Title

Do Biological Sex and Early Developmental Milestones Predict the Age of First Concerns and Eventual Diagnosis in Autism Spectrum Disorder?

Journal

Autism Research, 14(1)

ISSN

1939-3792

Authors

Harrop, Clare
Libsack, Erin
Bernier, Raphael
et al.

Publication Date

2021

DOI

10.1002/aur.2446

Peer reviewed

HHS Public Access

Author manuscript

Autism Res. Author manuscript; available in PMC 2021 November 01.

Published in final edited form as:

Autism Res. 2021 January ; 14(1): 156–168. doi:10.1002/aur.2446.

Do Biological Sex and Early Developmental Milestones Predict the Age of First Concerns and Eventual Diagnosis in Autism Spectrum Disorder?

Clare Harrop[1], **Erin Libsack**[2], **Raphael Bernier**[3,4], **Mirella Dapretto**[5], **Allison Jack**[6], **James C. McPartland**[7,8], **John Darrell Van Horn**[9], **Sara Jane Webb**[3,4], **Kevin Pelphrey**[10], **GENDAAR Consortium**

[1].University of North Carolina at Chapel Hill, Allied Health Sciences, Carr Mill Mall, Carrboro, NC, 27510

[2].Stony Brook University, Department of Psychology, Stony Brook, NY, 11794

[3].University of Washington Seattle, Department of Psychiatry and Behavioral Sciences, Seattle, WA, 98195

[4].Seattle Children's Research Institute, Center on Child Health, Behavior and Development, Seattle, WA, 98121

[5].University of California Los Angeles, Department of Psychiatry and Biobehavioral Sciences, Los Angeles, CA, 90024

[6].George Mason University, Department of Psychology, Fairfax, VA, 22030

[7].Yale School of Medicine, Department of Pediatrics, New Haven, CT, 06520

[8].Yale School of Medicine, Yale Child Study Center, New Haven, CT, 06519

[9].University of Virginia, Department of Psychology, Charlottesville, VA, 22904

[10].University of Virginia, Department of Neurology, Charlottesville, VA, 22903

Abstract

Despite advances in early detection, the average age of autism spectrum disorder (ASD) diagnosis exceeds four years and is often later in females. In typical development, biological sex predicts

Corresponding Author: Clare Harrop, University of North Carolina at Chapel Hill, Allied Health Sciences, Carr Mill Mall, Carrboro, NC 27510, Tel: 919 966 9796, clare_harrop@med.unc.edu.

GENDAAR Consortium:

Elizabeth Aylward, Raphael A. Bernier, Susan Y. Bookheimer, Mirella Dapretto, Nadine Gaab, Daniel H. Geschwind, Allison Jack, James C. McPartland, Charles A. Nelson, Kevin A. Pelphrey, John D. Van Horn, Sara J. Webb, Katy Ankenman, Sarah Corrigan, Dianna Depedro-Mercier, Desiree Guilford, Abha R. Gupta, Zachary Jacokes, Shafali Jeste, Cara M. Keifer, Anna Kresse, Erin Libsack, Jennifer K. Lowe, Erin MacDonnell, Nicole McDonald, Adam Naples, Emily Neuhaus, Megha Santhosh, Catherine A. W. Sullivan, Heidi Tsapelas, Carinna M. Torgerson, Pamela Ventola, Olivia Welker & Julie Wolf

Author Contributions

C.H and E.B initiated the idea for the research questions posed in collaboration with K.P, S.J.W and R.B. K.P, in collaboration with R.B, M.D., J.C.M, J.D.V.H, and S.J.W, developed the idea for the wider GENDAAR Network and secured funding through grants. R.B oversaw all behavioral phenotyping data in the GENDAAR Network. M.D, J.C.M, A.J., and S.J.W coordinated behavioral data collection at individual sites. J.D.V.H oversaw data management in the wider GENDAAR Network. C.H. oversaw data management, extraction and cleaning. C.H. and E.B analyzed the data in consultation with coauthors. C.H wrote the manuscript, with edits and contributions from all other authors. All authors read/approved the final manuscript.

inter-individual variation across multiple developmental milestones, with females often exhibiting earlier progression. The goal of this study was to examine sex differences in caregiver-reported developmental milestones (first word, phrase, walking) and their contribution to timing of initial concerns expressed by caregivers and eventual age of diagnosis. 195 (105 males) children and adolescents aged 8 to 17 years with a clinical diagnosis of ASD were recruited to the study (mean IQ = 99.76). While developmental milestones did not predict timing of diagnosis or age parents first expressed concerns, females had earlier first words and phrases than males. There was a marginal difference in the age of diagnosis, with females receiving their diagnosis one year later than males. Despite sex differences in developmental milestones and diagnostic variables, IQ was the most significant predictor in the timing of initial concerns and eventual diagnosis, suggesting children with lower IQ, regardless of sex, are identified and diagnosed earlier. Overall, biological sex and developmental milestones did not account for a large proportion of variance for the eventual age of ASD diagnosis, suggesting other factors (such as IQ and the timing of initial concerns) are potentially more influential.

NB:

In this paper, we use World Health Organization definitions for sex and gender; “sex” is genetically and biologically determined whereas “gender” represents a socio-cultural construct (World, Health Organization, 2010). In this paper, we use the words “male” and “female” to refer to biological sex.

Lay abstract:

In this study, a later age of diagnosis in females having ASD was confirmed; however biological sex was not the stronger predictor of age of diagnosis. Parents reported that females learned language more quickly than males, and parents noted their first concerns when females were older than males. In this sample, the strongest predictor of age of diagnosis was the age of first concerns.

Keywords

sex differences; early milestones; diagnosis; females; parental perceptions

Background

Despite advances in early detection and research indicating that a reliable diagnosis of autism spectrum disorder (ASD) is achievable as early as 24 months, the average age of ASD diagnosis often exceeds 4 years, with a significant lag between the time parents first report concerns and eventual diagnosis (Daniels & Mandell, 2014). A number of factors impact both the age and likelihood of receiving an ASD diagnosis, including demographic variables such as maternal education and family SES (Mandell, Ittenbach, Levy, & Pinto-Martin, 2007; Mandell, Listerud, Levy, & Pinto-Martin, 2002). Across a range of studies, female sex is associated with a later age of diagnosis (Begeer et al., 2013; McCormick et al., 2020; Salomone, Charman, McConachie, & Warreyn, 2015). In a recent study using a population-based cohort, McCormick and colleagues (2020) found that females are diagnosed nearly 18 months later than males. This was particularly the case for females with

more advanced language abilities. Similar findings reported by Salomone and colleagues (2015) in a large European sample with an interaction between sex and verbal ability in predicting age of diagnosis, showing females with higher verbal ability were older at the time of ASD diagnosis. Begeer et al. (2013) reported that compared to males, females with Asperger Syndrome received a diagnosis 1.8 years later, and the timing between parents' first concerns and receipt of an eventual diagnosis was four months longer, regardless of language ability and IQ. A handful of studies have reported no differences between males and females with ASD in the age of parental first concerns (Hiller, Young, & Weber, 2016), the type of first concern (Hiller et al., 2016), or the age at first ASD evaluation (Giarelli et al., 2010). However, the overall consensus is that females, particularly those with average to above average verbal ability, receive ASD diagnoses later compared to males (McCormick et al., 2020; Salomone et al., 2015), therefore delaying females' access to vital early intervention services during a critical developmental period.

Parental and clinician perceptions of ASD as a disorder that primarily affects males, and parents' differential expectations about what constitutes *typical* behavior across males and females in early development may influence the timing of ASD diagnosis. In neurotypical (NT) populations, a child's sex has been identified as a source of inter-individual variation in the timing of multiple developmental milestones, including language acquisition and social-emotional development, favoring earlier skill development in females (Fenson et al., 1994; Galsworthy, Dionne, Dale, & Plomin, 2000). However, despite the broad assumption of population-based sex differences in developmental achievements, empirical evidence supporting a female advantage in the timing of developmental milestones is mixed and/or lacking. For example, despite small effects showing a female advantage in language and communication variables during the first 30 months of life (Bauer, Goldfield, & Reznick, 2002; Fenson et al., 1994; Galsworthy et al., 2000; Özçalişkan & Goldin-Meadow, 2010) and slight differences (weighted toward females) in the timing of sitting and standing without support during infancy, no significant sex differences have been reported in terms of overall motor milestone achievements (World Health Organization, 2008). Conversely, other studies have suggested this advantage is weighted toward males (Reinisch, Rosenblum, Rubin, & Schulsinger, 1991). In two recent studies, females were reported as meeting milestones before males; Sheldrick et al. (2019) reported sex effects across early developmental milestones from over 41,000 infants, however cautioned against assuming females develop at a more rapid rate than males. Ertem et al. (2018) reported equivalence for 96% of milestones across 4949 males and females. Despite these mixed findings, there are widely held assumptions that females achieve milestones at a faster rate than males that may impact the identification of females with ASD.

While early developmental milestones have been studied extensively in ASD (see Barbaro & Dissanayake, 2009 for review), the potential impact of a child's sex on the timing of these milestones is not fully understood. Pre-diagnosis, differences in early development between males and females have not been found to be ASD specific (Messinger et al., 2015; Zwaigenbaum et al., 2012). For example, in a sample of siblings at high-risk of developing ASD, Messinger et al. (2015) reported that males had slower growth trajectories and lower cognitive performance compared to females. Øien and colleagues studied children who had negative screens for ASD at 18 months, but received a later diagnosis of ASD (termed false-

negatives; Øien et al., 2018). Children in the false-negative group, regardless of sex, had poorer fine motor skills and overall girls (false-negative and true-negative) were rated as having less advanced motor skills than boys. Girls who subsequently received an ASD diagnosis following a false-negative had poorer gross motor skills relative to boys who also fell in the false-negative group.

However, in a community sample of children later diagnosed with ASD, parents of males reported more social interaction concerns compared to those reported by parents of females (Little, Wallisch, Salley, & Jamison, 2017). Early milestones are predictive of a number of outcome markers in ASD, such as language, cognitive ability, and adaptive behaviors (Bedford, Pickles, & Lord, 2016; Mayo, Chlebowski, Fein, & Eigsti, 2013), however the impact of these on the timing of diagnostic variables is less clear.

Aims

Given potential sex differences in caregiver-reported timing of developmental milestones in neurotypical development and the sex imbalance observed in ASD diagnosis rates, we sought to (1) investigate potential sex differences in caregiver-reported timing of developmental milestones and diagnostic variables in a large sample of males and females with ASD. Then, after controlling for key demographic variables, we examined how (2) biological sex and developmental milestones contributed to the timing of initial parental concerns and eventual ASD diagnosis. We predicted that sex differences in language milestones (age of first word, age of first phrase) reported in neurotypical development in favor of females would be mirrored in children later diagnosed with ASD. Based on previous research, we expected parents of females would have later first concerns, females would be diagnosed later and experience a greater lag between initial concerns and eventual ASD diagnosis. We did not make any specific hypotheses regarding the impact of developmental milestones on diagnostic outcomes as the variables included in our models were dependent on the outcomes of Aim One.

Method

Participants.

Participants in this study were drawn from the NIH ACE GENDAAR Network, a research consortium focused on better understanding the causes and expression of ASD in females. Recruitment strategies therefore included over-sampling for females with ASD. Participating families were recruited across four research sites based in academic medical centers serving the Northwest, Southwest, and Northeast regions of the U.S. Eligible participants included 195 (105 males, 90 females; Table 1 and Supplementary Table 1) children and adolescents aged 8 to 17 years, with a clinical diagnosis of ASD. Additionally, eligible participants met the following inclusion criteria: verbal ability consistent with administration of the Autism Diagnostic Observation Schedule, 2nd edition (ADOS-2; Lord et al., 2012) Module 3 or 4; no current nor history of a significant medical disability, neurological disorder or developmental disability aside from ASD, known genetic syndrome (e.g., Fragile X Syndrome), nor significant cognitive impairment (measured as IQ < 70). Community ASD diagnoses were verified by a licensed, research reliable clinical psychologist at each site

using all available information and ensuring all participants met ADOS-2 ASD cutoff criteria and met Collaborative Programs of Excellence in Autism (CPEA) criteria (Risi et al., 2006) on the Autism Diagnostic Interview-Revised (ADI-R; Rutter, Le Couteur, & Lord, 2003). Eligibility criteria were confirmed, and diagnostic and cognitive assessments were administered at the first study visit. The current study was approved by the Institutional Review Board at each research site. All participating families provided informed consent, children provided written informed assent, and were compensated for their participation.

Measures.

Differential Ability Scales, Second Edition (DAS-II).—Child IQ was estimated upon enrollment using the Differential Ability Scales, Second Edition (DAS-II; Elliot, 2007) Children completed the School Years Battery. For this study, we used General Conceptual Ability (GCA) Standard Scores to provide an estimated full-scale IQ (FSIQ). The GCA is calculated based on scores from the following subscales; Pattern Construction, Matrices, Recall of Designs, Word Definitions, Verbal Similarities, and Sequential and Quantitative Reasoning.

NIH ACE Medical History Form.—Primary caregivers completed the standard NIH ACE Medical History Form (National Institutes of Health, 2012) upon entry into the study. This form covers a range of variables, including comorbid medical conditions, prescription and over-the-counter medications, pregnancy and birth complications, diagnostic experiences, and timing of early developmental milestones.

Autism Diagnostic Interview-Revised (ADI-R).—The ADI-R (Rutter et al., 2003) is a gold-standard, 111 item semi-structured parent interview that is administered by a trained clinician and used in tandem with the ADOS-2 to achieve gold-standard ASD diagnostic confirmation. The ADI-R is organized around DSM-IV and ICD-10 diagnostic criteria for ASD and has good reliability and validity for individuals 24 months and older. Parents are asked to report on a wide range of current and past behaviors associated with ASD spanning three main areas of functioning: quality of reciprocal social interaction, communication and language, and repetitive, restricted, and stereotyped patterns of behaviors. Most ADI-R items are coded on a Likert scale ranging from 0 to 2, with higher scores indicating more impairment/abnormality. Select items also include scoring of the child's age in months when certain behaviors were mastered.

Dependent Variables.

Dependent variables were drawn from the NIH ACE Medical History Form and the ADI-R (Supplementary Figure 1).

Developmental Milestones.—Analyses focused on three early developmental milestones; age of first single word, age of first three-word phrase, and age of walking (defined as 10-steps without support). These variables were selected based on prior literature that indicates (1) differences between high-risk and low-risk siblings are not ASD-specific in early childhood (Bedford, Jones, et al., 2016; Messinger et al., 2015; Zwaigenbaum et al., 2012); (2) biological sex potentially contributes to the timing of these milestones in NT

development (Bauer et al., 2002; Fenson et al., 1994; Galsworthy et al., 2000; Özçalişkan & Goldin-Meadow, 2010; Reinisch et al., 1991); (3) these variables have been linked to later outcomes in ASD (Bedford, Pickles, et al., 2016; Mayo et al., 2013); and (4) have been indicated as potential markers distinguishing distinct behavioral phenotypes for males and females with ASD (Hiller et al., 2016).

Both the Medical History Form and the ADI-R ask caregivers to report their child's age in months when these three developmental milestones were reached. Both forms also ask caregivers for the age of first concerns. Whenever possible, an average age was taken across the two measures. If values were missing from one form, values from the other form were used in the analyses. Participants with missing values on both measures for a single variable were excluded from analyses including that specific variable. The majority (70%) of variables across the two measures were within five months of one another. If there was a difference greater than five months, original data sources were checked. In the case of an *obvious* disagreement (e.g. caregiver reports in years on the Medical History Form but the examiner reports in months for the ADI-R, yet the values correspond – 48months vs. 4years – the ADI-R value was retained). As summarized in Supplementary Table 1, the majority of participants (187/195) had data for at least one developmental milestones. Eighty-eight percent of participants had data from both measures for age of first word and age of first phrase, and 73% of participants had data from both measures for age of first walking.

Diagnostic Variables.—Based on prior research indicating differences in timing of ASD diagnosis between males and females (Begeer et al., 2013; McCormick et al., 2020; Salomone et al., 2015), the analyses conducted here focused on three variables to assess diagnostic timing: child's age when parents first noticed developmental concerns (age of first concerns); child's age when first diagnosed with ASD (age at diagnosis); and the length of time that elapsed between the onset of parents' first concerns and their child's eventual ASD diagnosis (diagnostic lag). Age of first concerns was calculated as an average (wherever possible) from the Medical History Form and the ADI-R. Only one participant did not have data for age of first concern from either the ADI-R or Medical History form. Age at diagnosis was obtained from the Medical History Form only and over 90% of participants (N=177) had data reported for this variable (Supplementary Table 2). The 18 participants with missing data for this variable were excluded from associated analyses. Diagnostic lag was calculated as the difference (in months) between age of first concerns and age at diagnosis.

Data Analytic Plan.

After controlling for demographic variables (child FSIQ, maternal education, child race, child ethnicity, and study site) previously shown to influence timing of ASD diagnosis (Mandell et al., 2007; Mandell et al., 2002; Begeer et al., 2013; McCormick et al., 2020; Salomone et al., 2015), ANOVAs were used to test for sex differences (male, female) in timing of developmental milestones (walking, first word, three-word phrases) and diagnostic variables (first concerns, ASD diagnosis, and diagnostic lag). We also included child current age in the analytic models for developmental milestones based on the findings of Hus et al.

(2011) who reported caregiver reports of language delays in children with ASD increased over time.

The developmental milestones that showed significant between-sex effects in the initial analysis were then included in a stepwise regression model in order to investigate the relative contributions of child IQ, maternal education, race, ethnicity, biological sex, and timing of early developmental milestones in predicting diagnostic variables. Models included interactions between child biological sex and developmental milestones (mean centered). Significant interactions were plotted using the method outlined by Preacher, Curran, and Bauer (2006).

Results

Between-Sex Differences.

After controlling for demographic variables, there was one significant and one marginal between-sex difference for developmental milestones (Table 1; Figure 1): age of first three-word phrase ($F(1,149) = 4.807$, $p = .030$, $\eta_p^2 = .031$) and age of first word ($F(1,150) = 3.854$, $p = .051$, $\eta_p^2 = .025$). Compared to ASD males, ASD females spoke their first word on average three months earlier (17.31 vs. 20.57 months) and spoke their first three-word phrase nearly six months earlier (29.79 vs. 35.05 months; Figure 1). There was no difference between males ($M = 13.66$, $SD = 3.60$) and females ($M = 13.57$, $SD = 3.12$) in caregiver-reported age of walking ($p = .661$).

After controlling for demographic variables, there was a between-sex difference in age of first concerns $F(1,155) = 6.582$, $p = .011$, $\eta_p^2 = .041$), with ASD females on average being over seven months older than ASD males when their caregivers reported first concerns about their child's development (Table 1; Figure 2). The difference in age at diagnosis, with females being, on average, one year older than males, approached significance (Table 1; Figure 2; $F(1,152) = 3.527$, $p = .062$, $\eta_p^2 = .023$). There was no difference between males ($M = 41.71$, $SD = 38.86$) and females ($M = 47.80$, $SD = 38.36$) in diagnostic lag ($p = .414$).

Factors Predicting Timing of Diagnostic Variables.

Table 2 summarizes the linear regression models predicting age of first concerns and age at diagnosis. We did not examine the factors that predicted diagnostic lag as length of diagnostic lag did not differ between males and females. Only age of first word and age of first three-word phrase were entered into the regression models as predictors of diagnostic variables because these two developmental milestones showed between-sex differences.

Age of first concerns.—Due to the clinical significance of this variable and a difference of 12 months between males and females in the age of diagnosis (Table 1, Figure 2), we sought to determine the factors that impact age of diagnosis. While demographic variables alone did not reliably predict age of first concerns (Table 2; $R^2 = .036$, $p = .06$), within model one, current child IQ was a significant predictor of age of first concerns ($p = .006$); caregivers reported later first concerns for children with current higher IQs. With the inclusion of biological sex, model two was significant ($R^2 = .070$, $p = .010$). Both child IQ and child biological sex were significant predictors of age of first concerns (IQ: $t = 2.826$, p

= .005; sex: $t = 2.541$, $p = .012$). The inclusion of developmental milestones (age of first word and three-word phrase) did not alter the significant findings for model three. Finally, we tested the interaction between early developmental milestones and biological sex and their contribution to age of first concerns (model four). While the overall model significance did not change ($R^2 = .075$, $p = .018$), the interaction between age of first word and sex was significant ($t(154) = -2.030$, $p = .044$), such that caregivers reported earlier age of first concerns for males who spoke their first word later (Figure 3). Across all models, child IQ was the strongest predictor of age of first concerns, showing earlier age of first concerns for children with lower IQs, followed by child biological sex, with caregivers reporting earlier first concerns for males.

Age at ASD diagnosis.—Demographic variables did not predict age of diagnosis (Model one; Table 2), however child IQ emerged as a strong individual predictor ($p = .007$). Model significance did not change with the inclusion of child biological sex, nor developmental milestones (age of first word and three-word phrase), and child IQ remained the only significant predictor in models two, three and four (Table 2; $ps = .007$, .016 and 0.19), with earlier diagnoses for children with lower IQ. Interactions between early developmental milestones and biological sex were not significant predictors of age at diagnosis in model four. Due to the sex difference in age of first concerns, we added this variable in the final step of our model (Table 2). The inclusion of age of first concerns was highly significant ($p \geq .001$) in predicting age of first concerns; children whose caregivers expressed earlier first concerns received their diagnosis earlier.

Discussion

Early developmental milestones provide cognitive and behavioral benchmarks that caregivers and clinicians use to identify potential developmental delays and provide timely intervention when indicated. Due to the behavioral nature of ASD symptoms and the diagnostic instruments for identifying ASD in young children, understanding the timing of early developmental milestones in ASD and the factors that predict timing of such milestones is critically important for early identification and intervention services. The current study aimed to examine potential sex differences in the timing of early developmental milestones and diagnostic-related variables in ASD to understand how these variables predict the timing of ASD diagnosis.

Given sex differences observed in developmental markers in NT development (Galsworthy et al., 2000; Özçalişkan & Goldin-Meadow, 2010; Reinisch et al., 1991), and research suggesting potential early developmental differences between males and females with ASD (Bedford, Jones, et al., 2016; Little et al., 2017; Messinger et al., 2015), we sought to explore whether males and females with ASD in a large multi-site sample differed across three milestones considered pivotal in early development: age of first word, age of first three-word phrase, and age of walking. The approach builds on the strengths of previous retrospective report studies in small to medium sized samples of ASD diagnosed females (Hiller et al., 2016; Little et al., 2017) to examine retrospective caregiver reports of the timing of early milestones in a large, well-characterized sample of females with ASD.

On average, caregivers reported that females spoke their first word around 17 months of age and three months earlier than males. Additionally, females spoke their first three-word phrase nearly six months earlier than males. The language differences between males and females highlight the need for more guidance around the awareness, detection, and diagnosis of ASD for more verbally advanced females, such as more red flags focused on social development and more subtle social-communicative behaviors instead of language. While language delay was recently removed from DSM criteria for ASD (APA, 2013), it has been historically used as a primary indicator of ASD (Mitchell et al., 2006) though it may not extend in the same way to females.

Differences in language milestones reported between NT males and females appear to be mirrored in ASD. However, while females with ASD may have an advantage over males with ASD, their language milestones are still delayed compared to NT populations with the average age of first word in children with NT outcomes reported around 12 months of age (Darley & Winitz, 1961; Nelson, 1981; Sheldrick et al., 2019). In the current sample, while age of first word and age of first three-word phrase did not predict age of first concerns or age at diagnosis, these results are consistent with recent population-based findings suggesting that ASD females with more advanced language abilities are diagnosed later than ASD males (McCormick et al., 2020).

Few studies have examined sex differences in early developmental milestones in children later diagnosed with ASD (Hiller et al., 2016; Little et al., 2017; Messinger et al., 2015; Zwaigenbaum et al., 2012). These studies suggest that males with ASD exhibit slower cognitive growth and poorer social communication skills compared to females with ASD. However, our results suggest that language-specific milestones may differentiate males and females with ASD from one another during early development. Despite the sample being well-matched on developmental variables upon entry into the study, retrospective caregiver reports indicate that females may have a slight advantage in the timing of language related milestones. Alternatively, caregivers may demonstrate a *female bias* in perceptions of development and it is possible that differences in caregiver-reported milestones reflect differences in parental expectations, rather than evidence of empirical differences between the sexes. For example, mothers have been found to overestimate language abilities in infancy and early childhood for female children compared to male children (Ruble & Martin, 1998). Caregivers of children with ASD have also been found to retrospectively inflate their child's language delays over time, but not other developmental milestones (Hus et al., 2011).

There were no sex differences in the reported age of first walking, with both males and females starting to walk between 13 and 14 months. This aligns with reports from NT development showing age of first walking typically occurs around 13 months of age (Adolph & Robinson, 2013; World Health Organization, 2006), and is consistent with data suggesting minimal gross motor delays in ASD (Bhat, Landa, & Galloway, 2011; Green et al., 2002, 2009; Ozonoff et al., 2008; Provost, Lopez, & Heimerl, 2007). However, as gross motor skills have been reported to be an important indicator for cognitive and language development in NT development (Alcock & Krawczyk, 2010; He, Walle, & Campos, 2015; Libertus & Violi, 2016; Walle & Campos, 2014) and ASD (Bedford, Pickles, et al., 2016),

future work should seek to clarify potential sex effects on motor abilities using more fine-grained analyses of milestones.

Results reflect a later age of diagnosis in females, as reported by some previous studies (Begeer et al., 2013; McCormick et al., 2020; Salomone et al., 2015). Females in this study received their diagnosis on average one year later than males, however this only approached significance. Caregivers also reported first concerns about their child's development nearly 18 months later for females compared to males. It is possible that the observed female advantages in language may *sway* caregiver perceptions of development in females. However, neither age of first word nor age of first three-word phrase were individually predictive of age of first concerns across males and females. Another potential explanation for this sex discrepancy in timing of first concerns is caregivers' knowledge of ASD as a condition more commonly diagnosed in males.

While caregivers of females reported later age of first concerns and later age of diagnosis, the time between these events (diagnostic lag) did not differ significantly for males and females. Despite the lack of significance, the time between first concerns and eventual diagnosis was six months later for females (47.8 months) vs males (41.7 months). This aligns with previous reports of longer diagnostic lags in females (Begeer et al., 2013) and suggests that females may experience delays once their caregivers and/or teachers begin evaluation processes, which in turn could lead to intervention delays. It is worth noting that our sample had many markers of high SES, such as post-secondary education, income above the local median, and privately owned housing. While we cannot assume that SES at the time of data collection reflect that at the time of diagnosis, it is likely that many caregivers in our sample had the resources to seek out an evaluation and potentially push back against perception of ASD in females reported by others (Navot, Jorgenson, & Webb, 2017).

While not studied directly here, it is possible that differences in how parents socialize with their children may also contribute to how they retrospectively and prospectively report milestone for males and females. Research has shown that parents use different strategies and language when interacting with male and female children (Baker & Milligan, 2016; Bellinger & Gleason, 1982; Clearfield & Nelson, 2006; Pruden & Levine, 2017). These parental expectations and/or socialization differences may be especially important in ASD where the male dominance in diagnosis may bias parental perceptions of both female developmental advantages and the likelihood of receiving an ASD diagnosis, therefore increasing the need to examine the potential interplay between a child's sex and the timing of developmental milestones and ASD diagnosis.

Unlike previous studies, we did not find any impact of race and ethnicity on the age of first concerns or age of diagnosis. These factors have been highlighted as key mediators in the age of and access to an ASD diagnosis (Becerra et al., 2014; Mandell et al., 2007, 2002). However, due to our relatively small and mostly white and non-Hispanic sample, we were not powered to detect any important racial or ethnic differences. Future research should examine the intersectionality between race, ethnicity and biological sex in accessing and receiving an ASD diagnosis.

Child IQ was the strongest predictor of age of first concerns and also predicted age of diagnosis suggesting that overall intellectual functioning, which is viewed as relatively stable overtime (Bishop, Farmer, & Thurm, 2015; Dietz, Swinkels, Buitelaar, Van Daalen, & Van Engeland, 2007; Howlin, Savage, Moss, Tempier, & Rutter, 2014), is more likely to predict the timing of caregivers' first expressed concerns over their child's development and when their child receives their diagnosis. However, age of first concerns was the strongest predictor of age of diagnosis. Together these findings suggest that parents and clinicians are more likely to recognize ASD in females when there are additional factors suggesting developmental disability, evident earlier in development, and aligns with research indicating a less-skewed sex ratio in children with co-occurring intellectual disability (Banach et al., 2009; Volkmar, Szatmari, & Sparrow, 1993; Yeargin-Allsopp et al., 2003).

Although IQ was a stronger predictor in the statistical modeling conducted here, biological sex was a significant predictor of age of first concerns, with first concerns expressed earlier for males. Furthermore, the interaction between biological sex and age of first word was significant; when males had later first words, caregivers reported earlier concerns. Overall, IQ was the strongest predictor of retrospective caregiver concerns. Age of first concerns, which was higher in females, was predictive of age of diagnosis and more predictive than IQ.

Implications for Clinical Practice.

These results align with other studies indicating a later age of diagnosis for females but also extend this to a later age of first concerns expressed by caregivers. Females had earlier first words and phrases compared with males. This may suggest that a combination of more advanced language skills displayed by females and caregiver knowledge of differential diagnosis rates between males and females may contribute to later first concerns, and ultimately, to later age at ASD diagnosis for females. The finding that age of first concern, which were later in females, predicted age of diagnosis further supports the need for more awareness and targeted screening for females, especially those who are verbal. Our findings, together with previous research (McCormick et al., 2020), can help inform prospective screening practices and suggest that screening criteria might need to be modified to identify verbal females who may not get "flagged" as early if their language is not as delayed as males or developing in line with CDC milestones (Sheldrick et al., 2019).

Clinicians' knowledge of how ASD can uniquely manifest in females should include how developmental milestones may be less delayed in females compared to males with the disorder, therefore potentially hindering early detection particularly for females with ASD and average to above average verbal ability.

Limitations.

While this study included a large, well-matched sample of ASD females, there were some limitations. First, an NT control group was not included in this study. While NT controls were included in the ACE GENDAAR Network, NT participants did not complete the ADI-R which was one of the main sources of data for the current study; therefore, normative data on caregiver-reported early milestones was lacking in the NT sample. The IQ variable is

based on current IQ measured at study enrollment. Therefore, while predictive, current IQ may not be an exact reflection of the child's level of functioning at the age of diagnosis. Evidence does indicate that IQ remains relatively stable across childhood (Bishop et al., 2015; Dietz et al., 2007; Howlin et al., 2014), suggesting participants' current IQ would be relatively consistent with their early childhood IQ. Participation in the current study was limited to individuals with average to above average IQ and findings may therefore not be generalizable to the full range of cognitive abilities represented across the autism spectrum.

While the use of gold-standard measures (ADOS-2 and ADI-R) to confirm ASD diagnosis are a strength, these diagnostic tools may also *filter out* potential sex differences as females who meet gold-standard diagnostic criteria may align more with the male-conceptualization of ASD (Mandy & Lai, 2017). Therefore, females in our sample were included based on our current conventional conception of ASD and study inclusion criteria and similar findings may not be replicated in a broader population.

Results reported here were based on retrospective caregiver reports which tend to be subject to recall issues and bias. Using the ADI-R, Hus and colleagues (2011) reported significant "telescoping" of language abilities compared to other developmental milestones, with caregivers reporting more language delays in their children as they grew older. While current chronological age did not predict any developmental milestones, caution must be adopted due to our reliance upon retrospective, caregiver reports. Future early detection studies should therefore include variables related to developmental milestones to understand if these results translate to prospectively studied samples. Future studies may also seek to confirm caregivers' reported timing of developmental milestones via medical chart review. Any missing data was mitigated by calculating dependent variables from two caregiver report tools (ACE Family History and the ADI-R); however, there was missing data for a number of cases on one of the two measures. While we adopted a robust approach to account for any missing data by creating an average across the Medical History Questionnaire and ADI-R, it should be noted that these measures are collected differently; one through in-depth caregiver interview and the other by questionnaire.

Another potential limitation is the generalizability of these results and the representation of the ACE GENDAAR sample. All families were recruited via well-resourced ASD research centers. Given these resources, it is possible that males and females in this sample may not reflect males and females recruited using population based approaches. While there were no effects of site on our analyses, it should be noted that two sites (Los Angeles and New Haven) had lower age of diagnoses for females than the other two sites (Seattle, Boston) which may reflect site-specific expertise in identifying ASD females (Supplementary Table 2). Our sample was also limited to children with an IQ above 70 and all recruited children completed ADOS-2 Modules 3 or 4, therefore our findings may not be generalizable to minimally verbal and/or less cognitively able children.

Conclusions: Results reported here support recent research indicating females are diagnosed significantly later than males (McCormick et al., 2020). Caregivers of females reported later first concerns compared to caregivers of males. While developmental milestones did not predict timing of diagnostic variables, females had earlier first words and

phrases than males. Biological sex, in combination with IQ, predicted caregiver first concerns but did not contribute to age of diagnosis. The strongest predictor of age of diagnosis was age of first concerns, which were lower in males. Earlier concerns expressed by caregivers predicted earlier age of diagnosis, supporting the need for sex-sensitive screening measures that better detect ASD characteristics in females. Overall, biological sex and developmental milestones did not account for a large proportion of variance, suggesting other factors, are more influential in predicting timing of initial concerns. and diagnosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements.

We thank the families who participated in this research for their time and commitment. Research reported in this publication was supported by a KL2 Career Development Award awarded to C.H through the National Center for Advancing Translation Sciences Award (UL1TR001111; PI: Buse) and This work was supported by the National Institute of Mental Health (R01MH100028) to K.P. The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health. Portions of this data have been presented at the International Society for Autism Research 2019 Conference (Montreal, Canada).

References

National Institutes of Health. Retrieved May 26, 2020, from https://nda.nih.gov/ndarpublicweb/Documents/CommonMeasures/ACESubjectMedicalHistoryForm.pdf

Adolph K, & Robinson SR (2013). The road to walking: What learning to walk tells us about development. Oxford University Press.

Alcock KJ, & Krawczyk K (2010). Individual differences in language development: Relationship with motor skill at 21 months. Developmental Science, 13(5), 677–691. 10.1111/j.1467-7687.2009.00924.x [PubMed: 20712734]

American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders (DSM-5®).

Baker M, & Milligan K (2016). Boy-girl differences in parental time investments: Evidence from three countries. Journal of Human Capital, 10(4), 399–441. 10.1086/688899

Banach R, Thompson A, Szatmari P, Goldberg J, Tuff L, Zwaigenbaum L, & Mahoney W (2009). Brief report: Relationship between non-verbal IQ and gender in autism. Journal of Autism and Developmental Disorders, 39(1), 188–193. 10.1007/s10803-008-0612-4 [PubMed: 18594959]

Barbaro J, & Dissanayake C (2009). Autism Spectrum Disorders in Infancy and Toddlerhood: A Review of the Evidence on Early Signs, Early Identification Tools, and Early Diagnosis. Journal of Developmental & Behavioral Pediatrics, 30(5), 447–459. 10.1097/DBP.0b013e3181ba0f9f [PubMed: 19823139]

Bauer DJ, Goldfield BA, & Reznick JS (2002, 9). Alternative approaches to analyzing individual differences in the rate of early vocabulary development. Applied Psycholinguistics. 10.1017/S0142716402003016

Becerra TA, Von Ehrenstein OS, Heck JE, Olsen J, Arah OA, Jeste SS, … Ritz B (2014). Autism spectrum disorders and race, ethnicity, and nativity: A population-based study. Pediatrics, 134(1), e63–e71. 10.1542/peds.2013-3928 [PubMed: 24958588]

Bedford R, Jones EJH, Johnson MH, Pickles A, Charman T, & Gliga T (2016). Sex differences in the association between infant markers and later autistic traits. Molecular Autism, 7(1), 21. 10.1186/s13229-016-0081-0 [PubMed: 27034768]

Bedford R, Pickles A, & Lord C (2016). Early gross motor skills predict the subsequent development of language in children with autism spectrum disorder. Autism Research, 9(9), 993–1001. 10.1002/aur.1587 [PubMed: 26692550]

Begeer S, Mandell D, Wijnker-Holmes B, Venderbosch S, Rem D, Stekelenburg F, & Koot HM (2013). Sex differences in the timing of identification among children and adults with autism spectrum disorders. Journal of Autism and Developmental Disorders, 43(5), 1151–1156. 10.1007/s10803-012-1656-z [PubMed: 23001766]

Bellinger DC, & Gleason JB (1982). Sex differences in parental directives to young children. Sex Roles, 8(11), 1123–1139. 10.1007/BF00290968

Bhat AN, Landa RJ, & Galloway J. C. (Cole). (2011). Current Perspectives on Motor Functioning in Infants, Children, and Adults With Autism Spectrum Disorders. Physical Therapy, 91(7), 1116–1129. 10.2522/ptj.20100294 [PubMed: 21546566]

Bishop SL, Farmer C, & Thurm A (2015). Measurement of Nonverbal IQ in Autism Spectrum Disorder: Scores in Young Adulthood Compared to Early Childhood. Journal of Autism and Developmental Disorders, 45(4), 966–974. 10.1007/s10803-014-2250-3 [PubMed: 25239176]

Clearfield MW, & Nelson NM (2006). Sex differences in mothers' speech and play behavior with 6-, 9-, and 14-month-old infants. Sex Roles, 54(1–2), 127–137. 10.1007/s11199-005-8874-1

Daniels AM, & Mandell DS (2014). Explaining differences in age at autism spectrum disorder diagnosis: a critical review. Autism : The International Journal of Research and Practice, 18(5), 583–597. 10.1177/1362361313480277 [PubMed: 23787411]

Darley FL, & Winitz H (1961). Age of First Word: Review of Research. Journal of Speech and Hearing Disorders, 26(3), 272–290. 10.1044/jshd.2603.272

Dietz C, Swinkels SHN, Buitelaar JK, Van Daalen E, & Van Engeland H (2007). Stability and change of IQ scores in preschool children diagnosed with autistic spectrum disorder. European Child and Adolescent Psychiatry, 16(6), 405–410. 10.1007/s00787-007-0614-3 [PubMed: 17401607]

Elliot CD (2007). Differential Abilities Scales (DAS-II). Pearson.

Ertem IO, Krishnamurthy V, Mulaudzi MC, Sguassero Y, Balta H, Gulumser O, … Forsyth BWC (2018). Similarities and differences in child development from birth to age 3 years by sex and across four countries: a cross-sectional, observational study. The Lancet Global Health, 6(3), e279–e291. 10.1016/S2214-109X(18)30003-2 [PubMed: 29433666]

Fenson L, Dale PS, Reznick JS, Bates E, Thal DJ, Pethick SJ, … Stiles J (1994). Variability in Early Communicative Development. Monographs of the Society for Research in Child Development, 59(5), i. 10.2307/1166093 [PubMed: 8047076]

Galsworthy MJ, Dionne G, Dale PS, & Plomin R (2000). Sex differences in early verbal and non-verbal cognitive development. Developmental Science, 3(2), 206–215. 10.1111/1467-7687.00114

Giarelli E, Wiggins LD, Rice CE, Levy SE, Kirby RS, Pinto-Martin J, & Mandell D (2010). Sex differences in the evaluation and diagnosis of autism spectrum disorders among children. Disability and Health Journal, 3(2), 107–116. 10.1016/j.dhjo.2009.07.001 [PubMed: 21122776]

Green D, Baird G, Barnett AL, Henderson L, Huber J, & Henderson SE (2002). The severity and nature of motor impairment in Asperger's syndrome: A comparison with Specific Developmental Disorder of Motor Function. Journal of Child Psychology and Psychiatry and Allied Disciplines, 43(5), 655–668. 10.1111/1469-7610.00054

Green D, Charman T, Pickles A, Chandler S, Loucas T, Simonoff E, & Baird G (2009). Impairment in movement skills of children with autistic spectrum disorders. Developmental Medicine and Child Neurology, 51(4), 311–316. 10.1111/j.1469-8749.2008.03242.x [PubMed: 19207298]

He M, Walle EA, & Campos JJ (2015). A Cross-National Investigation of the Relationship Between Infant Walking and Language Development. Infancy, 20(3), 283–305. 10.1111/infa.12071

Hiller RM, Young RL, & Weber N (2016). Sex differences in pre-diagnosis concerns for children later diagnosed with autism spectrum disorder. Autism, 20(1), 75–84. 10.1177/1362361314568899 [PubMed: 25717130]

Howlin P, Savage S, Moss P, Tempier A, & Rutter M (2014). Cognitive and language skills in adults with autism: A 40-year follow-up. Journal of Child Psychology and Psychiatry and Allied Disciplines, 55(1), 49–58. 10.1111/jcpp.12115

Hus V, Taylor A, & Lord C (2011, 7). Telescoping of caregiver report on the Autism Diagnostic Interview - Revised. Journal of Child Psychology and Psychiatry and Allied Disciplines. J Child Psychol Psychiatry. 10.1111/j.1469-7610.2011.02398.x

Libertus K, & Violi DA (2016). Sit to talk: Relation between motor skills and language development in infancy. Frontiers in Psychology, 7(MAR). 10.3389/fpsyg.2016.00475

Little LM, Wallisch A, Salley B, & Jamison R (2017). Do early caregiver concerns differ for girls with autism spectrum disorders? Autism, 21(6), 728–732. 10.1177/1362361316664188 [PubMed: 27542396]

Lord C, Rutter ML, DiLavore PS, Risi S, Gotham K, & Bishop SL (2012). Autism Diagnostic Observation Schedule - Second Edition (ADOS-2). WPS.

Mandell DS, Ittenbach RF, Levy SE, & Pinto-Martin JA (2007). Disparities in diagnoses received prior to a diagnosis of autism spectrum disorder. Journal of Autism and Developmental Disorders, 37(9), 1795–1802. 10.1007/s10803-006-0314-8 [PubMed: 17160456]

Mandell DS, Listerud J, Levy SE, & Pinto-Martin JA (2002). Race differences in the age at diagnosis among medicaid-eligible children with autism. Journal of the American Academy of Child and Adolescent Psychiatry, 41(12), 1447–1453. 10.1097/00004583-200212000-00016 [PubMed: 12447031]

Mandy W, & Lai MC (2017, 8 1). Towards sex- and gender-informed autism research. Autism. SAGE Publications Ltd. 10.1177/1362361317706904

Mayo J, Chlebowski C, Fein DA, & Eigsti IM (2013). Age of first words predicts cognitive ability and adaptive skills in children with ASD. Journal of Autism and Developmental Disorders, 43(2), 253–264. 10.1007/s10803-012-1558-0 [PubMed: 22673858]

McCormick CEB, Kavanaugh BC, Sipsock D, Righi G, Oberman LM, Moreno De Luca D, … Morrow EM (2020). Autism Heterogeneity in a Densely Sampled U.S. Population: Results From the First 1,000 Participants in the RI-CART Study. Autism Research, aur.2261. 10.1002/aur.2261

Messinger DS, Young GS, Webb SJ, Ozonoff S, Bryson SE, Carter A, … Zwaigenbaum L (2015). Early sex differences are not autism-specific: A Baby Siblings Research Consortium (BSRC) study. Mol Autism, 6, 32. 10.1186/s13229-015-0027-y [PubMed: 26045943]

Mitchell S, Brian J, Zwaigenbaum L, Roberts W, Szatmari P, Smith I, & Bryson S (2006). Early language and communication development of infants later diagnosed with autism spectrum disorder. Journal of Developmental and Behavioral Pediatrics, 27(2 SUPPL. 2). 10.1097/00004703-200604002-00004

Navot N, Jorgenson AG, & Webb SJ (2017). Maternal experience raising girls with autism spectrum disorder: a qualitative study. Child: Care, Health and Development, 43(4), 536–545. 10.1111/cch.12470

Nelson K (1981). Individual differences in language development: Implications for development and language. Developmental Psychology, 17(2), 170–187. 10.1037/0012-1649.17.2.170

Øien RA, Schjølberg S, Volkmar FR, Shic F, Cicchetti DV, Nordahl-Hansen A, … Chawarska K (2018). Clinical Features of Children With Autism Who Passed 18-Month Screening. Retrieved from www.aappublications.org/news

Özçalişkan Ş, & Goldin-Meadow S (2010). Sex differences in language first appear in gesture. Developmental Science, 13(5), 752–760. 10.1111/j.1467-7687.2009.00933.x [PubMed: 20712741]

Ozonoff S, Young GS, Goldring S, Greiss-Hess L, Herrera AM, Steele J, … Rogers SJ (2008). Gross motor development, movement abnormalities, and early identification of autism. Journal of Autism and Developmental Disorders, 38(4), 644–656. 10.1007/s10803-007-0430-0 [PubMed: 17805956]

Preacher KJ, Curran PJ, & Bauer DJ (2006). Computational Tools for Probing Interactions in Multiple Linear Regression, Multilevel Modeling, and Latent Curve Analysis. Journal of Educational and Behavioral Statistics Winter (Vol. 31). Retrieved from http://www.quantpsy.org/.437

Provost B, Lopez BR, & Heimerl S (2007). A comparison of motor delays in young children: Autism spectrum disorder, developmental delay, and developmental concerns. Journal of Autism and Developmental Disorders, 37(2), 321–328. 10.1007/s10803-006-0170-6 [PubMed: 16868847]

Pruden SM, & Levine SC (2017). Parents' Spatial Language Mediates a Sex Difference in Preschoolers' Spatial-Language Use. Psychological Science, 28(11), 1583–1596. 10.1177/0956797617711968 [PubMed: 28880726]

Reinisch JM, Rosenblum LA, Rubin DB, & Schulsinger MF (1991). Sex Differences In Developmental Milestones During The First Year Of Life. Journal of Psychology and Human Sexuality, 4(2), 19–36. 10.1300/J056v04n02_03

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. 10.1097/01.chi.0000227880.42780.0e [PubMed: 16926617]

Ruble DN, & Martin CL (1998). Gender development. In Handbook of child psychology (pp. 933–1016).

Rutter M, Le Couteur A, & Lord C (2003). ADI-R. Autism Diagnostic Interview Revised Los Angeles: Western Psychological Services.

Salomone E, Charman T, McConachie H, & Warreyn P (2015). Child's verbal ability and gender are associated with age at diagnosis in a sample of young children with ASD in Europe. Child: Care, Health and Development, 42(1), 141–145. 10.1111/cch.12261

Sheldrick R, Schlichting L, Berger B, Pediatrics AC-, & 2019, undefined. (n.d.). Establishing new norms for developmental milestones. Am Acad Pediatrics. Retrieved from https://pediatrics.aappublications.org/content/144/6/e20190374.abstract?casa_token=wm9k86WSTZ8AAAAA:COTrB91HKdnw02xdiu72n6xM4cJFqxeHuTtXqMegKqiusfPds2sJGQ4kKV9kMk_z6v87TzwEMA

Volkmar FR, Szatmari P, & Sparrow SS (1993). Sex differences in pervasive developmental disorders. Journal of Autism and Developmental Disorders, 23(4), 579–591. 10.1007/BF01046103 [PubMed: 8106301]

Walle EA, & Campos JJ (2014). Infant language development is related to the acquisition of walking. Developmental Psychology, 50(2), 336–348. 10.1037/a0033238 [PubMed: 23750505]

WHO | Gender and Genetics. (2010). WHO.

WHO Motor Development Study: Windows of achievement for six gross motor development milestones WHO MULTICENTRE GROWTH REFERENCE STUDY GROUP 1,2. (n.d.). 10.1080/08035320500495563

Yeargin-Allsopp M, Rice C, Karapurkar T, Doernberg N, Boyle C, & Murphy C (2003). Prevalence of autism in a US metropolitan area. Journal of the American Medical Association, 289(1), 49–55. 10.1001/jama.289.1.49 [PubMed: 12503976]

Zwaigenbaum L, Bryson SE, Szatmari P, Brian J, Smith IM, Roberts W, … Roncadin C (n.d.). Sex Differences in Children with Autism Spectrum Disorder Identified Within a High-Risk Infant Cohort. 10.1007/s10803-012-1515-y

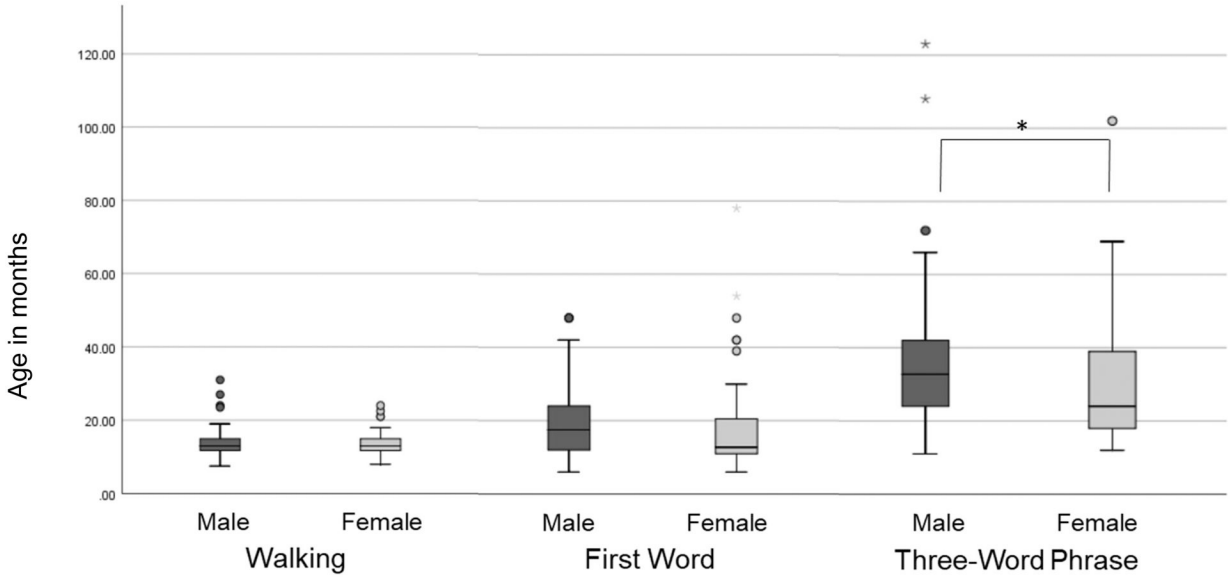

Figure 1:
Developmental Milestones by Biological Sex
* indicates significant to at least 0.05

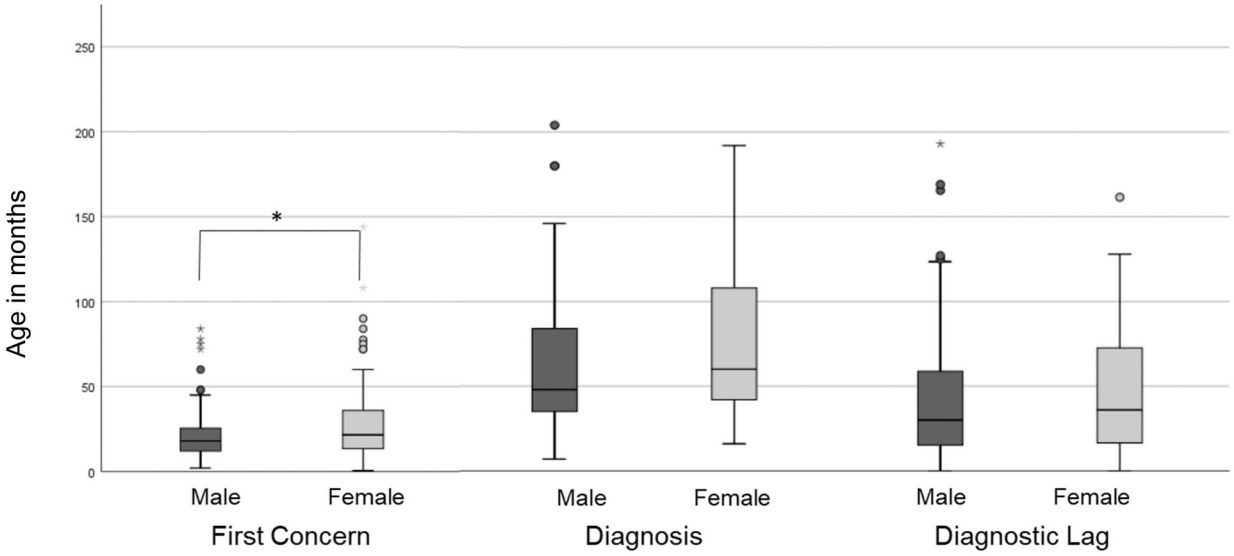

Figure 2:
Diagnostic Variables by Biological Sex
* indicates significant to at least 0.05

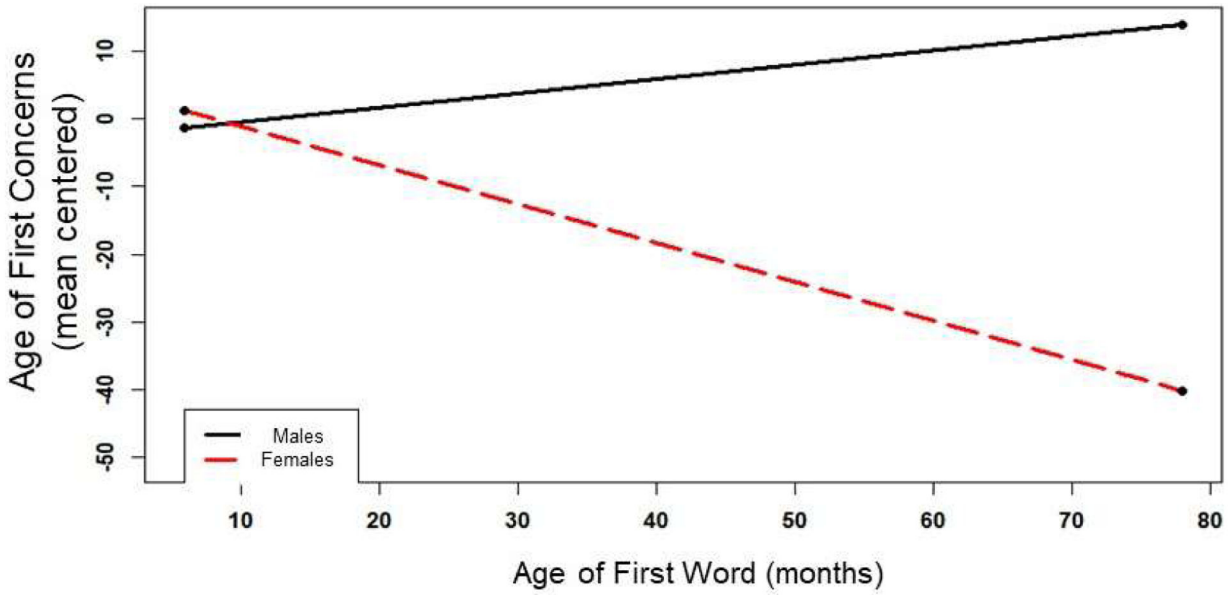

Figure 3.
Two-way interaction between sex and age of first word in predicting age of first concerns.

Table 1.

Participant Characteristics, Developmental Milestones and Diagnostic Variables by Sex

	Male (N = 105)	Female (N = 90)	F	p	η^2
Chronological age in months at entry into study	148.01 (35.50)	152.11 (35.42)	.648	.422	.003
Child Race			.474	.492	.003
White	68.6%	71.1%			
Black	2.9%	3.6%			
Asian	3.8%	5.6%			
Mixed-Race	14.3%	16.7%			
Native American	1.0%	1.1%			
Missing	9.5%	7.8%			
Child Ethnicity			1.545	.215	.009
Non-Hispanic	80.0%	74.4%			
Hispanic	11.4%	17.8%			
Missing	8.6%	7.8%			
Developmental Delay			.630	.429	.004
Yes	47.6%	52.2%			
No	39.0%	33.3%			
Missing	13.3%	14.4%			
IQ at entry into study	99.39 (19.60)	100.19 (21.68)	.073	.787	.000
ADOS-2 CSS at entry into study	7.38 (1.81)	6.39 (2.05)	11.597	.001**	.063
Mother's Education			.504	.479	.003
Less than high school	2.9%	1.1%			
High school	9.5%	6.7%			
Some college	14.3%	17.8%			
Associates degree	8.6%	5.6%			
Bachelor's degree	23.8%	18.9%			
Some graduate school	3.8%	6.7%			
Graduate degree	23.8%	25.6%			
Missing	13.3%	17.8%			

	Male (N = 105)	Female (N = 90)	F	p	η^2
Developmental Milestones					
Age of walking 10 steps (months)	13.66 (3.60)	13.57 (3.12)	.199	.656	.001
Age of first word (months)	20.57 (10.56)	17.31 (11.46)	3.854	.051	.025
Age of first three word phrase (months)	35.05 (17.96)	29.79 (15.06)	4.807	.030*	.031
Diagnostic Variables					
Age of first concerns (months)	21.46 (15.52)	28.88 (24.99)	6.582	.011*	.041
Age of ASD diagnosis (months)	63.61 (40.93)	75.62 (45.46)	3.527	.062	.023
Lag between first concerns and diagnosis (months)	41.71 (38.86)	47.80 (38.36)	.672	.414	.004

Table 2:

Predictors of Timing of Parental First Concerns and Age of Diagnosis

	Age First Concerns				Age of Diagnosis			
	ΔR^2	β	t	Sig	ΔR^2	β	t	Sig
Model 1	.036		−.049	.961	.049		.213	.832
Site		.071	.896	.372		.118	1.475	.124
Mother's Education		.089	1.091	.277		.112	1.482	.120
Race		−.073	−.912	.363		−.040	−.495	.621
Ethnicity		.019	.231	.817		.095	1.159	.248
IQ		.223**	2.797	.006		.219**	2.743	.007
Model 2	.070**		−.271	.787	.057		.091	.928
Site		.060	.762	.447		.110	1.370	.173
Mother's Education		.072	.906	.366		.110	1.337	.183
Race		−.081	−1.032	.304		−.043	−.537	.592
Ethnicity		−.001	−.016	.988		.082	.998	.320
IQ		.221**	2.826	.005		.220**	2.757	.007
Sex		.199*	2.541	.012		.119	1.479	.141
Model 3	.061		−.041	.968	.056		.440	.660
Site		.049	.614	.540		.089	1.090	.277
Mother's Education		.072	.883	.379		.123	1.476	.142
Race		−.087	−1.087	.279		−.046	−.571	.569
Ethnicity		.012	.146	.884		.112	1.321	.189
IQ		.206*	2.468	.015		.207*	2.446	.016
Sex		.190*	2.365	.019		.108	1.326	.187
Age of First Word		−.017	−.156	.876		.098	.875	.383
Age of 3-Word Phrase		.076	.685	.495		−.157	−1.379	.170
Step 4	.075		−.293	.770	.045		.561	.576
Site		.060	.729	.467		.100	1.189	.236
Mother's Education		.074	.913	.363		.123	1.469	.144
Race		−.058	−.715	.476		−.049	−.591	.556
Ethnicity		.011	.139	.890		.110	1.284	.201
IQ		.223**	2.671	.008		.204*	2.366	.019
Sex		.195**	2.452	.015		.111	1.352	.178
Age of First Word		.126	.920	.359		.060	.431	.667
Age of 3-Word Phrase		−.035	−.277	.782		−.168	−1.244	.216
Sex *First Word		−.311*	−2.030	.044		−.049	−.314	.754
Sex *Phrase		.251	1.712	.089		−.022	−.140	.889
Step 5 (Age of Dx only)					.172		.622	.535

	Age First Concerns				Age of Diagnosis			
	ΔR^2	β	t	Sig	ΔR^2	β	t	Sig
Site	-	-	-	-		.080	1.025	.307
Mother's Education	-	-	-	-		.100	1.272	.206
Race	-	-	-	-		−.032	−.410	.683
Ethnicity	-	-	-	-		.109	1.370	.173
IQ	-	-	-	-		.115	1.397	.165
Sex	-	-	-	-		.034	.430	.668
Age of First Word	-	-	-	-		.108	.827	.410
Age of 3-Word Phrase	-	-	-	-		−.183	−1.455	.148
Sex * First Word	-	-	-	-		.070	.468	.641
Sex * Phrase	-	-	-	-		−.117	−.803	.423
Age of First Concerns	-	-	-	-		.379**	4.729	.000

* p <.05

** p <.01