Table 9. Descriptive statistics for associated characteristics of extremely preterm (EP) and term born females with ASD

	ELGAN EP ASD (n=20)	SSC Term ASD (n=20)	t or X ² , p
Single words > 24 months			X ² = 3.2 (p=.075)
Yes	13 (68.4%)	8 (40%)	
No	6 (31.6%)	12 (60%)	
Phrase speech > 33 months			X ² = 1.6 (p=.20)
Yes	15 (79.0%)	12 (60%)	
No	4 (21.1%)	8 (40%)	
Gross motor delay/impairment at age 2 ¹			X ² = 0.3 (p=.59)
Yes	2 (10%)	3 (15.8%)	
No	18 (90%)	16 (84.2%)	
Anthropometrics/physical growth measures at age 10			
Head circumference, raw	51.7 (SD=2.3)	53.5 (SD=2.2)	t= 2.6 (p=.013)
Height, z-score ²	-0.5 (SD=0.9)	0.4 (SD=1.3)	t=2.6 (p=.014)
Weight, z-score	-0.06 (SD=1.4)	0.2 (SD=1.2)	t=0.7 (p=.51)
Body mass index, z-score	0.3 (SD=1.5)	0.2 (SD=1.0)	t=0.07 (p=.95)
Seizure disorder at age 10			
Yes	3 (15%)	3 (15%)	X ² = 0 (p=1.00)
No	17 (85%)	17 (85%)	
Psychiatric symptoms at age 10			
ADHD			
T ≥ 65	9 (45%)	12 (60%)	X ² = 0.9 (p=.34)
T < 65	11 (55%)	8 (40%)	
Anxiety			
T ≥ 65	3 (15%)	10 (50%)	X ² = 5.6 (p=.018)
T < 65	17 (85%)	10 (50%)	
Depression			
T ≥ 65	5 (25%)	8 (40%)	X ² = 1.0 (p=.31)
T < 65	15 (75%)	12 (60%)	

¹ The Gross Motor Function Classification System (GMFCS) was used to assess gross motor delay/impairment in the ELGAN sample. A score of 0 on the GMFCS indicates no limitations in lower extremity movement. Item 5 of the Autism Diagnostic Interview-Revised (ADI-R) was used to assess gross motor delay in the SSC cohort. On item 5, parents were asked at what age (in months) their child started walking unaided. Children who began walking at 24 months or later were designated as having gross motor delay/impairment. One SSC individual was missing data on ADI-R Item 5.

²Anthropometric z-scores are relative to CDC normative data, which are sex-adjusted and age-adjusted (to the nearest month). One ELGAN participant was missing anthropometric data.

DISCUSSION

The principal goal of this study was to identify similarities and differences in ASD symptoms between children born extremely preterm and children born at term who were matched for age, sex, and nonverbal IQ. The second goal was to examine characteristics commonly associated with ASD in term-born children, such as delayed developmental milestones, seizure disorders, and psychiatric symptoms, within an extremely preterm-born sample. Furthermore, we were interested in whether simplex/multiplex status or sex would influence any group differences in ASD symptoms or associated characteristics.

Regarding core ASD symptoms, whereas the ELGAN EP and SSC term groups did not differ in their social affect and restricted, repetitive behaviors scores as assessed at age 10 years on the basis of the ADOS-2, there were some differences between cohorts on the parent-reported symptoms as determined by the ADI-R. These differences related to the parent-report of verbal communication, specifically the use of stereotypic language, and restricted, repetitive behaviors, for which the ELGAN EP group exhibited lower scores. The ELGAN EP and SSC term groups did not differ on the ADI-R for nonverbal communication and reciprocal interaction scores or for the repetitive, restricted behavior scores.

Regarding the presence of associated characteristics, significant differences were found in developmental language milestones, height z-score, weight z-score, and head circumference, as well as anxiety and depression symptoms. The ELGAN EP sample demonstrated higher rates of delayed acquisition of single word speech (> 24 months)

and phrase speech (> 33 months). However, the EP and term groups did not differ in their rates of gross motor delay/impairment at the age of 2 years. At age 10, the EP group showed a lower height z-score, weight z-score, and head circumference, but the two groups did not differ on their BMI z-score. The ELGAN EP group had a lower prevalence of clinical anxiety and depression symptoms. However, the EP and term groups did not differ on ADHD symptoms or seizure disorder prevalence. These results did not change when multiplex individuals and their matched SSC subjects were excluded.

Results from the female-only analyses were also similar to the findings from the total sample. Differences in the ADI-R verbal communication and repetitive and restricted behavior domains, height z-score, head circumference, and anxiety symptoms scores persisted from the primary analyses. However, in contrast to primary and simplex-only analyses, there were no differences in speech developmental milestones, weight z-scores, or depression symptoms.

Differences in ASD symptomatology between term-born and preterm-born children have previously been explored in the literature, albeit with younger children. However, these previous studies have primarily studied moderate to late preterm-born individuals. The null finding on ADOS-2 domain scores is consistent with previous studies conducted with children aged 2 years and 5 years (Chen et al., 2019; Luu et al., 2020). Brayette et al. (2019) did not find any differences in ASD symptomatology between term and moderate-to-late preterm groups on clinician-report measures, but this study did not match groups on IQ, and the preterm and early term groups had

significantly lower nonverbal IQ than the full-term group. Chen et al. (2019) only found significant differences on the ADI-R in reciprocal social interaction, whereas findings from the present study demonstrated differences on the ADI-R in verbal communication and RRBs, and no group differences were noted in reciprocal social interaction.

One potential explanation for the discrepancy in parent-report findings from the ADI-R and the clinical-observation findings from the ADOS-2 may be related to the difference in recruitment strategies between the SSC and ELGAN cohorts. SSC participants were recruited based on having a prior clinical diagnosis of ASD (Fischbach & Lord, 2010). In contrast, only 64% (n=38) of ELGAN participants had a prior ASD diagnosis. Because ADI-R diagnostic algorithm scores are based on whether the symptom was present at ages 4-5 or whether the child had ever exhibited a given symptom, parents of children with a prior ASD diagnosis may have been more primed to identify symptoms, particularly stereotypic language and repetitive and restricted behaviors. We investigated this possibility and found that parents of the ELGAN children were much more likely to report these symptoms when their child had a prior clinical diagnosis. However, although the group differences were smaller, ELGAN EP participants with a prior clinical ASD diagnosis still had lower rates of stereotypic language (in the verbal communication domain) as well as repetitive, restricted behaviors as measured by ADI-R parent report. This suggests the possibility of a difference in the developmental ASD symptom phenotype of children born extremely preterm.

The group differences in anthropometrics observed in this study are consistent with previous studies of the overall EP-born population. While children born extremely

preterm do reach normal height and weight (standard deviation scores of -2.0 or higher), their heights and weights are consistently lower than those of term peers from early childhood to late adolescence (Ni et al., 2021; Roberts et al., 2013). Although the difference in weight z-scores gradually decreases across childhood, the difference in height z-scores remains consistent in magnitude (Roberts et al., 2013). Children born preterm also have shorter heights than expected based on their parents' heights (Rowe et al., 2011). Although age-adjusted z-scores could not be calculated for head circumference in this study, due to lack of HC reference data after the age of 3 years in the United States, mean differences in raw HC were similar to those reported for a UK cohort of children born extremely preterm (Ni et al., 2021). This difference in raw HC corresponded to a z-score difference of 1.05 standard deviations, based on UK normative data (Ni et al., 2021). However, it should be noted that while HC is positively associated with neurodevelopmental outcomes within the general population (Jaekel et al., 2019), larger HC is associated with greater ASD symptom severity among individuals with simplex ASD (Chaste et al., 2013).

Findings on language and motor developmental milestones are also relatively consistent with previously reported data. Among national cohorts of EP children, there are greater rates of language and motor delays (Månsson & Stjernqvist, 2014; Serenius et al., 2013). Although this study did not find differences in the prevalence of motor developmental delay, this may be due to our use of a relatively gross measure of walking unaided at the age of 24 months. High prevalence of delayed phrase speech acquisition has previously been reported within the SSC cohort (Wodka et al., 2013).

The increased risk of ASD associated with preterm birth may be partially accounted for by disruptions in prenatal environment. Maternal infection and subsequent inflammatory response are major risk factors for spontaneous preterm birth (Cappelletti et al., 2016; Meldrum et al., 2013), and these factors have also been associated with an increased ASD risk (Meltzer & Van De Water, 2017). In a national cohort, an inpatient diagnosis of maternal infection was associated with a 30% increased ASD risk (Lee et al., 2015). One potential explanation for the relationship between maternal immune response and increased ASD risk is elevated cytokines in response to maternal inflammation, which can influence neurological development (Jones et al., 2017; Meltzer & Van De Water, 2017). Infants born extremely preterm are at particular risk of neurological injury, as their developing brains are particularly vulnerable to increased inflammation (Meldrum et al., 2013).

Additionally, placental dysfunction or failure has also been associated with an increased prevalence of ASD and other neuropsychiatric disorders (Kratimenos & Penn, 2019). Placentas from ASD patients have less diffuse vasculature and are thicker and rounder than placentas from neurotypical controls (Chang et al., 2017; Park et al., 2018). The premature loss of placental support during spontaneous preterm birth may contribute to neurodevelopmental impairment (Kratimenos & Penn, 2019). Future studies that account for prenatal and perinatal factors, such as maternal inflammation or placental dysfunction, are needed to assess how disruptions in the maternal environment can affect ASD symptom presentation in children born preterm. In addition, future studies should also investigate potential differences between spontaneous preterm birth and medically

indicated preterm birth. However, the role of these environmental factors does not rule out the possibility that children born extremely preterm may also be at genetic risk for ASD.

Study Strengths and Limitations

Strengths of this study include the use of gold-standard ASD diagnostic measures, such as the ADI-R and ADOS-2, as well as the matching of multiple potential confounds, such as age, sex, and nonverbal IQ. Although the sample size of this study was relatively small, the sample size was larger or similar to those of previous papers (Brayette et al., 2019; Chen et al., 2019; Luu et al., 2020) investigating ASD phenotype in children born preterm versus born at term. There is the possibility that some of the null findings in the female-only analyses were the result of decreased statistical power from reduced sample size. Future studies with larger samples of female preterm-born participants are needed to further investigate sex differences in phenotype within children with ASD born preterm.

One weakness of this study was the use of different measures between the two groups of subjects for certain associated characteristics, such as using the CSI-4 and CBCL to measure psychiatric symptoms for the ELGAN and SSC cohorts, respectively. This was due to the use of different measures between the two research databases, which may not be fully comparable. Future research using identical measures and similar recruitment strategies for EP and term samples are needed to confirm the findings from the present study. Longitudinal studies comparing symptoms and associated characteristics at multiple time-points may also help to reconcile the disparate findings between studies of differently aged cohorts.

Recent findings suggest that verbal IQ has the strongest inverse association with ASD symptom severity, rather than nonverbal IQ or the difference between nonverbal and verbal IQ (Johnson et al., 2021). The two groups in this study were not matched on verbal IQ, and the ELGAN group had significantly lower verbal IQ. However, given the inverse association between verbal IQ and symptom severity, the SSC cohort having a higher verbal IQ would have been expected to have less severe symptoms, rather than more severe symptoms. Furthermore, Johnson et al. (2021) found that verbal IQ was inversely associated with ADOS-2 communication symptoms and was not associated with any ADI-R measures, whereas this study had null findings on all ADOS-2 scores.

Clinical Implications

Children born preterm are at increased risk of developing ASD, especially those born very or extremely preterm (Crump et al., 2021). In addition to low gestational age, perinatal factors such as maternal infection or inflammation may further increase risk for ASD (Joseph et al., 2016; Meltzer & Van De Water, 2017). Therefore, clinicians who work with young children born preterm should monitor for ASD symptoms at early ages, in order to facilitate early ASD interventions, and throughout childhood, given the high false-positive rate in screening preterm-born infants and toddlers for ASD (Cogley et al., 2021; Yaari et al., 2016). Clinicians should consider potential differences in ASD phenotype within the preterm population, as well as overlapping phenotypes of any co-occurring conditions.

Conclusions

Retrospective parent report on the ADI-R showed lower severity in stereotypic language and repetitive, restricted behaviors in the EP group. However, observational assessments at age 10 years with the ADOS-2 did not show any differences between the EP and term born samples. Parents of children with a prior ASD diagnosis may have more sensitive recall of ASD symptoms compared to parents of children without a prior ASD diagnosis, due to greater familiarity with ASD symptomatology. This potential explanation was supported by more severe parent-reported symptoms in the EP group with a prior clinical diagnosis compared to EP children without a prior clinical diagnosis. However, when analyses were conducted only with children who had a prior ASD diagnosis, the EP group still had less severe parent-reported stereotyped language and RRB symptoms. Apart from these parent-reported symptoms, ASD symptom presentation was overall similar between EP-born and term-born children. The EP group in this study also had decreased physical growth parameters and more delayed language milestones, consistent with more general studies of the EP-born population. Future investigations with larger sample sizes (particularly for females) and multiple time-points of data collection should be conducted to investigate possible differences in repetitive and restricted behaviors, including stereotypic language.

REFERENCES

- Achenbach, T. M., & Rescorla, L. A. (2001). *Manual for the ASEBA school-age forms & profiles: an integrated system of multi-informant assessment* Burlington, VT: University of Vermont. *Research Center for Children, Youth, & Families*.
- Agrawal, S., Rao, S. C., Bulsara, M. K., & Patole, S. K. (2018, September 1). Prevalence of autism spectrum disorder in preterm infants: A meta-Analysis. *Pediatrics*. American Academy of Pediatrics. <https://doi.org/10.1542/peds.2018-0134>
- Ament, K., Mejia, A., Buhlman, R., Erklin, S., Caffo, B., Mostofsky, S., & Wodka, E. (2015). Evidence for Specificity of Motor Impairments in Catching and Balance in Children with Autism. *Journal of Autism and Developmental Disorders*, 45(3), 742–751. <https://doi.org/10.1007/s10803-014-2229-0>
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). <https://doi.org/10.1176/appi.books.9780890425596>
- Anderson, P. J. (2014). Neuropsychological outcomes of children born very preterm. *Seminars in Fetal and Neonatal Medicine*. W.B. Saunders Ltd. <https://doi.org/10.1016/j.siny.2013.11.012>
- Antshel, K. M., & Russo, N. (2019, May 1). Autism Spectrum Disorders and ADHD: Overlapping Phenomenology, Diagnostic Issues, and Treatment Considerations. *Current Psychiatry Reports*. Current Medicine Group LLC 1. <https://doi.org/10.1007/s11920-019-1020-5>
- Antshel, K. M., Zhang-James, Y., Wagner, K. E., Ledesma, A., & Faraone, S. V. (2016, March 3). An update on the comorbidity of ADHD and ASD: A focus on clinical management. *Expert Review of Neurotherapeutics*. Taylor and Francis Ltd. <https://doi.org/10.1586/14737175.2016.1146591>
- Bai, D., Yip, B. H. K., Windham, G. C., Sourander, A., Francis, R., Yoffe, R., ... Sandin, S. (2019). Association of Genetic and Environmental Factors with Autism in a 5-Country Cohort. *JAMA Psychiatry*, 76(10), 1035–1043. <https://doi.org/10.1001/jamapsychiatry.2019.1411>
- Bhat, A. N., Landa, R. J., & Galloway, J. C. (2011). Current perspectives on motor functioning in infants, children, and adults with autism spectrum disorders. *Physical Therapy*, 91(7), 1116–1129. <https://doi.org/10.2522/ptj.20100294>
- Bhat, A. N. (2020). Is Motor Impairment in Autism Spectrum Disorder Distinct from Developmental Coordination Disorder A Report from the SPARK Study. *Physical Therapy*, 100(4), 633–644. <https://doi.org/10.1093/ptj/pzz190>

- Bishop, S. L., Hus, V., Duncan, A., Huerta, M., Gotham, K., Pickles, A., ... Lord, C. (2013). Subcategories of restricted and repetitive behaviors in children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 43(6), 1287–1297. <https://doi.org/10.1007/s10803-012-1671-0>
- Bolton, P. F., Carcani-Rathwell, I., Hutton, J., Goode, S., Howlin, P., & Rutter, M. (2011). Epilepsy in autism: Features and correlates. *British Journal of Psychiatry*, 198(4), 289–294. <https://doi.org/10.1192/bjp.bp.109.076877>
- Bowers, K., Wink, L. K., Pottenger, A., McDougale, C. J., & Erickson, C. (2015). Phenotypic differences in individuals with autism spectrum disorder born preterm and at term gestation. *Autism*, 19(6), 758–763. <https://doi.org/10.1177/1362361314547366>
- Bowers, K., Wink, L. K., Pottenger, A., McDougale, C. J., & Erickson, C. (2015). Phenotypic differences in individuals with autism spectrum disorder born preterm and at term gestation. *Autism*, 19(6), 758–763. <https://doi.org/10.1177/1362361314547366>
- Brayette, M., Saliba, E., Malvy, J., Blanc, R., Ponson, L., Tripi, G., ... Bonnet-Brilhault, F. (2019). Incomplete Gestation has an Impact on Cognitive Abilities in Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders*, 49(10), 4339–4345. <https://doi.org/10.1007/s10803-019-04105-x>
- Cappelletti, M., Della Bella, S., Ferrazzi, E., Mavilio, D., & Divanovic, S. (2016). Inflammation and preterm birth. *Journal of Leukocyte Biology*, 99(1), 67–78. <https://doi.org/10.1189/jlb.3mr0615-272rr>
- Centers for Disease Control and Prevention (2009, August 4). *Growth Charts – Percentile Data Files with LMS values*. Centers for Disease Control and Prevention. https://www.cdc.gov/growthcharts/percentile_data_files.htm
- Chang, J. M., Zeng, H., Han, R., Chang, Y. M., Shah, R., Salafia, C. M., ... Croen, L. (2017). Autism risk classification using placental chorionic surface vascular network features. *BMC Medical Informatics and Decision Making*, 17(1), 162. <https://doi.org/10.1186/s12911-017-0564-8>
- Chaste, P., Klei, L., Sanders, S. J., Murtha, M. T., Hus, V., Lowe, J. K., ... Kim, S. J. (2013). Adjusting head circumference for covariates in autism: Clinical correlates of a highly heritable continuous trait. *Biological Psychiatry*, 74(8), 576–584. <https://doi.org/10.1016/j.biopsych.2013.04.018>

- Chawarska, K., Campbell, D., Chen, L., Shic, F., Klin, A., & Chang, J. (2011). Early generalized overgrowth in boys with autism. *Archives of General Psychiatry*, *68*(10), 1021–1031. <https://doi.org/10.1001/archgenpsychiatry.2011.106>
- Chen, L. W., Wang, S. T., Wang, L. W., Kao, Y. C., Chu, C. L., Wu, C. C., ... Huang, C. C. (2019). Behavioral characteristics of autism spectrum disorder in very preterm birth children. *Molecular Autism*, *10*(1). <https://doi.org/10.1186/s13229-019-0282-4>
- Christensen, D., Maenner, M., Bilder, D., Constantino, J., Daniels, J., Durkin, M., ... Dietz, P. (2019). Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 4 Years — Early Autism and Developmental Disabilities Monitoring Network, Seven Sites, United States, 2010, 2012, and 2014. *MMWR Surveillance Summaries*, *68*(2), 1–19. <https://doi.org/10.15585/mmwr.ss6802a1>
- Cogley, C., O'Reilly, H., Bramham, J., & Downes, M. (2021). A Systematic Review of the Risk Factors for Autism Spectrum Disorder in Children Born Preterm. *Child Psychiatry and Human Development*, *52*(5), 841–855. <https://doi.org/10.1007/s10578-020-01071-9>
- Corsello, C. M., Akshoomoff, N., & Stahmer, A. C. (2013). Diagnosis of autism spectrum disorders in 2-year-olds: A study of community practice. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *54*(2), 178–185. <https://doi.org/10.1111/j.1469-7610.2012.02607.x>
- Craig, F., Margari, F., Legrottaglie, A. R., Palumbi, R., de Giambattista, C., & Margari, L. (2016, May 12). A review of executive function deficits in autism spectrum disorder and attention-deficit/hyperactivity disorder. *Neuropsychiatric Disease and Treatment*. Dove Medical Press Ltd. <https://doi.org/10.2147/NDT.S104620>
- Crump, C., Sundquist, J., & Sundquist, K. (2021). Preterm or early term birth and risk of autism. *Pediatrics*, *148*(3). <https://doi.org/10.1542/peds.2020-032300>
- Davis, J. M., Keeney, J. G., Sikela, J. M., & Hepburn, S. (2013). Mode of Genetic Inheritance Modifies the Association of Head Circumference and Autism-Related Symptoms: A Cross-Sectional Study. *PLoS ONE*, *8*(9). <https://doi.org/10.1371/journal.pone.0074940>
- Douglass, L. M., Heeren, T. C., Stafstrom, C. E., DeBassio, W., Allred, E. N., Leviton, A., ... Kuban, K. (2017). Cumulative Incidence of Seizures and Epilepsy in Ten-Year-Old Children Born Before 28 Weeks' Gestation. *Pediatric Neurology*, *73*, 13–19. <https://doi.org/10.1016/j.pediatrneurol.2017.05.009>
- Eigsti, I. M., De Marchena, A. B., Schuh, J. M., & Kelley, E. (2011, April). Language acquisition in autism spectrum disorders: A developmental review. *Research in*

Autism Spectrum Disorders. <https://doi.org/10.1016/j.rasd.2010.09.001>

El Achkar, C. M., & Spence, S. J. (2015, June 1). Clinical characteristics of children and young adults with co-occurring autism spectrum disorder and epilepsy. *Epilepsy and Behavior*. Academic Press Inc. <https://doi.org/10.1016/j.yebeh.2014.12.022>

Elliott, C.D. (2007). *Differential Ability Scales* (2nd ed.). San Antonio, Texas: Pearson.

Ferri, S. L., Abel, T., & Brodtkin, E. S. (2018). Sex Differences in Autism Spectrum Disorder: a Review. *Current Psychiatry Reports*, 20(2). <https://doi.org/10.1007/s11920-018-0874-2>

Fischbach, G. D., & Lord, C. (2010, October 21). The simons simplex collection: A resource for identification of autism genetic risk factors. *Neuron*. <https://doi.org/10.1016/j.neuron.2010.10.006>

Fitzallen, G. C., Taylor, H. G., & Bora, S. (2020, March 25). What Do We Know About the Preterm Behavioral Phenotype? A Narrative Review. *Frontiers in Psychiatry*. Frontiers Media S.A. <https://doi.org/10.3389/fpsy.2020.00154>

Flanagan, J. E., Landa, R., Bhat, A., & Bauman, M. (2012). Head lag in infants at risk for autism: A preliminary study. *American Journal of Occupational Therapy*, 66(5), 577–585. <https://doi.org/10.5014/ajot.2012.004192>

Fournier, K. A., Hass, C. J., Naik, S. K., Lodha, N., & Cauraugh, J. H. (2010). Motor coordination in autism spectrum disorders: A synthesis and meta-analysis. *Journal of Autism and Developmental Disorders*, 40(10), 1227–1240. <https://doi.org/10.1007/s10803-010-0981-3>

Flegal, K. M., & Cole, T. J. (2013). Construction of LMS parameters for the Centers for Disease Control and Prevention 2000 growth charts. *National Health Statistics Reports*, (63), 1–4.

Frazier, T. W., Georgiades, S., Bishop, S. L., & Hardan, A. Y. (2014). Behavioral and cognitive characteristics of females and males with autism in the simons simplex collection. *Journal of the American Academy of Child and Adolescent Psychiatry*, 53(3). <https://doi.org/10.1016/j.jaac.2013.12.004>

Gadow KD, S. J. (2002). *Child Symptom Inventory 4: Screening and Norms Manual*. Tony Brook, NY: Checkmate Plus.

Gotham, K., Brunwasser, S. M., & Lord, C. (2015). Depressive and anxiety symptom trajectories from school age through young adulthood in samples with autism spectrum disorder and developmental delay. *Journal of the American Academy of*

Child and Adolescent Psychiatry, 54(5), 369-376.e3.
<https://doi.org/10.1016/j.jaac.2015.02.005>

Gotham, K., Pickles, A., & Lord, C. (2009). Standardizing ADOS scores for a measure of severity in autism spectrum disorders. *Journal of Autism and Developmental Disorders*, 39(5), 693–705. <https://doi.org/10.1007/s10803-008-0674-3>

Grzadzinski, R., Dick, C., Lord, C., & Bishop, S. (2016). Parent-reported and clinician-observed autism spectrum disorder (ASD) symptoms in children with attention deficit/hyperactivity disorder (ADHD): Implications for practice under DSM-5. *Molecular Autism*, 7(1). <https://doi.org/10.1186/s13229-016-0072-1>

Hyman, S. L., Levy, S. E., Myers, S. M., Kuo, D. Z., Apkon, C. S., Davidson, L. F., ... Paul, L. (2020). Identification, evaluation, and management of children with autism spectrum disorder. *Pediatrics*, 145(1). <https://doi.org/10.1542/PEDS.2019-3447>

Jaekel, J., Sorg, C., Baeuml, J., Bartmann, P., & Wolke, D. (2019). Head growth and intelligence from birth to adulthood in very preterm and term born individuals. *Journal of the International Neuropsychological Society*, 25(1), 48–56. <https://doi.org/10.1017/S135561771800084X>

Johnson, C. N., Ramphal, B., Koe, E., Raudales, A., Goldsmith, J., & Margolis, A. E. (2021). Cognitive correlates of autism spectrum disorder symptoms. *Autism Research*, 14(11), 2405–2411. <https://doi.org/10.1002/aur.2577>

Jokiranta, E., Sourander, A., Suominen, A., Timonen-Soivio, L., Brown, A. S., & Sillanpää, M. (2014). Epilepsy among children and adolescents with autism spectrum disorders: A population-based study. *Journal of Autism and Developmental Disorders*, 44(10), 2547–2557. <https://doi.org/10.1007/s10803-014-2126-6>

Jones, K. L., Croen, L. A., Yoshida, C. K., Heuer, L., Hansen, R., Zerbo, O., ... Van De Water, J. (2017). Autism with intellectual disability is associated with increased levels of maternal cytokines and chemokines during gestation. *Molecular Psychiatry*, 22(2), 273–279. <https://doi.org/10.1038/mp.2016.77>

Joseph, R. M., Korzeniewski, S. J., Allred, E. N., O’Shea, T. M., Heeren, T., Frazier, J. A., ... Vogt, K. (2017). Extremely low gestational age and very low birthweight for gestational age are risk factors for autism spectrum disorder in a large cohort study of 10-year-old children born at 23-27 weeks’ gestation. *American Journal of Obstetrics and Gynecology*, 216(3), 304.e1-304.e16. <https://doi.org/10.1016/j.ajog.2016.11.1009>

- Joseph, R. M., O'Shea, T. M., Allred, E. N., Heeren, T., Hirtz, D., Jara, H., ... Kuban, K. C. K. (2016). Neurocognitive and academic outcomes at age 10 years of extremely preterm newborns. *Pediatrics*, *137*(4). <https://doi.org/10.1542/peds.2015-4343>
- Joseph, R. M., O'Shea, T. M., Allred, E. N., Heeren, T., Hirtz, D., Paneth, N., ... Kuban, K. C. K. (2017). Prevalence and associated features of autism spectrum disorder in extremely low gestational age newborns at age 10 years. *Autism Research*, *10*(2), 224–232. <https://doi.org/10.1002/aur.1644>
- Kaat, A. J., Shui, A. M., Ghods, S. S., Farmer, C. A., Esler, A. N., Thurm, A., ... Bishop, S. L. (2021). Sex differences in scores on standardized measures of autism symptoms: a multisite integrative data analysis. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *62*(1), 97–106. <https://doi.org/10.1111/jcpp.13242>
- Kaur, M., M. Srinivasan, S., & N. Bhat, A. (2018). Comparing motor performance, praxis, coordination, and interpersonal synchrony between children with and without Autism Spectrum Disorder (ASD). *Research in Developmental Disabilities*, *72*, 79–95. <https://doi.org/10.1016/j.ridd.2017.10.025>
- Kerns, C. M., Kendall, P. C., Berry, L., Souders, M. C., Franklin, M. E., Schultz, R. T., ... Herrington, J. (2014). Traditional and atypical presentations of anxiety in youth with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *44*(11), 2851–2861. <https://doi.org/10.1007/s10803-014-2141-7>
- Kerr-Wilson, C. O., MacKay, D. F., Smith, G. C. S., & Pell, J. P. (2012). Meta-analysis of the association between preterm delivery and intelligence. *Journal of Public Health (United Kingdom)*, *34*(2), 209–216. <https://doi.org/10.1093/pubmed/fdr024>
- Knutsen, J., Crossman, M., Perrin, J., Shui, A., & Kuhlthau, K. (2019). Sex differences in restricted repetitive behaviors and interests in children with autism spectrum disorder: An Autism Treatment Network study. *Autism*, *23*(4), 858–868. <https://doi.org/10.1177/1362361318786490>
- Kratimenos, P., & Penn, A. A. (2019, August 1). Placental programming of neuropsychiatric disease. *Pediatric Research*. Nature Publishing Group. <https://doi.org/10.1038/s41390-019-0405-9>
- Lai, M. C., Lombardo, M. V., Auyeung, B., Chakrabarti, B., & Baron-Cohen, S. (2015, January 1). Sex/Gender Differences and Autism: Setting the Scene for Future Research. *Journal of the American Academy of Child and Adolescent Psychiatry*. Elsevier Inc. <https://doi.org/10.1016/j.jaac.2014.10.003>
- LeBarton, E. S., & Landa, R. J. (2019). Infant motor skill predicts later expressive language and autism spectrum disorder diagnosis. *Infant Behavior and*

Development, 54, 37–47. <https://doi.org/10.1016/j.infbeh.2018.11.003>

- Le Couteur, A., Lord, C., & Rutter, M. (2003). The autism diagnostic interview-revised (ADI-R). Los Angeles, CA: Western Psychological Services.
- Lee, B. K., Magnusson, C., Gardner, R. M., Blomström, Å., Newschaffer, C. J., Burstyn, I., ... Dalman, C. (2015). Maternal hospitalization with infection during pregnancy and risk of autism spectrum disorders. *Brain, Behavior, and Immunity*, 44, 100–105. <https://doi.org/10.1016/j.bbi.2014.09.001>
- Levy, S. E., Giarelli, E., Lee, L. C., Schieve, L. A., Kirby, R. S., Cunniff, C., ... Rice, C. E. (2010). Autism spectrum disorder and co-occurring developmental, psychiatric, and medical conditions among children in multiple populations of the United States. *Journal of Developmental and Behavioral Pediatrics*, 31(4), 267–275. <https://doi.org/10.1097/DBP.0b013e3181d5d03b>
- Licari, M. K., Alvares, G. A., Varcin, K., Evans, K. L., Cleary, D., Reid, S. L., ... Whitehouse, A. J. O. (2020). Prevalence of Motor Difficulties in Autism Spectrum Disorder: Analysis of a Population-Based Cohort. *Autism Research*, 13(2), 298–306. <https://doi.org/10.1002/aur.2230>
- Loomes, R., Hull, L., & Mandy, W. P. L. (2017, June 1). What Is the Male-to-Female Ratio in Autism Spectrum Disorder? A Systematic Review and Meta-Analysis. *Journal of the American Academy of Child and Adolescent Psychiatry*. Elsevier Inc. <https://doi.org/10.1016/j.jaac.2017.03.013>
- Lord, C., Petkova, E., Hus, V., Gan, W., Lu, F., Martin, D. M., ... Risi, S. (2012). A multisite study of the clinical diagnosis of different autism spectrum disorders. *Archives of General Psychiatry*, 69(3), 306–313. <https://doi.org/10.1001/archgenpsychiatry.2011.148>
- Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S. L. (2012). Autism diagnostic observation schedule, (ADOS-2) modules 1-4. Los Angeles, California: Western Psychological Services.
- Luu, J., Jellett, R., Yaari, M., Gilbert, M., & Barbaro, J. (2020). A Comparison of Children Born Preterm and Full-Term on the Autism Spectrum in a Prospective Community Sample. *Frontiers in Neurology*, 11. <https://doi.org/10.3389/fneur.2020.597505>
- Maenner, M. J., Shaw, K. A., Baio, J., Washington, A., Patrick, M., DiRienzo, M., ... Dietz, P. M. (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(4), 1–12.

<https://doi.org/10.15585/MMWR.SS6904A1>

- Månsson, J., & Stjernqvist, K. (2014). Children born extremely preterm show significant lower cognitive, language and motor function levels compared with children born at term, as measured by the Bayley-III at 2.5 years. *Acta Paediatrica, International Journal of Paediatrics*, *103*(5), 504–511. <https://doi.org/10.1111/apa.12585>
- Martin, J. A., Hamilton, B. E., Osterman, M. J. K., Driscoll, A. K., Schwartz, S., & Horon, I. (2021). Births: Final data for 2019. *National Vital Statistics Reports*, *70*(2).
- Masi, A., DeMayo, M. M., Glozier, N., & Guastella, A. J. (2017, April 1). An Overview of Autism Spectrum Disorder, Heterogeneity and Treatment Options. *Neuroscience Bulletin*. Science Press. <https://doi.org/10.1007/s12264-017-0100-y>
- Mayes, S. D., & Calhoun, S. L. (2011). Impact of IQ, age, SES, gender, and race on autistic symptoms. *Research in Autism Spectrum Disorders*, *5*(2), 749–757. <https://doi.org/10.1016/j.rasd.2010.09.002>
- McElrath, T. F., Allred, E. N., Kuban, K., Hecht, J. L., Onderdonk, A., O’Shea, T. M., ... Leviton, A. (2010). Factors associated with small head circumference at birth among infants born before the 28th week. *American Journal of Obstetrics and Gynecology*, *203*(2), 138.e1-138.e8. <https://doi.org/10.1016/j.ajog.2010.05.006>
- Meldrum, S. J., Strunk, T., Currie, A., Prescott, S. L., Simmer, K., & Whitehouse, A. J. O. (2013). Autism spectrum disorder in children born preterm-role of exposure to perinatal inflammation. *Frontiers in Neuroscience*. Frontiers Research Foundation. <https://doi.org/10.3389/fnins.2013.00123>
- Meltzer, A., & Van De Water, J. (2017, January 1). The Role of the Immune System in Autism Spectrum Disorder. *Neuropsychopharmacology*. Nature Publishing Group. <https://doi.org/10.1038/npp.2016.158>
- Moore, P. S., Mokrova, I., Frazier, J. A., Joseph, R. M., Santos, H. P., Dvir, Y., ... Kuban, K. C. K. (2021). Anxiety and Depression Correlates at Age 10 in Children Born Extremely Preterm. *Journal of Pediatric Psychology*, *46*(4), 422–432. <https://doi.org/10.1093/jpepsy/jsaa118>
- Muhle, R. A., Reed, H. E., Stratigos, K. A., & Veenstra-VanderWeele, J. (2018, May 1). The emerging clinical neuroscience of autism spectrum disorder a review. *JAMA Psychiatry*. American Medical Association. <https://doi.org/10.1001/jamapsychiatry.2017.4685>
- Ni, Y., Lancaster, R., Suonpera, E., Bernardi, M., Fahy, A., Larsen, J., ... Marlow, N. (2021). Growth in extremely preterm children born in England in 1995 and 2006:

- The EPICure studies. *Archives of Disease in Childhood: Fetal and Neonatal Edition*, F1–F8. <https://doi.org/10.1136/archdischild-2020-321107>
- Norrelgen, F., Fernell, E., Eriksson, M., Hedvall, Å., Persson, C., Sjölin, M., ... Kjellmer, L. (2015). Children with autism spectrum disorders who do not develop phrase speech in the preschool years. *Autism*, *19*(8), 934–943. <https://doi.org/10.1177/1362361314556782>
- O’Shea, T. M., Allred, E. N., Dammann, O., Hirtz, D., Kuban, K. C. K., Paneth, N., & Leviton, A. (2009). The ELGAN study of the brain and related disorders in extremely low gestational age newborns. *Early Human Development*, *85*(11), 719–725. <https://doi.org/10.1016/j.earlhumdev.2009.08.060>
- Palisano, R. J., Hanna, S. E., Rosenbaum, P. L., Russell, D. J., Walter, S. D., Wood, E. P., ... Galuppi, B. E. (2000). Validation of a model of gross motor function for children with cerebral palsy. *Physical Therapy*, *80*(10), 974–985. <https://doi.org/10.1093/ptj/80.10.974>
- Pan, P. Y., Bölte, S., Kaur, P., Jamil, S., & Jonsson, U. (2021). Neurological disorders in autism: A systematic review and meta-analysis. *Autism*, *25*(3), 812–830. <https://doi.org/10.1177/1362361320951370>
- Park, B. Y., Misra, D. P., Moye, J., Miller, R. K., Croen, L., Dani Fallin, M., ... Salafia, C. M. (2018). Placental gross shape differences in a high autism risk cohort and the general population. *PLoS ONE*, *13*(8). <https://doi.org/10.1371/journal.pone.0191276>
- Peralta-Carcelen, M., Schwartz, J., & Carcelen, A. C. (2018, September 1). Behavioral and Socioemotional Development in Preterm Children. *Clinics in Perinatology*. W.B. Saunders. <https://doi.org/10.1016/j.clp.2018.05.003>
- Pezzimenti, F., Han, G. T., Vasa, R. A., & Gotham, K. (2019, July 1). Depression in Youth with Autism Spectrum Disorder. *Child and Adolescent Psychiatric Clinics of North America*. W.B. Saunders. <https://doi.org/10.1016/j.chc.2019.02.009>
- Risi, S., Lord, C., Gotham, K., Corsello, C., Chrysler, C., Szatmari, P., ... Pickles, A. (2006). Combining information from multiple sources in the diagnosis of autism spectrum disorders. *Journal of the American Academy of Child and Adolescent Psychiatry*, *45*(9), 1094–1103. <https://doi.org/10.1097/01.chi.0000227880.42780.0e>
- Roberts, G., Cheong, J., Opie, G., Carse, E., Davis, N., Duff, J., ... Doyle, L. (2013). Growth of extremely preterm survivors from birth to 18 years of age compared with term controls. *Pediatrics*, *131*(2). <https://doi.org/10.1542/peds.2012-1135>
- Robertson, J., Hatton, C., Emerson, E., & Baines, S. (2015, July 1). Prevalence of

- epilepsy among people with intellectual disabilities: A systematic review. *Seizure*. W.B. Saunders Ltd. <https://doi.org/10.1016/j.seizure.2015.03.016>
- Rose, V., Trembath, D., Keen, D., & Paynter, J. (2016). The proportion of minimally verbal children with autism spectrum disorder in a community-based early intervention programme. *Journal of Intellectual Disability Research*, *60*(5), 464–477. <https://doi.org/10.1111/jir.12284>
- Rosen, T. E., Mazefsky, C. A., Vasa, R. A., & Lerner, M. D. (2018, January 2). Co-occurring psychiatric conditions in autism spectrum disorder. *International Review of Psychiatry*. Taylor and Francis Ltd. <https://doi.org/10.1080/09540261.2018.1450229>
- Rowe, D. L., Derraik, J. G. B., Robinson, E., Cutfield, W. S., & Hofman, P. L. (2011). Preterm birth and the endocrine regulation of growth in childhood and adolescence. *Clinical Endocrinology*, *75*(5), 661–665. <https://doi.org/10.1111/j.1365-2265.2011.04116.x>
- Russell, G., Mandy, W., Elliott, D., White, R., Pittwood, T., & Ford, T. (2019, March 1). Selection bias on intellectual ability in autism research: A cross-sectional review and meta-analysis. *Molecular Autism*. BioMed Central Ltd. <https://doi.org/10.1186/s13229-019-0260-x>
- Sacco, R., Gabriele, S., & Persico, A. M. (2015). Head circumference and brain size in autism spectrum disorder: A systematic review and meta-analysis. *Psychiatry Research - Neuroimaging*, *234*(2), 239–251. <https://doi.org/10.1016/j.psychresns.2015.08.016>
- Serenius, F., Ewald, U., Farooqi, A., Fellman, V., Hafström, M., Hellgren, K., ... Källén, K. (2016). Neurodevelopmental outcomes among extremely preterm infants 6.5 years after active perinatal care in Sweden. *JAMA Pediatrics*, *170*(10), 954–963. <https://doi.org/10.1001/jamapediatrics.2016.1210>
- Simons Foundation Autism Research Initiative. (2014). *SFARI Base / SSC / Simons VIP researcher welcome packet*. <https://sfari.org/resources/sfari-base>
- Sprafkin, J., Gadow, K. D., Salisbury, H., Schneider, J., & Loney, J. (2002). Further evidence of reliability and validity of the Child Symptom Inventory-4: parent checklist in clinically referred boys. *Journal of Clinical Child and Adolescent Psychology*, *31*(4), 513-524.
- Stevens, T., Peng, L., & Barnard-Brak, L. (2016). The comorbidity of ADHD in children diagnosed with autism spectrum disorder. *Research in Autism Spectrum Disorders*, *31*, 11–18. <https://doi.org/10.1016/j.rasd.2016.07.003>

- Supekar, K., Iyer, T., & Menon, V. (2017). The influence of sex and age on prevalence rates of comorbid conditions in autism. *Autism Research, 10*(5), 778–789. <https://doi.org/10.1002/aur.1741>
- Tager-Flusberg, H., & Kasari, C. (2013, December). Minimally verbal school-aged children with autism spectrum disorder: The neglected end of the spectrum. *Autism Research*. <https://doi.org/10.1002/aur.1329>
- Takano, T., & Sawai, C. (2014). Early and Late-Onset Epilepsy in Autism: High Rate of Secondly Generalized Seizures. *Autism-Open Access, 04*(02). <https://doi.org/10.4172/2165-7890.1000130>
- Tillmann, J., Ashwood, K., Absoud, M., Bölte, S., Bonnet-Brilhault, F., Buitelaar, J. K., ... Charman, T. (2018). Evaluating Sex and Age Differences in ADI-R and ADOS Scores in a Large European Multi-site Sample of Individuals with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders, 48*(7), 2490–2505. <https://doi.org/10.1007/s10803-018-3510-4>
- van 't Hof, M., Tisseur, C., van Berckeleer-Onnes, I., van Nieuwenhuyzen, A., Daniels, A. M., Deen, M., ... Ester, W. A. (2021, May 1). Age at autism spectrum disorder diagnosis: A systematic review and meta-analysis from 2012 to 2019. *Autism*. SAGE Publications Ltd. <https://doi.org/10.1177/1362361320971107>
- Vasa, R. A., Kalb, L., Mazurek, M., Kanne, S., Freedman, B., Keefer, A., ... Murray, D. (2013). Age-related differences in the prevalence and correlates of anxiety in youth with autism spectrum disorders. *Research in Autism Spectrum Disorders, 7*(11), 1358–1369. <https://doi.org/10.1016/j.rasd.2013.07.005>
- Viscidi, E. W., Johnson, A. L., Spence, S. J., Buka, S. L., Morrow, E. M., & Triche, E. W. (2014). The association between epilepsy and autism symptoms and maladaptive behaviors in children with autism spectrum disorder. *Autism, 18*(8), 996–1006. <https://doi.org/10.1177/1362361313508027>
- Walani, S. R. (2020, July 1). Global burden of preterm birth. *International Journal of Gynecology and Obstetrics*. John Wiley and Sons Ltd. <https://doi.org/10.1002/ijgo.13195>
- Werling, D. M., & Geschwind, D. H. (2013, April). Sex differences in autism spectrum disorders. *Current Opinion in Neurology*. <https://doi.org/10.1097/WCO.0b013e32835ee548>
- WHO. (2018). *Preterm birth*. <https://www.who.int/en/news-room/fact-sheets/detail/preterm-birth>

- Wodka, E. L., Mathy, P., & Kalb, L. (2013). Predictors of phrase and fluent speech in children with Autism and severe language delay. *Pediatrics*, *131*(4).
<https://doi.org/10.1542/peds.2012-2221>
- Yaari, M., Yitzhak, N., Harel, A., Friedlander, E., Bar-Oz, B., Eventov-Friedman, S., ... Yirmiya, N. (2016). Stability of early risk assessment for autism spectrum disorder in preterm infants. *Autism*, *20*(7), 856–867.
<https://doi.org/10.1177/1362361315614758>
- Yudkin, P. L., Aboualfa, M., Eyre, J. A., Redman, C. W. G., & Wilkinson, A. R. (1987). New birthweight and head circumference centiles for gestational ages 24 to 42 weeks. *Early Human Development*, *15*(1), 45–52. [https://doi.org/10.1016/0378-3782\(87\)90099-5](https://doi.org/10.1016/0378-3782(87)90099-5)
- Zampella, C. J., Wang, L. A. L., Haley, M., Hutchinson, A. G., & de Marchena, A. (2021, October 1). Motor Skill Differences in Autism Spectrum Disorder: a Clinically Focused Review. *Current Psychiatry Reports*. Springer.
<https://doi.org/10.1007/s11920-021-01280-6>
- Zwaigenbaum, L., Bauman, M. L., Choueiri, R., Kasari, C., Carter, A., Granpeesheh, D., ... Natowicz, M. R. (2015). Early Intervention for children with autism spectrum disorder under 3 years of age: Recommendations for practice and research. In *Pediatrics* (Vol. 136, pp. S60–S81). American Academy of Pediatrics.
<https://doi.org/10.1542/peds.2014-3667E>

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