Early Behavioral and Environmental Predictors of Language Skills in Infants at High and Low Risk for Autism Spectrum Disorder

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Abstract

Autism spectrum disorder (ASD) is characterized by deficits in social communication and repetitive and stereotyped behaviors. In addition to having the core features of the disorder, approximately 70% of children with ASD experience language delays and deficits. Language skill is one of the most robust predictors of long-term social and educational outcomes of children. Thus, finding reliable predictors of language skills is important for early identification of children who need language interventions and the development of effective prevention and intervention strategies promoting optimal child language development. Despite recognition of the importance of language skills, our knowledge of the factors that set the foundation for early language learning, especially in infants at risk for ASD, remains limited.

This dissertation examines early behavioral and environmental factors associated with language development in infants at high and low familial risk for ASD, using a prospective, longitudinal design. In Study 1, I investigate developmental trajectories of fine motor skills between 6 and 24 months in relation to expressive language skills at 36 months. In Study 2, I examine the extent to which early gesture production at 12 months predicts 24-month receptive language skills and eventual ASD diagnosis. In Study 3, I explore relations between parent input and child language development between 12 and 36 months. Together, these three studies contribute to the field's effort to identify early emerging factors that predate and predict language skills in ASD high- and low-risk infants.

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GENERAL INTRODUCTION

Autism spectrum disorder (ASD) is characterized by deficits in social communication and interaction and the presence of repetitive or stereotyped behaviors (American Psychiatric Association, 2013). Currently, ASD is estimated to affect 1 in 58 children in the United States (Baio et al., 2018), and similar prevalence rates have been reported throughout the world, regardless of culture, geographic region, and socioeconomic factors (Baxter et al., 2015; Elsabbagh et al., 2012). An extensive body of literature suggests that early identification and interventions are the key for promoting optimal development of children with ASD (Barbaro & Dissanayake, 2009; Koegel, Koegel, Ashbaugh, & Bradshaw, 2014; Zwaigenbaum, Bauman, Choueiri, et al., 2015). Research has shown that early language skill, in particular, is robustly associated with positive long-term outcomes in children with ASD (Howlin, Goode, Hutton, & Rutter, 2004; Kover, Edmunds, & Ellis Weismer, 2016). Although language skills of children with ASD have been well documented in prior literature, relatively less is known about the factors that set the foundation for language learning in ASD. Understanding the factors that shape language learning can help facilitate early identification of children who need language interventions and inform the development of effective interventions that may significantly improve outcomes in children with or at risk for ASD (Bradshaw, Steiner, Gengoux, & Koegel, 2015; Warren et al., 2011).

In this dissertation I examine early behavioral and environmental factors that predict language skills in infants at high and low risk for ASD. Specifically, I focus on fine motor skills, gestures, and parent input – factors that are associated with language learning in children with typical development (Iverson, 2010; Rowe, 2012; Tamis-LeMonda, Kuchirko, & Song, 2014), but have not been extensively studied in infants at high risk for ASD. In the rest of this chapter, I present a targeted review of the relevant literature, followed by an overview of three studies included in the present dissertation.

ASD and Language

According to the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-V), the diagnostic criteria for ASD include two clusters of symptoms: (1) persistent impairments in social communication and interaction; and (2) repetitive behaviors or restricted interests (American Psychiatric Association, 2013). In addition to these core features, many children with ASD experience atypical language development. For example, children with ASD often achieve language milestones later than children with typical development (Howlin, 2003; Tager-Flusberg, 2016). Moreover, about 30% of children with ASD remain minimally verbal (Tager-Flusberg & Kasari, 2013). On the other hand, there is a subgroup of children with ASD who are verbally fluent and do not show difficulties with structural aspects of language (Tager-Flusberg, Edelson, & Luyster, 2011). Taken together, these studies demonstrate substantial heterogeneity in the language profiles of children with ASD.

Previous studies have also reported that language in early childhood strongly predicts social and educational outcomes in individuals with ASD. Howlin et al. (2004) found that among children with ASD, those who had speech at 5 years of age had significantly higher social competence and used fewer residential support services later in adulthood, compared to children who had no speech at 5 years. More recent studies revealed that the age of first words (Kover et al., 2016; Mayo, Chlebowski, Fein, & Eigsti, 2013) and the onset of first phrases (Kenworthy et al., 2012) are associated with later cognitive ability and adaptive functioning in children with ASD. Furthermore, studies with typically developing children suggest that early language ability predicts school readiness and academic achievement later in childhood (Durand, Loe, Yeatman,

& Feldman, 2013; Hoff, 2013). Collectively, these findings suggest that identifying reliable predictors of early language skills could be useful in maximizing the potential of not only children with ASD, but of all children.

Examining factors that are related to language outcomes is of theoretical and practical interest for researchers, educators, and parents. First, from a theoretical perspective, understanding risk factors for language impairment may help parse heterogeneity in communicative and language abilities of children with ASD (Messinger et al., 2013; Tager-Flusberg et al., 2011). Investigating mechanisms underlying early language learning in ASD can, in turn, lead to a better understanding of individual differences in ASD. Second, from clinical and educational perspectives, discovering risk factors that predict language outcomes can help identify children in need of interventions at a younger age than would be possible if we waited until language deficits or delays became apparent (Tager-Flusberg, 2016). Relatedly, examining risk factors for language deficits can help inform educational strategies used in early interventions to significantly improve developmental outcomes of children with ASD (Dawson et al., 2010; Kasari et al., 2014; Schreibman et al., 2015). For example, if difficulties with gesture are observed in children at risk for ASD and are related to later language deficits, it would be important to promote gestural use among young children at risk for language difficulties later in life. Early interventions that target precursors to language can be particularly effective during critical periods in development, when the brain is most open to the influences of experiences and relationships (Dawson, 2008; Wade, Jenkins, Venkadasalam, Binnoon-Erez, & Ganea, 2018; Werker & Hensch, 2015). In sum, investigating early predictors of language skills is a critical step for developing effective prevention and intervention strategies promoting language development.

Infant at High Risk for ASD

One way to identify factors associated with early language skills in ASD is to study infants who have an older sibling with ASD and are considered at high familial risk for developing ASD (hereafter, “high-risk”). High-risk infants represent a unique population who can provide insight on the emergence and progression of ASD-associated features. A large, multi-site infant sibling study reported that approximately 18.7% of high-risk infants develop ASD (Messinger et al., 2015; Ozonoff et al., 2011). These infants are not only at high risk for ASD but also at elevated risk for associated language delays and deficits (see Drumm & Brian, 2013 for review) as well as other clinical outcomes (Charman et al., 2017). Comparing high-risk infants to infants who have no immediate family history of ASD and are therefore at low familial risk for ASD (hereafter, “low-risk”), allows early detection of risk factors that predict later outcomes. During the past decade, a handful of prospective longitudinal ‘infant sibling’ studies have reported significant group differences between high- and low-risk infants in multiple domains of development (see Jones, Gliga, Bedford, Charman, & Johnson, 2014 for review).

Fine Motor Skills. One specific domain in which significant group difference have been found between high- and low-risk infants is motor development (see a meta-analysis by Garrido, Petrova, Watson, Garcia-Retamero, & Carballo, 2017). However, because motor skills are not part of the diagnostic criteria for ASD, they have been less examined in the infant sibling literature, relative to the core features of ASD. Also, a small number of studies have explicitly investigated whether early motor skills relate to later language outcomes in high-risk infants, despite the growing evidence that suggests significant association between motor and language skills in typical and atypical development (Iverson, 2010; Leonard & Hill, 2014). In particular, the relation between fine motor skills, defined as the ability to make fine-grained hand movements, and language outcomes remains unclear in high-risk infants (LeBarton & Iverson, 2013). Thus, examining whether and to what extent early motor skills are associated with later language skills in high-risk infants is warranted.

Gestures. Another domain of development that researchers have studied in high-risk infants is early social communication. For example, deficits in gestures[1], which are hand or body movements that speakers produce as forms of intentional communication, have been fairly well documented as a potential early risk factor of ASD in high-risk infants (see Manwaring, Stevens, Mowdood, & Lackey, 2018 for review). However, several limitations exist in prior research on early gesture production of high-risk infants. First, there has been a predominant emphasis on the amount and types of gestures, leaving our knowledge of gestures produced in conjunction with or without speech (hereafter, "gesture-speech combinations") limited. Studying gesture-speech combinations is crucial, as it may help parse variability in the communicative and language profiles of high-risk infants (Messinger et al., 2013). Second, despite the robust evidence that early gesture predicts later language in children with typical development (e.g., Rowe & Goldin-Meadow, 2009), gesture has not been extensively studied in relation to later language skills in high-risk infants. Examining whether the gesture-language relation holds within high-risk infants, despite the expected language difficulties associated with their ASD risk, has potential to guide targeted intervention approaches for high-risk infants.

Parent Input. While previous infant sibling studies have focused on behaviors such as fine motor skills and gestures (see above), less attention has been paid to the linguistic environment of high- and low-risk infants. Previous studies with typically developing children suggest that parent input is an important environmental factor that is directly relevant to child

[1]Note that gesture overlaps with fine motor skills. The distinction between gesture and fine motor skills is that gesture is primarily communicative (e.g., infant showing an object to parent), while fine motor skill does not have to be communicative (e.g., infant picking an object up).

language development (Rowe, 2012; Tamis-LeMonda, Bornstein, & Baumwell, 2001). However, less is known about the role of parent input in the infant sibling context (Leezenbaum, Campbell, Butler, & Iverson, 2014; Talbott, Nelson, & Tager-Flusberg, 2016). Furthermore, most previous studies in the ASD literature have examined parent-to-child effects in the domain of language and paid less attention to child-to-parent effects (Fusaroli, Weed, Fein, & Naigles, 2019). Thus, an open question remaining in the literature is whether high-risk infants can contribute to their own linguistic experiences. For example, some infants may influence parent language through providing fewer opportunities for parents to respond, which then may have cascading effects on infant language development (Leezenbaum et al., 2014).

In addition to the gaps in the literature reviewed above, there are other general limitations of previous infant sibling studies that need to be acknowledged. First, many studies have focused on comparing high- and low-risk infants and have not provided information on diagnostic outcomes of high-risk infants. Nevertheless, it is important to consider both ASD risk and diagnostic outcomes in order to assess the specificity of early risk markers associated with the disorder. That is, when a difference between high- and low-risk infants is found, is the difference driven by a subset of infants later diagnosed with ASD? Or is the difference a characteristic of high-risk infants as a group, suggesting that the difference may reflect a broader autism phenotype (i.e., a trait present in unaffected family members)? Examining both infants' risk for and diagnosis of ASD will allow evaluation of the specificity of risk markers and aid in early detection of the disorder and its related features. Second, the majority of prior work has been cross-sectional, which limits our ability to see a holistic longitudinal picture of early development involved in ASD. Longitudinal examinations of risk markers can extend our knowledge of how features associated with ASD unfold across development and inform the design of targeted and developmentally sensitive interventions for children.

The Present Dissertation

In this dissertation, I present three studies aimed at identifying early behavioral and environmental factors associated with language development in high- and low-risk infants, some of whom were eventually diagnosed with ASD. Of particular interest are fine motor skills, gestures, and caregiver input, all of which have been shown to provide a critical foundation for language learning in typical development (Iverson, 2010; Rowe, 2012; Tamis-LeMonda et al., 2014), but have been less studied in high-risk infants.

The three studies draw data from a prospective longitudinal investigation of early development of high- and low-risk infants. Between 6 and 36 months of age, infants were administered a comprehensive battery of behavioral assessments as well as numerous other measures. For the present dissertation, data were drawn from direct standard assessments and naturalistic interactions between infants and their caregivers. Also, to address the limitations of prior infant sibling research, all three studies in this dissertation leverage data on infants' final ASD outcomes and include a larger number of infants later diagnosed with ASD than most previous studies. Moreover, data were collected at multiple time points to examine longitudinal development of factors associated with language skills. Below I introduce each of the three specific studies in turn.

In Study 1, I examine whether the developmental trajectories of fine motor skills between 6 and 24 months predict expressive language skills at 36 months. Although impairments in motor skills are not core symptoms of ASD, a growing body of evidence suggests that there are subtle disruptions in motor development of high-risk infants, compared to low-risk infants (Garrido et al., 2017; Iverson et al., 2019). Furthermore, while links between motor and language skills have been found in typical development (e.g., Iverson, 2010), such relations have been less explored in high-risk infants. In light of these limitations, I investigate the relations between fine motor skills and later language outcomes in high-risk infants with eventual ASD diagnosis, high-risk infants with no ASD diagnosis, and low-risk infants with no ASD diagnosis in Study 1.

In Study 2, I assess the extent to which early gesture production (with or without speech) between 12 and 24 months predicts 24-month language skills and eventual ASD diagnosis of infants. As noted above, while previous research has been informative in identifying reduced gestural production as a risk factor for ASD, it has paid less attention to gesture-speech combinations in high-risk infants (Manwaring et al., 2018). Moreover, our knowledge of the predictive power of early gesture use, observed during naturalistic interactions, in relation to later language and eventual ASD diagnosis is limited. To address these issues, I use a detailed coding of videotaped sessions of caregiver-infant interactions at 12, 18, and 24 months to examine gesture use with or without speech and the degree to which early gesture relates to subsequent language and ASD outcomes in high- and low-risk infants in Study 2.

Finally, I investigate an environmental factor – specifically, parent input – associated with infants' language development between 12 and 36 months in Study 3. The important role of parent input in children's language acquisition has been well documented in typical development (Hirsh-Pasek et al., 2015; Rowe, 2012; Tamis-LeMonda et al., 2014). In contrast, most previous studies on language development in ASD have not examined the influence of parent input in children's language learning in comprehensive ways (Fusaroli et al., 2019). Furthermore, the potential reciprocal influences between parents and their high- and low-risk infants remain unknown. In an effort to extend our knowledge of the language learning environment of high-risk infants, I characterize parent input between 12 and 24 months and examine the effects of parent input on children's later language skills and vice versa in the first three years of life in Study 3.

Overall, findings from this dissertation provide a more comprehensive picture of multiple factors at the behavioral and environmental levels that shape early language development of high- and low-risk infants. Also, the findings will have implications for clinical and educational practice, facilitating early identification of infants who will likely experience language difficulties associated with ASD and informing the design of interventions that can improve language and long-term outcomes for these children.

STUDY 1:

Development of Fine Motor Skills is Associated with Expressive Language Outcomes in Infants at High and Low Risk for Autism Spectrum Disorder[2]

Abstract

A growing body of research suggests that fine motor abilities are associated with skills in a variety of domains in both typical and atypical development. In this study, we investigated developmental trajectories of fine motor skills between 6 and 24 months in relation to expressive language outcomes at 36 months in infants at high and low familial risk for autism spectrum disorder (ASD). Participants included 71 high-risk infants without ASD diagnoses, 30 high-risk infants later diagnosed with ASD, and 69 low-risk infants without ASD diagnoses. As part of a prospective, longitudinal study, fine motor skills were assessed at 6, 12, 18, and 24 months of age and expressive language outcomes at 36 months using the Mullen Scales of Early Learning. Diagnosis of ASD was determined at the infant's last visit to the lab (18, 24, or 36 months) using the Autism Diagnostic Observation Schedule. Hierarchical linear modeling revealed that high-risk infants who later developed ASD showed significantly slower growth in fine motor skills between 6 and 24 months, compared to their typically developing peers. In contrast to group differences in growth from age 6 months, cross-sectional group differences emerged only in the second year of life. Also, fine motor skills at 6 months predicted expressive language outcomes at 3 years of age. These results highlight the importance of utilizing longitudinal approaches in measuring early fine motor skills to reveal subtle group differences in infancy between ASD high-risk and low-risk infant populations and to predict their subsequent language outcomes.

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[2]Choi, Leech, Tager-Flusberg, & Nelson (2018). Development of fine motor skills is associated with expressive language outcomes in infants at high and low risk for autism spectrum disorder. *Journal of Neurodevelopmental Disorders, 10*(14).

Background

Autism spectrum disorder (ASD) is characterized by deficits in social communication and interaction, and repetitive and restricted behaviors (American Psychiatric Association, 2013). While the hallmarks of ASD are impairments in social communication and interaction, a growing body of evidence suggests that the disorder is also associated with impaired motor development. For example, a meta-analysis reported that individuals with ASD show substantial impairments in motor coordination, compared with typically developing control participants (Fournier, Hass, Naik, Lodha, & Cauraugh, 2010). A comprehensive review on motor functioning in ASD suggested that children and adults with ASD exhibit persistent difficulties across a wide set of motor behaviors including fine and gross motor skills and postural control (Bhat, Landa, & Galloway, 2011).

Fine motor skills are one specific domain for which deficits and delays are common in ASD (Bhat et al., 2011; LeBarton & Iverson, 2013). These skills refer to one's ability to make fine hand movements that often require sophisticated object manipulation, and appear more vulnerable to delay in ASD relative to general gross motor behaviors such as walking (Landa, Gross, Stuart, & Bauman, 2012). In fact, children and adults with ASD show difficulties in fine motor skills ranging from grasping toys to handwriting (Bhat et al., 2011). Moreover, infants with an older sibling with ASD, who have an approximately 20% chance of developing the disorder themselves (Ozonoff et al., 2011), exhibit deficits and delays in fine motor skills in the first few years of life (Estes et al., 2015; Landa & Garrett-Mayer, 2006; LeBarton & Iverson, 2013; Leonard et al., 2014; Libertus, Sheperd, Ross, & Landa, 2014; Toth, Dawson, Meltzoff, Greenson, & Fein, 2007). A recent meta-analysis of 34 studies reported that high-risk infants as a group show significantly poorer fine motor skills measured on the Mullen Scales of Early

Learning (Mullen, 1995), compared to low-risk infants who do not have a family history of ASD (Garrido et al., 2017). Specifically, the study identified 12-months as the earliest point when differences in fine motor skills can be reliably detected between high- and low-risk groups. Relatedly, another study found that among high-risk infants, those who subsequently developed ASD exhibited more pronounced and persistent motor difficulties, relative to high-risk infants who were later typically developing (LeBarton & Iverson, 2013).

Furthermore, a growing number of studies have suggested that motor abilities are associated with skills in other domains such as language in both typical and atypical development (Iverson, 2010; Leonard & Hill, 2014). In children with ASD specifically, motor skills in the first two years predict expressive language at 4 years (Stone & Yoder, 2001) and later speech fluency (Gernsbacher, Sauer, Geye, Schweigert, & Goldsmith, 2008). In high-risk infants, fine motor skills between 12 and 24 months significantly predict expressive language scores at 3 years (LeBarton & Iverson, 2013). And, more recently, early motor skills were found to be associated with the rate of expressive language development in high-risk infants who develop ASD (Leonard, Bedford, Pickles, & Hill, 2015). These findings thus suggest that motor and language skills are interrelated in development.

One possible explanation for the relation between motor and language skills is that development of skills in one domain (i.e., motor) can extend across other domains (i.e., language) over time to influence an outcome – a concept known as *developmental cascades* (Masten & Cicchetti, 2010). Specifically, infants with new motor skills have new learning opportunities to interact with the environment and people, which may subsequently influence how others interact with them, which in turn facilitates child language development. For instance, a previous study found that 13-month-olds who could walk shared objects with their mothers more frequently than those who could only crawl (Karasik, Tamis-LeMonda, & Adolph, 2014). Also, mothers of walking infants, in turn, were twice as likely to respond to their infants than mothers of crawling infants. Similarly, infants who can pick up objects such a toy block are more likely to share it with their caregivers, who can then provide the label for the object (e.g., "do you want to build blocks?"). The response, in turn, helps the infant learn the word "block." In short, a change in fine motor skills can alter how infants interact with objects and people, which may facilitate their language learning.

Given evidence of the motor-language links in development, deficits in early fine motor skills may help identify children who are likely to have language difficulties at a later age. Examining this possibility seems particularly relevant to infants at high risk for ASD who also have an increased prevalence of language and communication delays (Iverson & Wozniak, 2007; Messinger et al., 2013; Mitchell et al., 2006). Identifying children at risk for future language difficulties would be useful so that targeted intervention programs can be made available to them in a timely fashion.

Despite the promising research benefits of studying early fine motor skills in ASD, there are several limitations to previous work that must be acknowledged. First, although subtle group differences in early fine motor skills at single time points have been noted, growth trajectories of fine motor skills in infants at high and low risk infants for ASD have yet to be thoroughly studied across infancy (Estes et al., 2015; Iverson & Wozniak, 2007). Studying how children's fine motor skills develop over time may help depict a more complete picture of early development in infants at high and low risk for ASD than collecting a snapshot of their abilities at a single age. Relatedly, it remains unclear whether and to what extent growth trajectories of early fine motor skills are related to later language skills in infants at high and low risk for ASD. Previous research has pooled fine motor skill data across different time points (i.e., using composite scores of fine motor skills) to predict language outcomes (Gernsbacher et al., 2008; LeBarton & Iverson, 2013). Although useful, prior research thus leaves the open question of which specific growth parameters of fine motor skills (i.e., a child's status, velocity, and acceleration in fine motor skills) may help predict subsequent language skills.

In the current study, we studied growth, or change over time, in fine motor skills between 6 and 24 months in relation to expressive language scores at 36 months in infants at high and low familial risk for ASD. By examining growth, we investigated whether groups differed in their trajectories of fine motor skills and determined which growth parameters of fine motor skills were linked to later language outcomes. First, we employed a unique growth modeling approach to ask whether growth in fine motor skills may differentiate three diagnostic groups: high-risk infants who were later diagnosed with ASD (HRA+), high-risk infants with no ASD diagnosis (HRA-), and low-risk control infants with no diagnosis (LRC). We then used individual growth parameters of fine motor skills to predict expressive language at 36 months. Our specific research questions were as follows:

1. Do HRA+, HRA-, and LRC infants differ in their growth trajectories of fine motor skills between 6 and 24 months of age?
2. Do growth parameters of early fine motor skills (i.e., a child's status, velocity, and acceleration in fine motor skills) predict expressive language at 36 months?

Methods

Participants

Participants were drawn from a prospective, longitudinal study of infants at high and low risk for ASD across the first three years of life. Eligibility criteria for all infants included a gestational age of at least 36 weeks, no known prenatal or perinatal complications, and no known genetic disorders. For the present study, the sample included infants who had fine motor skill data available for at least one time point at 6, 12, 18, and/or 24 months and an ASD evaluation at their last visit to the lab (either at 18, 24, or 36 months). The final analysis sample included 170 infants.

Of the 170 infants, 101 infants were classified as high risk for autism (HRA) because they had an older sibling with a community diagnosis of ASD. To verify older siblings' ASD diagnoses, we used the Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000) and/or age-appropriate screeners including the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003) for probands older than four, and the Pervasive Developmental Disorders Screening Test-II (PDDST-II; Siegel, 2004) for probands younger than four, with the best clinical judgment by a psychologist, where required.

ASD diagnoses in 52 older siblings of HRA infants (51% of the HRA sample in the current study) were verified using both the ADOS and SCQ. Four HRA older siblings (4%) had the ADOS. Thirty-seven older siblings (37%) had their diagnosis verified using the SCQ and three older siblings (3%) had the PDDST-II, as they did not have the ADOS. Five older siblings (5%) did not have an ADOS, SCQ, or PDDST-II, and therefore were unable to have their diagnoses verified; however, all five of them had received their ASD diagnoses in specialist clinics, and data from their younger siblings were included in the current study.

Sixty-nine infants were classified as low-risk infants (LRC) if they had a typically developing older sibling and no first- or second-degree family members with ASD. ASD diagnoses in 48 older siblings of LRC infants (70% of the LRC sample) were verified using both the ADOS and SCQ. Three older siblings (4%) had the ADOS. Thirteen older siblings (19%) had the SCQ and one sibling (1%) had the PDDST-II, as they did not have the ADOS. Finally, four LRC older siblings (6%) did not have an ADOS, SCQ, or PDDST-II; however, data from their younger siblings were included in the study, as their parents reported no clinical concerns in the older siblings.

For purposes of analyses, infants were further categorized into three groups based on their risk status (high- vs. low-risk) and an eventual ASD diagnosis (ASD vs. no ASD). Of the 101 HRA infants, 30 later met criteria for ASD (HRA+), and 71 did not meet criteria for ASD (HRA-). Of the 69 LRC infants, none met criteria for ASD (LRC).

Demographic characteristics for participants were collected at the first laboratory visit and are shown in Table 1.1, broken down by three groups and age. Infants in the three groups did not differ significantly on their race/ethnicity, sex distributions, and household income. However, there was a significant group difference in maternal education[3]. For data analysis, a composite score for socioeconomic status (SES) was generated by combining household income and maternal education using Principal Component Analysis, as the two variables were significantly and positively related to each other (r = .29, p = .0004). The first principal component weighted maternal education and income positively and equally and explained about 64% of the original variance (M = 0, SD = 1.14). The group difference remained significant in the SES composite such that HRA+ infants had the lowest level of SES.

Procedures

This study was approved by the Institutional Review Boards (IRB) at Boston Children's Hospital and Boston University. Written, informed consent was obtained from all caregivers

[3]LRC mothers demonstrated the highest levels of maternal education. Although our sample as a whole was recruited from a relatively high socioeconomic areas of greater New England area, our LRC families, in particular, had unusually high levels of maternal education. Specifically, the majority of mothers of LRC infants (60 out of 62 families; 97%) had at least four-year college degree, and the remaining two families (3%) indicated community college/two-year degree as the highest education level attained.

Table 1.1. Sample characteristics, by age and group

	HRA+	HRA-	LRC	*p* (3-group)
Sex (% female)	30.0 *N* = 30	53.5 *N* = 71	44.9 *N* = 69	.09
Race/ethnicity (% White)	83.3 *N* = 30	95.7 *N* = 71	88.4 *N* = 69	.08
[a] Household income	7.08 (2.02) *N* = 24	7.69 (0.91) *N* = 67	7.52 (1.38) *N* = 58	.79
[b] Mother's level of education	5.04 (1.72) *N* = 25	5.74 (1.65) *N* = 68	6.65 (1.22) *N* = 62	< .001***
Actual age at visits				
6 months	5.91 (0.43) *N* = 22	5.96 (0.28) *N* = 50	5.97 (0.36) *N* = 61	.79
12 months	11.93 (0.45) *N* = 30	11.94 (0.38) *N* = 67	11.87 (0.42) *N* = 67	.54
18 months	18.12 (0.78) *N* = 25	17.91 (0.42) *N* = 67	18.01 (0.27) *N* = 67	.11
24 months	24.16 (0.55) *N* = 25	24.03 (0.55) *N* = 61	24.10 (0.56) *N* = 63	.60
36 months	36.09 (0.68) *N* = 22	36.57 (1.50) *N* = 51	36.33 (0.64) *N* = 54	.20

Note. Data are reported as group means with standard deviations in parentheses. [a] Income was reported on an eight-point scale: (1) less than $15,000, (2) $15,000-$25,000, (3) $25,000-$35,000, (4) $35,000-$45,000, (5) $45,000-$55,000, (6) $55,000-$65,000, (7) $65,000-$75,000, (8) more than $75,000. [b] Education was reported as highest level attained on a 9-point scale: (1) some high school, (2) high school graduate, (3) some college, (4) community college/two-year degree, (5) four-year college degree, (6) some graduate school, (7) master's degree, (8) doctoral degree, (9) professional degree.

$^{***}p < 0.001$.

prior to their infants' participation in the study. Infants were recruited and allowed to enter the study at different ages (e.g., 6 or 12 months) as long as their first visit took place no later than 12 months of age.

At 6, 12, 18, 24, and 36 months of age, trained examiners administered the Mullen Scales of Early Learning (MSEL; Mullen, 1995) to children who visited the laboratory. ASD diagnoses were made at 18, 24, and 36 months. At the child's last visit (either 18, 24, or 36 months), final ASD diagnoses for children were determined on the basis of the ADOS using the revised algorithm, with the best clinical judgment by a psychologist. If there were multiple diagnostic evaluations (e.g., children completed ASD evaluations at 18, 24, and 36 months), the ultimate categorization was made at the last visit (e.g., 36 months) by a licensed psychologist. Depending on the child's last visit, ASD outcome classifications were made at 18 months for 13 children (8% of the sample in the present study; $n_{\text{HRA+}} = 3$; $n_{\text{HRA-}} = 4$; $n_{\text{LRC}} = 6$), at 24 months for 24 children (14%; $n_{\text{HRA+}} = 3$; $n_{\text{HRA-}} = 13$; $n_{\text{LRC}} = 8$), or at 36 months for 133 children (78%; $n_{\text{HRA+}} = 24$; $n_{\text{HRA-}} = 54$; $n_{\text{LRC}} = 55$). Although the majority of our children had their ASD outcome classifications made at 36 months, the rest of children had their ASD outcomes made at earlier age points (18 or 24 months) due to sample attrition. As prior research suggests the high diagnostic stability of ASD at 18 and 24 months (Ozonoff et al., 2015; Zwaigenbaum et al., 2016), infants with ASD diagnoses made between 18 and 36 months were included in the current study, similar to previous studies (Levin, Varcin, O'Leary, Tager-Flusberg, & Nelson, 2017; Talbott et al., 2016).

Measures

Mullen Scales of Early Learning (MSEL; Mullen, 1995). The MSEL is a standardized, normed, developmental assessment for children from 0 to 68 months and provides an overall index of cognitive ability and potential delay. The MSEL consists of five scales: Gross Motor, Visual Reception, Fine Motor, Expressive Language, and Receptive Language. In this study, we used the MSEL Fine Motor, Expressive Language, and Visual Reception scales. More specifically, we used raw scores from the Fine Motor scale at 6, 12, 18, and 24 months to study longitudinal trajectories of children's fine motor skills development. We used children's raw scores from the Expressive Language scale at 36 months to assess children's expressive language outcomes. Raw scores from the Visual Reception scale at 6 months were used as a covariate to control for nonverbal cognition in regression analyses of fine motor and expressive language relations, as variation in children's early fine motor skills may arise from differences in general nonverbal skill (LeBarton & Iverson, 2013). The possible ranges of raw scores for the Fine Motor scale are 0 to 49, and 0 to 50 for the Expressive Language and Visual Reception scales. We used raw scores rather than standardized scores (i.e., T scores), as raw scores allowed us to better capture individual differences in skills across time. Relatedly, we used child exact age at each visit as our measure of time to control for differences in age of testing (Table 1.1), which might affect children's raw scores on MSEL.

Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000). The ADOS is a semi-structured play assessment of social interaction, communication, and restricted interests/ repetitive behavior. Research staff with extensive experience in testing children with developmental disorders administered and scored children's ADOS. In addition, an ADOS-reliable researcher co-scored the ADOS via video recording. When children met the criteria for ASD on the ADOS or came within three points of cutoffs, a licensed clinical psychologist reviewed the ADOS scores and behavioral assessment videos to determine final clinical judgment: ASD or no ASD.

Data Reduction and Analysis

Because of data attrition associated with longitudinal design (e.g., infants not yet enrolled in study, visits missed by families), 6-month fine motor skill data were available for n = 133, 12-month data for n = 164, 18-month data for n = 159, and 24-month data for n = 149 children. Of note, 110 of 170 infants contributed fine motor skills data at all four time points.

In order to address our research goals, we carried out analyses in two stages. In the first step, to explore group differences, we used hierarchical linear modeling (HLM) to best characterize each group's fine motor skills growth between 6 and 24 months (see Appendix A). HLM allowed us to model developmental trajectories of each individual, and accommodate the nested, hierarchical nature of the data (i.e., multiple measurements within infants) and missing data in our longitudinal design. Applications of HLM for growth involved a two-level hierarchical structure, where we first modeled each child's change over time in fine motor skills (Level 1), and then determined whether fine motor skills among the groups showed differences in growth parameters (Level 2). Specifically, at Level 1 (within children), we included time-variant predictors such as a linear age variable (*age)* and a quadratic age variable (age^2). We centered age at the earliest data collection point, 6 months or 0.5 years, so that parameters are more interpretable (Singer & Willett, 2003) and reflect children's fine motor skills and rate of growth at 6 months. In addition, we performed post-hoc analyses by re-centering time so that the trajectories' intercept systematically varied by age (i.e., $age_{ti} – 12$, $age_{ti} – 18$, $age_{ti} – 24$). Re-centering time allowed us to examine the point at which the divergence of developmental trajectories between outcome groups became statistically significant. If we did not center age, the model would estimate growth rates when children are at birth (i.e., 0 months), for which we would expect no measurable fine motor skill or growth. The quadratic age variable (age^2)

represents the acceleration (or deceleration) in the rate of change and was calculated by squaring the centered linear age variable. At Level 2 (between children), time-invariant predictors included groups (*group*; HRA+, HRA-, LRC). The fully specified equation for our model is summarized in Appendix A.

In the second step, our goal was to determine which growth parameters of early fine motor skills (i.e., status, velocity, and acceleration) between 6 and 24 months explain significant variance in children's expressive language outcomes at 36 months. Thus, we employed individual growth rates of fine motor skills from our Level-1 HLM model as independent variables to predict later expressive language skills in regression analyses (see Appendix B). That is, we used a prediction model, in which we calculated individual growth rates, or Empirical Bayes' posterior means (Raudenbush & Bryk, 2002), using the random effects and fixed effects coefficients from our HLM model that includes only Level 1 predictors. An estimate was created for each child computed from a weighted combination of the individual child's growth trajectory (the random effect coefficient) as well as the average trajectory of the entire sample (the fixed effect coefficient). The rationale for using the method of Empirical Bayes stems from prior work that shows these Empirical Bayes' predictions from models are unbiased and precise (i.e., more similar to true values) than the predictions generated from a standard ordinary least squares (OLS) regression (Raudenbush & Bryk, 2002). Similar to previous work employing the same analytic strategy (Rowe, Raudenbush, & Goldin-Meadow, 2012), we found that the three predictors were too collinear to include simultaneously into one regression model. Thus, we fit three separate models for each predictor. All analyses were conducted using Stata and R, and HLM models were fit with the lmer package within R (Bates, Mächler, Bolker, & Walker, 2014).

Results

Modeling Fine Motor Skills Growth

Descriptive data on cross-sectional fine motor skills, as measured on MSEL, between 6 and 24 months are presented in Table 1.2. Of note, although HRA+ infants as a group demonstrated lower raw scores on the MSEL Fine Motor scale, compared to HRA- and LRC infants, the scores of all groups were within the range of typical development.

To best characterize the developmental trajectories of fine motor skills between 6 and 24 months in HRA+, HRA-, and LRC infants, we used the following model building strategies. Preliminary visual inspection of the raw data suggested fine motor skills followed a curvilinear trajectory between 6 and 24 months. Statistical analyses confirmed this pattern: the best fitting model to the data contained both a linear and quadratic growth term, *-2 log likelihood* = -1231, $\chi^2(7) = 1481$, $p < .001$. Next, we added the interaction between group (HRA+, HRA-, LRC) and age (both linear and quadratic) to determine whether change in fine motor skills differed between groups. Results revealed that the groups significantly differed from one another in the linear growth only, $\hat{\beta}_{HRA+*AGE} = -0.83$, $SE_{HRA+*AGE} = 0.39$, $p = .04$; $\hat{\beta}_{HRA-*AGE} = -0.51$, $SE_{HRA-*AGE} = 0.30$, $p = .09$. A model with a group x quadratic age interaction fit the data no better than a model without it. As such, we removed this term and retained only the group x linear age interaction in subsequent models. We completed our model building process by adding demographic covariates (i.e., sex and SES). Neither of the covariates significantly predicted fine motor skills and were thus not included in the final model.

Our final HLM model summaries are presented in Table 1.3. The final model considered between-child associations of groups with status (intercept), velocity (linear growth), and acceleration (quadratic growth) in fine motor skills, and an interaction effect between groups and linear growth at 6 months. Note that we entered the LRC group into all models as a reference

Table 1.2. Descriptive statistics, group comparisons, and effect sizes of pairwise comparisons of cross-sectional data from the MSEL Fine Motor subscale, by age and group

Age	HRA+	HRA-	LRC	*p* (3-group)	*d (HRA+ vs. HRA-)*	*d (HRA+ vs. LRC)*	*d (HRA- vs. LRC)*
6	7.86 (1.21) 6-11 *N* = 22	8.42 (1.28) 6-12 *N* = 50	8.13 (1.27) 6-12 *N* = 61	0.20	-0.44	-0.22	0.23
12	16.5 (2.08) 12-21 *N* = 30	17.27 (1.80) 12-20 *N* = 67	16.58 (1.63) 12-20 *N* = 67	0.04	-0.41	-0.05	0.40
18	20.36 (1.66) 16-24 *N* = 25	21.03 (1.64) 17-24 *N* = 67	20.96 (1.54) 19-25 *N* = 67	0.19	-0.41	-0.38	0.04
24	24.12 (2.42) 19-28 *N* = 25	25.13 (2.12) 20-29 *N* = 61	25.56 (2.59) 20-32 *N* = 63	0.04	-0.46	-0.57	-0.18

Table 1.3. Final growth model of group predicting growth trajectories for fine motor skills (age centered at 6 months; *N* = 170)

	Coefficient	SE
Intercept	8.38***	0.19
Linear growth	17.71***	0.44
Quadratic growth	-4.38***	0.27
HRA+	0.08	0.34
HRA-	0.58*	0.26
Linear x HRA+	-0.83*	0.39
Linear x HRA-	-0.51	0.30
Variance Components		
Goodness of fit (-2 log likelihood)	-1226.94	
Variance in intercept	0.27	
Variance in growth rate	1.70	
Variance in acceleration	1.72	

Note. $^{***}p < 0.001$, $^{*}p < 0.05$.

group; therefore, the coefficients generated for HRA+ and HRA- groups reflected deviations in intercept, slope, and acceleration from the LRC group. The final model shows that, on average, LRC infants at 6 months had estimated fine motor skills of approximately 8 points, with an increase in fine motor skills at this age at a rate of 17.71 points per year. Of note, after studying how high-risk infants differed in their fine motor skills development from those of low-risk infants (i.e., LRC as a reference group), we systematically rotated which group served as the comparison to examine potential differences in growth trajectories among three groups. Estimated growth trajectories of fine motor skills from 6 to 24 months are presented for all three groups in Figure 1.1.

As can be seen in the figure, when we compared *status* of fine motor skills (i.e., intercept) among three groups, HRA+ infants did not significantly differ from their typically developing peers (both HRA- and LRC) at 6 months, indicating that three groups were indistinguishable by their fine motor skills at 6 months. However, when age was re-centered at 12, 18, and 24 months to identify points of divergence in developmental trajectories of fine motor skills, HRA+ infants showed significantly lower fine motor skills than HRA- infants starting at 12 months, $t = 2.45$, $p = .015$, and than LRC infants at 18 months, $t = -2.34$, $p = .020$. Thus, these results indicate that infants later diagnosed with ASD began to diverge from their typically developing peers by their first birthday, although when these groups diverged depended on whether they were infants at high or low risk for autism. Interestingly, at 6 months, HRA- infants had significantly stronger fine motor scores compared to LRC infants, $t = 2.19$, $p = .030$, but this difference no longer reached significance beginning at 12 months.

When we compared *velocity* in fine motor skills (i.e., linear growth) among the three groups, HRA+ infants had significantly slower growth rates than LRC infants at 6 months

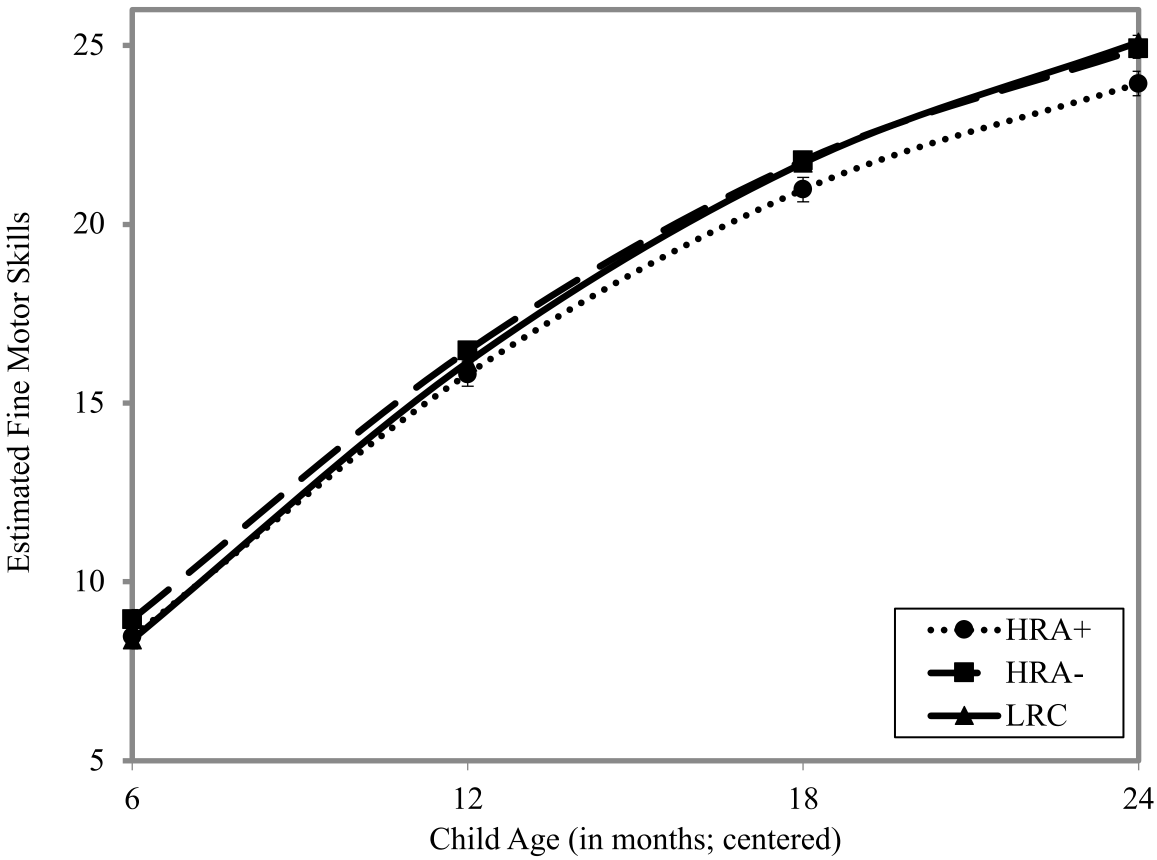

Figure 1.1. The average growth in fine motor skills for three groups. Error bars represent the standard error of the mean.

through 24 months, $t = -2.11$, $p = .036$. Specifically, the average growth rate for HRA+ group ($M = 16.88$, $SE = 0.39$) was approximately two standard errors below the mean of LRC group ($M = 17.71$, $SE = 0.44$). The HRA- infants also had slower growth rates than the LRC group between 6 and 24 months, but this difference did not reach statistical significance, $t = -1.68$, $p = .094$. Thus, while the groups demonstrated comparable status of fine motor skills at 6 months, HLM revealed subtle group differences in growth in fine motor skills from 6 months.

Using Growth Parameters of Fine Motor Skills to Predict Expressive Language Outcomes

To investigate which growth parameters of fine motor skills between 6 and 24 months predict expressive language outcomes at 36 months, we first examined descriptive statistics on the language outcomes (Table 1.4) and found significant group differences on 36-month expressive language scores. Specifically, high-risk infants scored significantly lower on the MSEL Expressive Language scale at 36 months, compared to low-risk infants. Next, we fitted a series of regression models with each of the growth parameters as the independent variable and expressive language scores as the dependent variable. In regression analyses, we controlled for children's nonverbal cognition, as indexed by MSEL visual reception scores at 6 months, to evaluate whether variance in expressive language skills was accounted for by the fine motor growth parameters above and beyond any variance accounted for by children's general nonverbal skill. The visual reception scores, assessed independently of children's motor abilities, did not differ across groups at 6 months (Table 1.4). In addition, child sex and SES, which significantly differed across groups and also are identified as related to children's language skills in previous research (Fernald, Marchman, & Weisleder, 2013; Hart & Risley, 1992), were included as covariates.

Table 1.4. Mean and standard deviation for MSEL Expressive Language subscale raw scores at 36 months and MSEL Visual Reception subscale raw scores at 6 months

	HRA+	HRA-	LRC	*p (*3-group)
MSEL Expressive Language at 36 months	31.32 (4.28) $N = 22$	35.02 (4.53) $N = 51$	37.26 (3.89) $N = 54$	< .001***
MSEL Visual Reception at 6 months	8.41 (1.74) $N = 22$	8.6 (1.54) $N = 50$	8.44 (1.65) $N = 61$	.85

Note. $^{***}p < 0.001$.

Table 1.5 shows the results of regression analyses. Specifically, the status of fine motor skills at 6 months (Model 1) was a significant, positive predictor of 36-month expressive language scores, when controlling for 6-month visual reception scores, sex, and SES. In other words, these results illustrate that when accounting for children's general nonverbal cognition, sex, and SES, a child whose 6-month fine motor skills scored at the sample mean had an expressive language score of 35 points at 36 months, and every one unit increment in fine motor skills at 6 months was associated with approximately four-point difference (*SE* = 1.22) in 36-month language scores, $t = 3.64$, $p < .001$, $R^2 = 23.6\%$, 95% CI = [2.02, 6.88]. When accounting for the covariates, the velocity in fine motor skills (Model 2) was marginally significant in predicting later expressive language scores, $t = 1.81$, $p = .07$, $R^2 = 14.4\%$. The acceleration (Model 3) did not result in significant variance explained in later language skills, $t = -.03$, $p = .98$, $R^2 = 10.9\%$. As the models were not nested, we compared Bayesian Information Criterion (BIC) estimates to determine which growth parameter best accounted for variance in the language outcomes. This comparison suggests that the model with the status of fine motor skills had the lowest BIC (510) value, relative to the models with the velocity or acceleration parameters (*BICs* = 520, 523, respectively). Together, a child's 6-month fine motor skills provided the most helpful information to estimate the child's expressive language at 3 years of age.

Finally, we included interaction terms between each of growth parameters and group (e.g., linear x group) to determine whether the relations between growth parameters of fine motor skills and expressive language outcomes differ across groups (not shown). A model resulted in no significant interactions between growth parameters and groups, suggesting that the effect of

Table 1.5. Growth models predicting 36-month expressive language skills, when controlling for nonverbal cognition, SES, and sex

	Model 1	Model 2	Model 3
Intercept	34.89***	33.28***	31.82***
Predicted status at 6 months	4.45***		
Predicted velocity at 6 months		1.14~	
Predicted acceleration at 6 months			-0.02
Nonverbal cognition at 6 months	0.07	0.25	0.39
SES	1.45**	1.54**	1.50**
Sex	0.08	0.63	0.97
R^2	23.6%	14.4%	10.9%
BIC	510	520	523

Note. $^{***}p < 0.001$, $^{**}p < 0.01$, $\sim p < 0.1$

fine motor skills on later expressive language outcomes did not differ for HRA+, HRA-, and LRC infants.

Discussion

In the current study we examined growth trajectories of fine motor skills between 6 and 24 months and determined which growth parameters of fine motor skills predict language outcomes at 36 months in high-risk infants later diagnosed with ASD, high-risk infants with no ASD diagnosis, and low-risk infants with no ASD diagnosis. Our key findings were that the development of fine motor skills was slower between 6 and 24 months in high-risk infants later diagnosed with ASD, compared to that of their typically developing peers, and that early fine motor skills were associated with subsequent expressive language skills at 36 months in all three groups.

Growth Trajectories of Early Fine Motor Skills

HLM revealed that infants at high risk for ASD who themselves later developed ASD had slower growth in fine motor skills between 6 and 24 months of age, compared to infants at low risk for ASD. This finding is consistent with those of previous studies that also employed longitudinal approaches and examined infants' performance on the MSEL. Specifically, a prior study reported that high-risk infants later diagnosed with ASD deviated from unaffected infants at around 14 months and developed more slowly through 24 months on the MSEL Fine Motor scale (Landa & Garrett-Mayer, 2006). Similarly, another study using latent class analysis identified slower developmental trajectories of fine motor skills in children with ASD between 6 and 36 months, compared to children without ASD (Landa, Gross, Stuart, & Faherty, 2013). This study thus adds to the existing research suggesting slower development in infancy in children with ASD. However, while these group differences between high-risk infants with ASD diagnoses and low-risk infants without ASD diagnoses were statistically significant, they were subtle and small (Figure 1.1; Table 1.2). Moreover, fine motor scores for all groups were within the range of typical development, indicating that these modest group differences may not rise to the level of detection by parents or clinicians in many cases.

Our data indicated that although high-risk infants later diagnosed with ASD showed slower growth in fine motor skills between the 6- to 24-month period, relative to that of high-risk infants without ASD diagnoses, this difference was not statistically significant. This non-significant difference between the two high-risk groups suggests that slower fine motor growth may not be specific to ASD. Our finding is consistent with those from prior research indicating that fine motor differences may be a characteristic of infants at high risk for ASD, rather than a core characteristic of the disorder (Libertus et al., 2014).

With regard to the status of fine motor skills at 6 months, there was no statistically significant difference between high-risk infants who later developed ASD and typically developing high- and low-risk infants. Only beginning in the second year of life did high-risk infants who later developed ASD score significantly lower on the MSEL Fine Motor scale than high- and low-risk infants without eventual diagnosis. The non-significant group difference in status of fine motor skills at 6 months stands in contrast to some of prior findings that reported high-risk infants tend to show differences in fine motor skills, relative to their low-risk peers as early as 6 months (Libertus et al., 2014). Given mixed evidence of fine motor differences in infancy (i.e., 6-7 month), future research is needed to replicate the examination of fine motor skill development with larger samples, particularly within the first year of life in ASD risk populations.

To our surprise, high-risk infants who did not develop ASD showed stronger fine motor scores than low-risk infants at 6 months, but the difference was transient, with these infants showing comparable fine motor scores from 12 months onward. This difference may reflect a random sampling error. Alternatively, strong early fine motor skills may function as a protective factor, rather than a risk factor, for some high-risk infants. That is, while all high-risk infants presumably carry genetic risk factors for ASD, those with stronger fine motor skills may require greater familial etiologic load to manifest the ASD phenotype (Szatmari, 2017). Examining the extent to which fine motor skills may act as a protective or risk factor for high-risk infants will be an important avenue for future research.

The results of the first part of our study highlight the importance of investigating the course of developmental change in skills over time. Studies of other behavioral domains lend support for this need to focus on developmental change (Zwaigenbaum, Bauman, Stone, et al., 2015). For example, an eye-tracking study reported that infants later diagnosed with ASD showed a decline in fixation to the eye region of the face from 2 to 6 months and were distinguishable from their typically developing peers by change over time; however, cross-sectional group differences in eye fixation emerged only later in the first year (Jones & Klin, 2013). Thus, while cross-sectional research identifies group differences at individual time points, longitudinal approaches can capture developmental change over time and depict a more comprehensive and nuanced picture of early development in infants at high and low risk for ASD.

Fine Motor Growth Trajectories Predict Expressive Language Outcomes

In our analysis to determine which growth parameters of early fine motor skills predict subsequent expressive language outcomes at 36 months, we found that the status of fine motor skills from the 6- to 24-month growth model was a significant, positive predictor of later expressive language outcomes, even after controlling for nonverbal cognition scores, sex, and SES. In other words, infants with poorer fine motor skills across the first two years of life scored significantly lower on expressive language at 36 months, even when the covariates were taken into account. On the other hand, the velocity in fine motor skills was marginally associated with subsequent expressive language outcomes, and the acceleration was not significantly associated with the outcomes, when controlling for the covariates. Thus, it appears that status of early fine motor skills may provide the most useful information about later expressive language skills among the growth parameters (i.e., status, velocity, and acceleration).

Also, the significant, positive associations between early fine motor skills and subsequent expressive language outcomes did not differ across all three groups, suggesting that differences in fine motor skills over time can have cascading effects on language outcomes for both high-risk infants who later developed ASD and typically developing high- and low-risk infants. These findings align with prior work on developmental motor-language cascades (LeBarton & Iverson, 2013; Libertus & Violi, 2016) demonstrating that children's early motor skills are significantly and positively related to later expressive language skills in both typical and atypical development.

Finally, the associations between early fine motor skills and later language abilities highlight a potential avenue for early intervention practices. Given that the findings of this study suggest that fine motor skills in infancy may influence subsequent expressive language outcomes, an assessment of early fine motor skills holds promise for early identification of difficulties in language which emerge later in life in high-risk infants (Iverson & Wozniak, 2007; Mitchell et al., 2006). By identifying and addressing infants' difficulties in fine motor skills in a timely fashion, we may then prevent cascading effects of motor impairments on children's language development. In fact, a growing body of literature suggests promising effects of early motor training on other domains of development. For example, 'sticky mittens' with Velcro strips are associated with increased object exploration behaviors in infants that are shown positively related to subsequent language development (Koterba, Leezenbaum, & Iverson, 2014; Libertus, Joh, & Needham, 2015).

Our findings should be interpreted in light of key limitations. First, due to the high levels of maternal education, our sample may not be a nationally representative sample of infants at high and low risk for ASD. Therefore, findings may not be generalizable to the larger population of infants at high and low risk for ASD. Second, our study focused on examining the relations between early fine motor skill development and later expressive language outcomes in infants at risk for ASD. More studies are needed to closely investigate the motor-language relations in other neurodevelopmental disorders such as developmental language disorders and dyslexia. Third, ASD outcomes of 22% of our participants were made at 18 or 24 months instead of at 36 months, when diagnosis can be reliably made (Chawarska, Klin, Paul, & Volkmar, 2007). Therefore, it is possible that those diagnosed at 18 or 24 months would or would not have met criteria for ASD at 36 months. However, the best clinical judgment was made by an expert clinician for those children using comprehensive data including developmental history and standardized tools. In addition, recent studies suggest high diagnostic stability for infants at high familial risk at this age (Ozonoff et al., 2015; Zwaigenbaum et al., 2016). While we made a decision to include those with ASD outcomes made at 18-36 months to maximize our sample size, future research could minimize the variation in age of diagnosis until there is more evidence for stable diagnosis as early as 18 months of age. Despite these limitations, our findings have the potential to promote longitudinal examinations of infants at increased risk for ASD and influence how we intervene to promote their optimal language outcomes.

Conclusions

Overall, our results suggest that fine motor skills growth between 6 and 24 months is significantly slower in high-risk infants with eventual ASD diagnosis, compared to high- and low-risk peers without eventual diagnosis, and predicts expressive language skills at three years of age. This work highlights the importance of studying children's skills within the context of developmental trajectories. Specifically, examining children's developmental change over time may create a more complete picture than collecting a snapshot of their abilities at a single age. Finally, poor performance on early fine motor skills may indicate an increased risk for language difficulties in children and be addressed early in life to promote children's optimal language outcomes. Targeting early fine motor skills in infancy seems promising, considering that these skills seem amenable to intervention (Koterba et al., 2014; Libertus et al., 2015), and that children can have the most gains during sensitive periods when their brains are receptive to the environment (Fox, Levitt, & Nelson, 2010). Altogether, our results suggest that closer attention to developmental trajectories of fine motor skills in relation to later developmental outcomes may be warranted in infants at high familial risk for ASD.

STUDY 2:

Gesture Development, Caregiver Responsiveness, and Language and Diagnostic Outcomes in Infants at High and Low Risk for Autism[4]

Abstract

We investigated gesture production in infants at high and low risk for autism spectrum disorder (ASD) and caregiver responsiveness between 12 and 24 months of age and assessed the extent to which early gesture predicts later language and ASD outcomes. Participants included 55 high-risk infants, 21 of whom later met criteria for ASD, 34 low-risk infants, and their caregivers. Results indicated that a) infants with ASD outcomes used fewer gestures and a lower proportion of developmentally advanced gesture-speech combinations; b) caregivers of all the infants provided similar rates of contingent responses to their infants' gestures; and c) gesture production at 12 months predicted subsequent receptive language and ASD outcomes within the high-risk group.

[4]Choi, Shah, Rowe, Nelson, & Tager-Flusberg (in press.) Gesture development, caregiver responsiveness, and language and diagnostic outcomes in infants at high and low risk for autism. *Journal of Autism and Developmental Disorders*, 1-17.

Background

Deficits in nonverbal communicative behaviors are among the hallmark features of autism spectrum disorder (ASD; American Psychiatric Association, 2013). In particular, deficits in gestures, which are hand or body movements that speakers produce as forms of intentional communication, have been well documented in the autism literature. Previous studies suggest that infants with ASD produce significantly fewer gestures than infants without ASD as early as 12–14 months (Landa, Holman, & Garrett-Mayer, 2007; Manwaring, Stevens, Mowdood, & Lackey, 2018; Zwaigenbaum et al., 2005), and that atypicality of gesture usage persists into childhood and adulthood (de Marchena & Eigsti, 2010; Morett, O'Hearn, Luna, & Ghuman, 2016). Furthermore, a number of prospective studies have examined gesture as a potential early sign in infants with an older sibling with ASD, who are at high familial risk for the disorder (hereafter, "high-risk"; Ozonoff et al., 2011). Significant group differences between high-risk infants and infants with no family history of ASD (hereafter, "low-risk") have been found in previous studies, with high-risk infants producing fewer gestures, compared to their low-risk peers (Cassel et al., 2007; Goldberg et al., 2005; Leezenbaum, Campbell, Butler, & Iverson, 2014; Manwaring et al., 2018; Mitchell et al., 2006; Toth, Dawson, Meltzoff, Greenson, & Fein, 2007; Yirmiya et al., 2006; Zwaigenbaum et al., 2005).

While the studies that examined risk group differences have been informative in suggesting that gesture may be a risk factor for ASD, these studies do not include information on diagnostic outcomes of the high-risk infants, making it impossible to determine whether the differences between high- and low-risk infants were driven by the subset of high-risk infants who were later diagnosed with ASD. However, research comparing high-risk infants who later developed ASD (HRA+) and unaffected high-risk infants (HRA-) suggests large variability in gesture production within the high-risk group (LeBarton & Iverson, 2016; Rozga et al., 2011; Talbott, Nelson, & Tager-Flusberg, 2015a; Winder, Wozniak, Parladé, & Iverson, 2013; Zwaigenbaum et al., 2005). For example, Rozga et al. (2011) found that HRA+ infants produced fewer pointing and showing gestures than HRA- and low-risk comparison (LRC) infants on a semi-structured assessment at 12 months, whereas there were no significant group differences between HRA- and LRC infants. Similarly, Talbott et al. (2015a) reported that HRA+ infants produced significantly fewer total gestures than HRA- and LRC infants during interactions with mothers or examiners at 12 months, and again, there was no significant group difference between HRA- and LRC infants. More recently, LeBarton and Iverson (2016) found that HRA+ toddlers produced fewer overall gestures than their high-risk peers with language delay or with no diagnosis during interactions with mothers at 24 months. Taken together, these findings highlight the need to go beyond the comparisons between high- and low-risk groups and investigate gesture production in infants based on both risk for ASD and diagnostic outcomes (e.g., HRA+, HRA-, LRC).

Another limitation of prior research is that there has been a predominant emphasis on the amount and types of gestures that high-risk infants produce. Relatively little is known about gestures produced in conjunction with or without speech (Manwaring et al., 2018; Özçalışkan, Adamson, Dimitrova, & Baumann, 2017). A comprehensive review by Manwaring et al. (2018) reported that only one of the 19 studies on deictic gestures, which indicate objects, people, or locations in the immediate environment, in toddlers with or at risk for ASD examined gesture paired with speech (hereafter, “gesture–speech combinations”). In particular, Winder et al. (2013) found that high-risk infants integrated deictic gestures with communicative non-word vocalizations at a significantly lower rate, compared to low-risk infants, at 13 and 18 months. A related study that included not only deictic but also other types of gestures found that the trajectory of gesture–speech combinations was significantly slower in HRA+ infants than LRC infants between 8 and 18 months (Parladé & Iverson, 2015). Recently, Özçalışkan et al. (2017) found that children with ASD or with Down syndrome produced significantly fewer overall gestures and types of gesture–speech combinations than typically developing children. Together, these studies suggest that gesture–speech combinations have been less explored and merit closer examination in high-risk infants. Investigating gesture–speech combinations may be useful in parsing the variability in early communicative profiles of the high-risk ASD population (Ozonoff et al., 2014; Talbott, Nelson, & Tager-Flusberg, 2016).

An important question related to group differences in infant gesture production is whether the differences in infants' gestures affect how their caregivers respond to gestures. For example, high-risk infants who produce fewer gestures than low-risk peers may give fewer opportunities for their caregivers to provide contingent input (Leezenbaum et al., 2014). Alternatively, caregivers of high-risk infants may be even more attuned to their infant's communicative behaviors and provide more contingent responses, compared to caregivers of low-risk infants (Tager-Flusberg, 2016). Leezenbaum et al. (2014) studied maternal responses to gestural and vocal communication in high- and low-risk infants at 13 and 18 months of age and found that maternal response rates did not vary across the two groups. More recently, Dimitrova, Özçalışkan, and Adamson (2016) reported that parents of children with ASD, children with Down syndrome, and typically developing children provided similar rates of contingent responses to their children's gestures. Considering the significance of reciprocal influences between child and caregiver communicative behaviors, it is surprising that only a few studies have explored whether the differences in infant gesture influence caregivers' responsiveness. In the current study, we examined both raw numbers (which measure the absolute quantity of parental responses that infants receive) and proportions (which control for differences in infant gestures) of contingent caregiver responses, which, in turn, may shape children's language development (Goldin-Meadow, Goodrich, Sauer, & Iverson, 2007; Tamis-LeMonda, Kuchirko, & Song, 2014).

Finally, while the relation between early gesture use and later language is well established in typical development (Acredolo & Goodwyn, 1988; Iverson & Goldin-Meadow, 2005; Rowe & Goldin-Meadow, 2009a; Rowe, Özçalişkan, & Goldin-Meadow, 2008), this relation has not been extensively studied in high-risk infants. In fact, previous findings have been mixed, with some studies showing positive, significant relations between early gesture and later vocabulary in children with ASD (Braddock et al., 2015; Medeiros & Winsler, 2014; Özçalışkan, Adamson, & Dimitrova, 2016), whereas others reported no significant relations between gesture and language in ASD (So, Wong, Lui, & Yip, 2015). Examining the relation between gesture and language may be useful in revealing whether such relation holds within the high-risk population and in predicting which infants will have subsequent language difficulties. Thus, exploring whether and to what extent early gesture may be related to later language skills within the high-risk population is warranted.

Similarly, it is of both practical and theoretical relevance to identify factors that may be associated with increased probability of receiving an ASD diagnosis. To date, several studies have identified gesture as an early marker for an eventual ASD diagnosis. For example, through using a developmental surveillance assessment, Barbaro and Dissanayake (2013) reported that pointing gestures were recurring early markers for ASD during the second year of life. Veness, Prior, Eadie, Bavin, and Reilly (2014), using parent reports of infant communicative behaviors, also found that gesture use at 8 months was significantly associated with an ASD diagnosis by 7 years. However, to our knowledge, no study has yet evaluated the predictive power of gesture observed during naturalistic interactions in relation to a later ASD diagnosis.

The Present Study

In light of the background and limitations discussed above, we examined infant production of gestures (with or without speech), caregiver responsiveness to gestures, and relations among gesture, caregiver responsiveness, later language, and/or ASD outcomes in HRA+, HRA-, and LRC families, using detailed coding of videotaped sessions of caregiver-infant interactions. Infant gesture and caregiver responsiveness were examined during naturalistic interactions in the lab at 12, 18, and 24 months. Infants' language skills were measured using Mullen Scales of Early Learning (MSEL; Mullen, 1995) at 24 months, and ASD outcomes were determined using a combination of the Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000) and best clinical judgment between 18 and 36 months. Our specific research questions were as follows:

1. Do HRA+, HRA-, and LRC infants differ in overall production and distribution of gestures (with or without speech) at 12, 18, and 24 months?
2. Do caregivers of HRA+, HRA-, and LRC infants differ in immediate, contingent responsiveness to infant gestures (with or without speech) at 12, 18, and 24 months?
3. Does early gesture or caregiver responsiveness relate to later language skills?
4. Does early gesture relate to ASD outcomes?

Methods

Participants

A total of 89 infants and their caregivers participated in this study. Participants were drawn from a larger prospective, longitudinal study of infants at high and low familial risk for ASD. For the present study, we included caregiver-infant dyads who participated in a 10-min free play interaction in the lab at least once at 12, 18, or 24 months and had ASD outcomes determined between 18 and 36 months. There were 70 caregiver-infant dyads at 12 and 18 months and 69 dyads at 24 months. Of note, sample attrition was due to visits missed by families, malfunction of video recording equipment, and infants becoming fussy and not doing caregiver-infant interactions during visits.

Fifty-five infants were enrolled as high risk for autism (HRA); parents of these infants reported a community diagnosis of ASD in the older siblings (probands) of these infants. To confirm ASD diagnosis of probands of HRA infants, we used the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003) and/or the ADOS (Lord et al., 2000). Community diagnosis of ASD were confirmed for 52 probands of HRA infants (95% of the HRA sample). Specifically, both the SCQ and ADOS were used to confirm diagnosis in 27 probands of HRA infants (49%); the SCQ was used for 21 probands (38%); and the ADOS was used for four probands (7%). Three probands of HRA infants (5%) did not have the ADOS or SCQ and therefore were unable to have their diagnosis confirmed. However, all three received their diagnosis by expert clinicians in the community, and data from their younger siblings were included in the study.

Thirty-four infants were enrolled as low risk comparison (LRC), as they had typically developing older siblings and no first- or second-degree family members with ASD. To ensure probands of LRC infants did not have ASD, we used the SCQ and/or ADOS. Specifically, both the ADOS and SCQ were used to verify no ASD diagnosis for 29 older siblings of the LRC infants (85% of the LRC sample); the SCQ was used for four probands (12%); and the ADOS was used for one proband (3%).

For the data analyses, infants were classified based on their risk for ASD (high or low) and also eventual ASD outcomes (ASD or no ASD; see the section "ASD outcome classification"). Of the 55 high-risk infants, 21 were later diagnosed with ASD (HRA+), and 34 were not diagnosed with ASD (HRA-). Notably, we oversampled high-risk infants who later met criteria for ASD to ensure their sufficient representation in the present study. All 34 low-risk infants were not later diagnosed with ASD.

Infant and caregiver characteristics are provided in Table 2.1 for the three groups. While the groups were comparable in infant race and household income, infant sex and caregiver education differed significantly across the groups. Specifically, the percentage of female infants was significantly lower in the HRA+ group than the HRA- group, $p = 0.013$. Also, the level of parental education was significantly lower in the HRA+ group than the LRC group, $z = -3.354$, $p < 0.001$. These variables were controlled for in data analyses. All infants were recruited before 12 months of age, were full-term, and had no genetic or neurological disorders. All caregivers spoke English in the home as the primary language (> 80% of the time).

Procedure and Measures

We obtained Institutional Review Board approvals from Boston Children's Hospital and Boston University and written, informed consent from caregivers of all infants.

Table 2.1. Infant and caregiver demographic data for group comparison (*N* = 89)

	HRA+	HRA-	LRC	*p* (3-group)
Sample size				
12 Months	17	25	28	
18 Months	16	25	29	
24 Months	15	25	29	
Child Characteristics				
Sex (% Female)	28.6% *N* = 21	64.7% *N* = 34	50.0% *N* = 34	.038*
Race/ethnicity (% White)	81.0% *N* = 21	94.1% *N* = 34	88.2% *N* = 34	.269
[a] MSEL VR at 12 months	51.24 (6.71) *N* = 21	53.88 (10.09) *N* = 34	58.12 (7.55) *N* = 34	.012*
MSEL VR at 18 months	46.32 (9.26) *N* = 19	50.88 (7.67) *N* = 32	50.97 (8.86) *N* = 34	.122
MSEL VR at 24 months	52.06 (12.24) *N* = 18	54.41 (10.07) *N* = 29	56.09 (9.71) *N* = 34	.417
[b]ADOS CSS	4.90 (2.30) *N* = 21	1.47 (0.75) *N* = 34	1.47 (1.05) *N* = 34	< .001***
Parent Characteristics				
[c] Household Income	6.78 (2.26) *N* = 18	7.65 (1.05) *N* = 31	7.22 (1.83) *N*= 27	.306
[d] Caregiver Education	4.92 (1.73) *N* = 19	5.77 (1.71) *N* = 31	6.47 (1.01) *N* = 30	.008**

Note. Data are reported as group means with standard deviations in parentheses.
[a]MSEL VR represents children's T scores on the Visual Reception subscale of the Mullen Scales of Early Learning.
[b]ADOS calibrated severity scores (range 1-10) reflect the severity of ASD symptoms on the basis of raw total ADOS scores, with higher values indicating greater symptom severity (Gotham, Pickles, & Lord, 2009).
[c]Income was reported on an eight-point scale: (1) less than $15,000, (2) $15,000-$25,000, (3) $25,000-$35,000, (4) $35,000-$45,000, (5) $45,000-$55,000, (6) $55,000-$65,000, (7) $65,000-$75,000, (8) more than $75,000.
[d]Caregiver education was reported as the highest level attained on a nine-point scale: (1) some high school, (2) high school graduate, (3) some college, (4) community college/two-year degree, (5) four-year college degree, (6) some graduate school, (7) master's degree, (8) doctoral degree, (9) professional degree. For three of our infants, either their mothers or fathers participated in caregiver-child interactions at 12, 18, and 24 months; for them, parental education levels were calculated by averaging paternal and maternal education levels. For two of our infants, only fathers participated in caregiver-child interactions, and paternal education levels were used. Maternal education levels were used for the rest of the participants.
* $p < .05$, ** $p < .01$, *** $p < .001$.

Caregiver-infant interaction[5]. At 12, 18, and 24 months of age, caregiver-infant dyads were videotaped while engaging in free play in the lab for 10 min. Dyads were instructed to play as they would normally do at home. Age-appropriate toys were provided.

ASD outcome classification. At the infant's final visit to the lab, which occurred either at 18, 24, or 36 months, a final ASD diagnosis (+/−) was determined on the basis of the ADOS (Lord et al. 2000) and with clinical judgment by a licensed clinical psychologist. The ADOS was administered by research staff with extensive experience in testing children with developmental disorders and co-scored by an ADOS-reliable researcher via recording. If infants met criteria for ASD or received a score within three points of the cutoff scores on the ADOS, a licensed clinical psychologist reviewed videos of the behavioral assessments along with the ADOS scores and determined final clinical judgment: ASD, no ASD, or other (e.g., ADHD, anxiety, language concerns). For the purposes of the current study, we excluded infants who were classified as 'other.' If there were multiple diagnostic evaluations at 18, 24, and 36 months (e.g., children completed all visits at three time points), we used information from their most recent visit for ultimate categorization. ASD evaluation was made at 18 months for four children ($n_{\text{HRA+}} = 3$; $n_{\text{HRA-}} = 1$; $n_{\text{LRC}} = 0$), at 24 months for ten children ($n_{\text{HRA+}} = 2$; $n_{\text{HRA-}} = 8$; $n_{\text{LRC}} = 0$), and 36 months for 75 children ($n_{\text{HRA+}} = 16$; $n_{\text{HRA-}} = 25$; $n_{\text{LRC}} = 34$). Given the high diagnostic stability of ASD at 18 and 24 months (Ozonoff et al., 2015; Zwaigenbaum et al., 2016), infants with ASD diagnosis made between 18 and 36 months were included in the present study to maximize sample size.

Language outcomes. At age 24 months, children were administered the MSEL (Mullen, 1995). We used children's standardized t-scores from the MSEL Receptive and Expressive Language subscales as our measures of children's language outcomes. We chose the MSEL as

[5]Of note, caregiver-infant interactions were also collected at 36 months as part of the larger study; however, recordings from 36-month interactions were not transcribed, as we were primarily interested in studying early gesture production in the first two years of life in relation to later language and ASD outcomes.

our language measure, as it is standardized and independent of our gesture and speech production measures from naturalistic interactions.

Control variables. Because one of our research goals was to examine relations between early gesture and subsequent language skills, we controlled for several variables such as nonverbal cognition (measured from 12-month MSEL Nonverbal Developmental Quotient), infant sex, and parent education, which have all been reported to be associated with children's gestural or language skills (Hoff, 2003; Özçalişkan & Goldin-Meadow, 2010; Wray, Norbury, & Alcock, 2016). In addition, we controlled for infants' 12-month number of different words (from caregiver-infant interactions) and language skills (from the MSEL Verbal Developmental Quotients, which reflect infants' performance on the MSEL Receptive and Expressive Language subscales) in our analyses to study relations between 12-month gestures and ASD outcomes.

Transcription and Coding

Speech. Speech from the videotaped sessions were transcribed using the CHAT (Codes for the Human Analysis of Transcripts) conventions of the CHILDES (Child Language Data Exchange System; MacWhinney, 2000) and verified by two trained research assistants. Following prior work (Pan, Rowe, Singer, & Snow, 2005), speech was transcribed at the level of utterance, which was defined as a sequence of speech that is preceded and followed by a pause, a change in conversational turn, or a change in intonational pattern. Consistent with previous work (Parladé & Iverson, 2015), we classified infant vocal utterances into words and communicative non-word vocalizations (e.g., babbling). Dictionary words, onomatopoetic sounds (e.g., "meow"), and evaluative sounds (e.g., "uhoh") were counted as words. The number of different words (word types) infants produced during the 10-min interaction served as a measure of productive vocabulary. Vegetative noises, laughter, crying, and other non-speech sounds were not coded.

Infant gesture. Occurrences of the infants' gestures were identified and coded to indicate gesture categories and their relation to speech, following earlier work (Özçalışkan & Goldin-Meadow, 2009). Specifically, we classified gestures into one of three main categories: deictic, conventional, or representational. Deictic gestures indicate objects, people, or locations in the environment (e.g., pointing, reaching, showing, giving). Conventional gestures are culturally-agreed-upon hand or body movements with a specific meaning (e.g., nodding the head to convey yes). Representational gestures indicate objects, actions, or relations by recreating an aspect of the referent's shape or movement (e.g., flapping arms in the air to mean flying).

In addition, we coded whether gesture occurred on its own or combined with speech. When gesture occurred with speech, it was first determined whether it occurred with a word or a communicative non-word vocalization. When gesture occurred with a word, it was categorized as reinforcing, supplementary, or disambiguating (e.g., Özçalışkan et al., 2017). Reinforcing gesture–speech combinations provide the same information in both gesture and speech (e.g., pointing to cookie + "cookie"). In supplementary gesture–speech combinations, gesture adds semantic information to the message conveyed in speech (e.g., showing a book + "open"). In disambiguating gesture–speech combinations, gesture clarifies the message conveyed in speech (e.g., pointing to book + "this").

Gesture coding reliability was assessed regularly between two coders. Approximately 20% of the transcripts (*n* = 45) were randomly selected and double coded to calculate interrater agreement. Percent agreement and Cohen's kappa were calculated for each gesture category:

deictic (99.7%, *k* = 0.996, *n* = 336), conventional (95.4%, *k* = 0.941, *n* = 86), and representational (80.0%, *k* = 0.762, *n* = 5). Percent agreement and Cohen's kappa were also calculated for classifying gesture based upon its relation to accompanying speech: gestures alone (93.5%, *k* = 0.934, *n* = 155), gestures with nonword vocalizations (93.8%, *k* = 0.935, *n* = 81), reinforcing combinations (91.5%, *k* = 0.905, *n* = 94), supplementary combinations (88.7%, *k* = 0.875, *n* = 62), and disambiguating combinations (81.0%, *k* = 0.769, *n* = 21).

Caregiver responsiveness. Immediate responses by the caregiver to the gestures were coded as contingent or noncontingent. Specifically, if a parent's verbal or nonverbal behavior was related to the infant's gesture and was produced within the first utterance following the gesture, the response was coded as contingent (e.g., an infant points to a ball, and a parent says "Do you want the ball?"). If a parent produced no response or a response that was unrelated to the infant's gesture within the first utterance following the gesture, the response was coded as noncontingent (e.g., an infant points to a ball, and a parent redirects the infant's attention and says "Let's do this puzzle"). Both raw numbers and proportions of contingent parental responses were calculated. Approximately 15% of the transcripts (*n* = 33) were double coded to assess interrater agreement (97.5%, *k* = 0.960, *n* = 326).

Data Analysis

To address our first research question about group differences in infant production of gesture with or without speech, we converted all gesture variables from frequency to rates per 10 min, as the lengths of the interactions varied across caregiver-infant pairs (*M* = 9.4 min, *SD* = 2.2)[6]. Visual examination of the gesture variables showed non-normal distributions of data. Therefore, we employed nonparametric analyses (Kruskal-Wallis H tests) to examine early

[6]There was no group difference in mean lengths of caregiver-infant interaction videos (HRA+: *M* = 9.21, *SD* = 1.90; HRA-: *M* = 9.31, *SD* = 2.25; LRC: *M* = 9.77, *SD* = 2.04).

gesture production in three groups of infants. Mann-Whitney U tests were used as post-hoc pairwise comparison tests. Regarding our second research question about group differences in caregiver responsiveness to the gestures, we calculated frequencies and proportions of contingent caregiver responses to infant gestures. Proportions were calculated for each infant by dividing the total number of contingent responses to gestures by total responses to gestures and then averaged across infants in each group. As these data were proportional, we applied an arcsine transformation to data and compared group differences in caregiver responsiveness using non-parametric analyses (Kruskal-Wallis H tests). Finally, regarding our third and fourth research questions, we performed correlation and/or regression analyses to determine whether early gesture use and caregiver responsiveness were related to later language skills, and whether early gesture was predictive of ASD diagnosis. We conducted all statistical analyses using Stata 14 (StataCorp, 2015).

Results

Gesture Production from 12 to 24 Months

Total number of gestures. We first investigated a total number of gestures that HRA+, HRA-, and LRC infants produced at 12, 18, and 24 months (Table 2.2). We found that there were significant group differences in the overall amount of gesturing at 12 months, $\chi2(2, N = 70) = 9.46$, $p = 0.009$, and 18 months, $\chi2(2, N = 70) = 7.86$, $p = 0.020$, but not at 24 months. Post-hoc pairwise comparisons revealed that at 12 months, HRA- infants produced significantly more total gestures than HRA+ infants, $U = 106$, $z = -2.73$, $p = 0.006$, $d = 0.9$, and than LRC infants, $U = 226$, $z = 2.21$, $p = 0.027$, $d = 0.4$. At 18 months, LRC infants produced significantly more gestures, compared to both HRA+ infants, $U = 142$, $z = -2.13$, $p = 0.033$, $d = 0.7$, and to HRA-

Table 2.2. Means, standard deviations, range, and Ns for total number of gestures, gestures produced with speech, and gestures produced without speech, for HRA+, HRA-, and LRC infants at 12, 18, and 24 months

		Total Gestures (a+b)	Gestures Produced with Speech (a)	Gestures Produced without Speech (b)
12 months	HRA+	7.4 (6.3) 0.9-22.4 *N* = 17	2.0 (3.6) 0-13.7 *N* = 17	5.4 (5.5) 0.9-22.4 *N* = 17
	HRA-	13.6 (7.3) 2.4-32 *N* = 25	4.1 (3.8) 0-12.4 *N* = 25	9.4 (5.5) 1.6-20.6 *N* = 25
	LRC	10.0 (9.4) 1.6-49.5 *N* = 28	3.8 (5.6) 0-28.5 *N* = 28	6.2 (5.1) 0-21 *N* = 28
18 months	HRA+	7.2 (6.2) 0-17.6 *N* = 16	4.1 (4.7) 0-16.0 *N* = 16	3.2 (4.1) 0-13.2 *N* = 16
	HRA-	7.5 (7.1) 0-31.9 *N* = 25	4.6 (4.3) 0-14.2 *N* = 25	2.9 (4.2) 0-19.1 *N* = 25
	LRC	12.3 (8.3) 0.9-40.7 *N* = 29	8.9 (7.9) 0.8-37.8 *N* = 29	3.4 (2.7) 0-10.0 *N* = 29
24 months	HRA+	12.0 (11.7) 1.0-40.8 *N* = 15	8.7 (8.6) 1.0-29.1 *N* = 15	3.3 (4.3) 0-15.2 *N* = 15
	HRA-	14.9 (7.6) 3.0-32.2 *N* = 25	11.2 (7.3) 0.8-30.4 *N* = 25	3.7 (2.8) 0-9.7 *N* = 25
	LRC	14.3 (9.8) 0-45.1 *N* = 29	11.0 (8.2) 0-39.2 *N* = 29	3.4 (4.5) 0-25 *N* = 29

infants, $U = 217.5$, $z = -2.52$, $p = 0.012$, $d = 0.6$. All other group differences were not statistically significant at 12 and 18 months.

Number of gestures produced with or without speech. We next broke down the total number of gestures and examined gestures produced with or without speech (Table 2.2). When examining the number of gestures produced with speech, we found that the three groups differed significantly at 12 months, $\chi 2(2, N = 70) = 6.50$, $p = 0.038$, and 18 months, $\chi 2(2, N = 70) = 9.64$, $p = 0.008$, but not at 24 months. Specifically, at 12 months, HRA- infants produced a significantly larger number of gesture–speech combinations than HRA+ infants, $U = 117$, $z = -2.48$, $p = 0.013$, $d = 0.6$. LRC infants showed a trend toward more gesture–speech combinations than HRA+ infants, $U = 163$, $z = -1.82$, $p = 0.070$, $d = 0.4$. At 18 months, LRC infants produced a significantly larger number of combinations than HRA+ infants, $U = 124$, $z = -2.56$, $p = 0.010$, $d = 0.7$, and than HRA- infants, $U = 214$, $z = -2.58$, $p = 0.010$, $d = 0.7$. When comparing the number of gestures produced without speech, the three groups differed significantly only at 12 months, $\chi 2(2) = 8.73$, $p = 0.013$. Post-hoc pairwise comparisons revealed that HRA- infants produced significantly more gestures than HRA+ infants, $U = 111.5$, $z = -2.59$, $p = 0.010$, $d = 0.7$, and than LRC infants, $U = 220$, z = 2.32, $p = 0.021$, $d = 0.6$.

Distribution of gesture categories. We examined the distribution of gesture categories (Table 2.3). The majority of gestures that infants produced at all three ages were deictic gestures, with averages of 86% in HRA+ infants, 83% in HRA- infants, and 86% in LRC infants, across the ages. Infants also produced conventional gestures, with averages of 14% in HRA+ infants, 17% in HRA- infants, and 13% in LRC infants, across the ages. There were almost no representational gestures in our infant data. Specifically, at 24 months only 1% of gestures were

Table 2.3. Mean proportions and standard deviations for gestures belonging to each category (deictic, conventional, representational) for HRA+, HRA-, and LRC infants at 12, 18, and 24 months

	12 months			18 months			24 months		
	HRA+	HRA-	LRC	HRA+	HRA-	LRC	HRA+	HRA-	LRC
Deictic	0.88 (0.20)	0.89 (0.22)	0.93 (0.12)	0.84 (0.21)	0.79 (0.24)	0.84 (0.22)	0.85 (0.19)	0.81 (0.17)	0.82 (0.19)
Conventional	0.12 (0.20)	0.11 (0.22)	0.07 (0.12)	0.16 (0.21)	0.21 (0.24)	0.16 (0.22)	0.15 (0.19)	0.18 (0.17)	0.16 (0.19)
Representational	0	0	0	0	0	0	0	0.01 (0.02)	0.01 (0.04)

coded in the representational category for HRA- and LRC infants. In sum, at all three ages, there was no significant group difference in the proportion of gestures belonging to each category.

Distribution of types of gesture–speech combinations. We also investigated the distribution of types of gesture–speech combinations (Table 2.4). At 12 months, there was no significant group difference in the distribution of types of gesture–speech combinations. Most of the gesture–speech combinations that infants produced at 12 months were gestures with non-word vocalizations, with averages of 98% in HRA+ infants, 93% in HRA- infants, and 96% in LRC infants. At 18 months, there was a trend toward significant group difference in reinforcing types, $\chi 2(2, N = 62) = 5.75$, $p = 0.057$, with HRA- and LRC infants producing 21% and 22% reinforcing types, respectively, compared to 8% in HRA+ infants. At 24 months, there was a significant group difference in disambiguating types, $\chi 2(2, N = 68) = 6.70$, $p = 0.035$. Again, HRA- infants and LRC infants produced a significantly higher proportion of disambiguating types, compared to HRA+ infants, $U = 109.5$, $z = -2.29$, $p = 0.022$, $d = 0.4$; $U = 118.5$, $z = -2.42$, $p = 0.015$, $d = 0.5$, respectively.

Contingent Caregiver Responses to Gestures

Descriptive information on the raw numbers and proportions of contingent caregiver responses is presented in Table 2.5. Similar to our findings with infant gestures, we found group differences in the *number* of contingent caregiver responses at 12 and 18 months, but not at 24 months. Specifically, there was a significant group difference at 12 months, $\chi 2(2, N = 70) = 5.98$, $p = 0.050$, and a significant group difference at 18 months, $\chi 2(2, N = 66) = 6.44$, $p = 0.040$. Post-hoc pairwise comparisons revealed that at 12 months, HRA+ caregivers provided significantly fewer contingent responses to infant gestures than HRA- caregivers, $U = 118.5$, $z = -2.42$, $p = 0.016$, $d = -0.8$. At 18 months, HRA+ caregivers made significantly fewer contingent responses

Table 2.4. Mean proportions and standard deviations for gesture-speech combinations belonging to each type (nonword vocalization, reinforcing, supplementary, disambiguating) for HRA+, HRA-, and LRC infants at 12, 18, and 24 months

	12 months			18 months			24 months		
	HRA+	HRA-	LRC	HRA+	HRA-	LRC	HRA+	HRA-	LRC
NWV	0.98 (0.06)	0.93 (0.22)	0.96 (0.11)	0.78 (0.35)	0.62 (0.35)	0.57 (0.32)	0.13 (0.27)	0.08 (0.17)	0.05 (0.12)
R	0.02 (0.06)	0.01 (0.04)	0.03 (0.09)	0.08 (0.20)	0.21 (0.27)	0.22 (0.23)	0.45 (0.38)	0.49 (0.32)	0.44 (0.28)
S	0	0.04 (0.15)	0.01 (0.05)	0.14 (0.31)	0.16 (0.24)	0.20 (0.31)	0.30 (0.30)	0.19 (0.21)	0.25 (0.21)
D	0	0.02 (0.07)	0	0	0.01 (0.02)	0.01 (0.02)	0.12 (0.27)	0.24 (0.29)	0.25 (0.26)

Note. NWV, R, S, and D stand for nonword vocalizations, reinforcing combinations, supplementary combinations, and disambiguating combinations, respectively.

Table 2.5. Contingent caregiver responses to infant gesture, by group and age

Child Age	HRA+	HRA-	LRC
Frequencies			
12 months	5.18 (4.11) *N* = 17	9.32 (5.81) *N* = 25	7.82 (6.53) *N* = 28
18 months	5.93 (4.99) *N* = 15	7.59 (6.45) *N* = 22	11.45 (9.54) *N* = 29
24 months	10.13 (10.95) *N* = 15	12.8 (7.07) *N* = 25	12.61 (6.84) *N* = 28
Proportions			
12 months	.82 (.26) *N* = 17	.84 (.23) *N* = 25	.85 (.18) *N* = 28
18 months	.91 (.17) *N* = 15	.91 (.11) *N* = 22	.91 (.12) *N* = 29
24 months	.88 (.17) *N* = 15	.86 (.11) *N* = 25	.89 (.16) *N* = 28

Note. Untransformed proportional data are reported in table. We excluded infants from all analysis of parents' responses to infant gestures, if the infant did not produce any gesture during the 10-minute interaction.

than LRC caregivers, $U = 129.5$, $z = -2.19$, $p = 0.029$, $d = -0.7$; HRA- caregivers also provided fewer contingent responses relative to LRC parents, $U = 217.5$, $z = -1.94$, $p = 0.053$, $d = -0.5$.

When examining the *proportions* of contingent caregiver responses that control for the differences in infant gestures, we found that caregivers of the three groups of children did not differ in the proportions of contingent responses: 12 months: $\chi 2(2, N = 70) = 0.07$, $p = 0.965$; 18 months: $\chi 2(2, N = 66) = 0.91$, $p = 0.634$; 24 months: $\chi 2(2, N = 68) = 2.85$, $p = 0.240$. Also, caregivers of the three groups showed high response rates to child gestures, ranging from 82% to 91% across all ages.

Relations Between Early Gesture, Caregiver Responsiveness, and Later Language Skills

Demographic data for the sample included in the correlation and regression analyses are presented in Table 2.6. We first examined descriptive information on MSEL standardized t-scores and found significant group differences in 24-month receptive and expressive language scores (Table 2.7). The total number of gestures at 12 months was significantly and positively correlated with receptive language scores at 24 months, $r = 0.256$, $p = 0.039$, but not with expressive language scores at 24 months, $r = 0.226$, $p = 0.070$. The number of word types infants produced at 12 months was not significantly correlated with receptive or expressive language scores at 24 months, $r = -.072$, $p = 0.572$; $r = 0.075$, $p = 0.553$, respectively, presumably because there was little variation in the number of word types infants produced at 12 months.

Given the results of these correlational analyses on early gesture, word types, and MSEL language outcomes, we used linear regression models to investigate whether early gesture predicted later receptive language skills (Table 2.8). Model 1 in Table 2.8 indicates that the total number of gestures at 12 months on its own significantly positively predicted receptive language scores at 24 months, $b = 0.30$, $t(63) = 2.11$, $p = 0.039$, 95% CI [0.02, 0.58]. We then included the

Table 2.6. Demographic characteristics for regression sample, by group (*N* = 70)

	HRA+	HRA-	LRC	*p* (3-group)
Child Characteristics				
Sex (% Female)	29.4% *N* = 17	64.0% *N* = 25	50.0% *N* = 28	.098~
Race/ethnicity (% White)	82.4% *N* = 17	92.0% *N* = 25	85.7% *N* = 28	.668
Parent Characteristics				
[a] Household Income	6.53 (2.42) *N* = 15	7.52 (1.20) *N* = 23	7.68 (1.09) *N* = 22	.224
[b] Caregiver Education	4.83 (1.62) *N* = 15	5.61 (1.73) *N* = 23	6.46 (0.98) *N* = 24	.006**

Note. Data are reported as group means with standard deviations in parentheses.
[a]Income was reported on an eight-point scale: (1) less than $15,000, (2) $15,000-$25,000, (3) $25,000-$35,000, (4) $35,000-$45,000, (5) $45,000-$55,000, (6) $55,000-$65,000, (7) $65,000-$75,000, (8) more than $75,000.
[b]Caregiver education was reported as highest level attained on a nine-point scale: (1) some high school, (2) high school graduate, (3) some college, (4) community college/two-year degree, (5) four-year college degree, (6) some graduate school, (7) master's degree, (8) doctoral degree, (9) professional degree.
~ $p < .1$, ** $p < .01$.

Table 2.7. Means and standard deviations for children's speech (word types), verbal developmental quotient (MSEL), and nonverbal developmental quotient (MSEL) at 12 months and receptive and expressive language scores (MSEL) at 24 months for regression sample (*N* = 70)

	HRA+	HRA-	LRC	*p* (3-group)
Word types at 12 months	0.99 (1.39) *N* = 17	1.14 (1.91) *N* = 25	0.83 (1.36) *N* = 28	.769
MSEL VDQ at 12 months	87.84 (18.31) *N* = 17	98.56 (13.20) *N* = 25	99.11 (12.74) *N* = 28	.028*
MSEL NDQ at 12 months	115.90 (12.03) *N* = 17	122.85 (13.97) *N* = 25	124.16 (10.78) *N* = 28	.085~
MSEL RL at 24 months	51.80 (10.75) *N* = 15	55.86 (8.63) *N* = 22	59.43 (7.70) *N* = 28	.029*
MSEL EL at 24 months	49.00 (11.60) *N* = 15	55.23 (9.71) *N* = 22	57.93 (7.95) *N* = 28	.017*

Note. The number of different words (word types) infants produced is derived from the 10-minute interaction. MSEL Verbal Developmental Quotient (VDQ) reflects infants' performance on the Receptive Language (RL) and Expressive Language (EL) subscales of the Mullen Scales of Early Learning (MSEL), adjusted for chronological age. MSEL Nonverbal Developmental Quotient (NDQ) reflects infants' performance on the Visual Reception and Fine Motor subscales of the Mullen Scales of Early Learning (MSEL), adjusted for chronological age.
~ $p < .1$, * $p < .05$.

Table 2.8. A series of regression models predicting child receptive language skills (MSEL) at 24 months based on early gesture use (12 months), controlling for word types, risk status for ASD, sex, caregiver education, and nonverbal developmental quotient

	Model 1	Model 2	Model 3	Model 4
Intercept	53.47*** (1.80)	53.73*** (1.79)	56.61*** (2.10)	35.88** (12.04)
12-month gestures	0.30* (0.14)	0.39* (0.15)	0.39* (0.15)	0.29* (0.14)
12-month word types		-1.44 (0.91)	-1.36 (0.88)	-1.17 (0.84)
Risk status			-5.12* (2.13)	-4.30~ (2.31)
Nonverbal cognition				0.15 (0.09)
Sex				-2.63 (2.24)
Caregiver education				0.76 (0.74)
N	65	65	65	58
R^2 statistic (%)	6.6%	10.2%	18.0%	24.8%

Note. Nonverbal cognition was measured using nonverbal developmental quotient from Mullen Scales of Early Learning at 12 months. Risk status was coded as LRC = 0, HRA = 1. Sex was coded as female = 1, male = 0.
~ $p < .1$, * $p < .05$, ** $p < .01$, *** $p < .001$.

number of word types produced at 12 months in the regression model to control for early speech and found that gesture at 12 months continued to significantly predict 24-month receptive language skills, even after controlling for the number of different words (Table 2.8, Model 2), $b = 0.39$, $t(62) = 2.58$, $p = 0.012$, 95% CI [0.09, 0.70]. This significant relation between gesture and language continued to hold when we added an infant's risk status for autism (Table 2.8, Model 3), $b = 0.39$, $t(61) = 2.66$, $p = 0.010$, 95% CI [0.10, 0.69]. Notably, risk status was also a significant predictor in Model 3 such that high-risk status was associated with lower receptive language scores, while controlling for the other variables, $b = -5.12$, $t(61) = -2.41$, $p = 0.019$, 95% CI [− 9.38, − 0.87]. When we included 12-month nonverbal cognition and demographic covariates (i.e., infant sex and caregiver education), gesture remained a significant positive predictor of later language (Table 2.8, Model 4), $b = 0.29$, $t(51) = 2.06$, $p = 0.044$, 95% CI [0.08, 0.58], and risk status was a marginal negative predictor of later language, $b = -4.30$, $t(51) = -1.86$, $p = 0.069$, 95% CI [− 8.95, 0.34]. In short, 12-month gesture was related to 24-month receptive language, even with risk status controlled (and vice versa, although to a lesser extent). Finally, we added an interaction term between gesture and group (not shown) and found no significant interaction effect, suggesting that the gesture–language relation was similar across risk status groups. Taken together, controlling for 12-month language, risk status, nonverbal cognition, and demographic covariates, gesture use at 12 months was a significant positive predictor of Mullen receptive language scores at 24 months in infants.

In the next step, we examined whether the relation we found between early gesture and language skills was driven by caregiver responsiveness. We found that the relation between the number of contingent parent responses and children's receptive language scores was positive and significant, $r = 0.305$, $p = 0.014$. However, this relation was no longer significant when controlling for the number of infant gestures, $r = 0.179$, $p = 0.158$. Similarly, the relation between the proportion of contingent parent responses and children's receptive language scores was weak and not statistically significant, $r = 0.077$, $p = 0.542$.

Relation Between Early Gesture and ASD Diagnosis

Finally, we conducted binomial logistic regression analyses to determine whether early gesture use predicted eventual ASD diagnosis among high-risk infants (Table 2.9). We found that the number of gestures at 12 months was significantly negatively related to autism diagnosis (Table 2.9, Model 1), $z = -2.46$, $p = 0.014$, 95% CI [− 0.256, − 0.029], suggesting that higher gesture use was associated with a lower probability of receiving an ASD diagnosis in high-risk infants. Early gesture remained a significant predictor of an ASD diagnosis when we controlled for infants' 12-month word types (Table 2.9, Model 2), $z = -2.63$, $p = 0.008$, 95% CI [− 0.294, − 0.043]; the same pattern of results emerged when we controlled for infants' 12-month MSEL Verbal Developmental Quotients (Table 2.9, Model 3), $z = -1.92$, $p = 0.055$, 95% CI [− 0.238, 0.002], although the effect of gesture was trending towards significant when standardized language scores were included in the model. Finally, the results held when we added infant sex and caregiver education (Table 2.9, Model 4), $z = -2.26$, $p = 0.024$, 95% CI [− 0.311, − 0.022]. To interpret this significant finding, we used the regression equation from the final model (Table 2.9, Model 4) and calculated estimated probabilities of receiving an ASD diagnosis for a high-risk male infant whose 12-month gesture use was at the 10^{th} percentile of the sample and a child whose gesture use was at the 90th percentile, holding their word types and caregivers' education constant at the sample mean (see Supplementary Material for calculations). We found that for a high-risk boy whose gesture use was at the 10th percentile, the probability of receiving an ASD diagnosis was 83.6%, whereas for a boy at the 90th percentile, the probability was 17.4%,

Table 2.9. Logistic regression results predicting an ASD diagnosis from early gesture use (12 months) in high-risk infants

	Model 1	Model 2	Model 3	Model 4
Intercept	1.06~ (0.64)	1.04 (0.63)	3.18 (2.13)	4.41* (1.71)
Gestures at 12 months	-0.14* (0.06)	-0.17** (0.06)	-0.12~ (0.06)	-0.17* (0.07)
Word types at 12 months		0.29 (0.26)		0.57~ (0.34)
VDQ at 12 months			-0.03 (0.02)	
Sex				-1.78~ (1.00)
Caregiver education				-0.57* (0.27)
χ^2	8.00	9.23	9.15	15.97
df	1	2	2	4
Deviance	48.68	47.46	47.54	35.01
N	42	42	42	38
Pseudo-R^2	14.1%	16.3%	16.0%	31.3%

Note. Verbal Developmental Quotients (VDQ) reflect infants' performance on the Expressive Language and Receptive Language subscales of the Mullen Scales of Early Learning, adjusted for chronological age. ASD diagnosis was coded as ASD = 1, no-ASD = 0. Sex was coded as female = 1, male = 0.
~ $p < .1$, * $p < .05$, ** $p < .01$.

holding word types and parental education constant. Therefore, higher gesture use at 12 months was associated with a lower probability of an ASD diagnosis in high-risk infants[7].

Discussion

In this study on early gesture in high-risk infants, we had three main findings. First, we found group differences in gesture production in high-risk infants later diagnosed with ASD, high-risk infants without ASD diagnosis, and low-risk infants at 12 and 18 months of age. Second, the differences in infant gesture did not alter responsiveness of caregivers of three infant groups, with caregivers of all three groups providing similar, high rates of contingent responses to infant gestures. Third, gesture use at 12 months was a significant predictor of infants' later receptive language skills and ASD diagnosis. Below we discuss each of these main findings.

Infant Gesture Production

We found that infants in the three groups showed differences in total amount of gesture production at 12 and 18 months. Specifically, at 12 months, high-risk infants later diagnosed with ASD and low-risk infants produced significantly fewer gestures, on average, than high-risk infants who did not develop ASD. Higher gesture production of high-risk infants without ASD, compared to that of low-risk infants, was somewhat unexpected, considering prior work that suggests lower gesture use in high-risk infants than in low-risk infants (e.g., Cassel et al., 2007). This difference could reflect the heterogeneity in early communicative profiles among high-risk infants (Ozonoff et al., 2014; Talbott, Nelson, & Tager-Flusberg, 2016). It is also possible that higher infant gesture production in high-risk infants without ASD may be due, in part, to higher gesture use in their mothers, as a positive relation between child and parent gesture has been reported in the literature (Iverson, Capirci, Longobardi, & Cristina Caselli, 1999; Rowe,

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[7]We conducted a sensitivity analysis in which we removed data from four high-risk infants whose ASD outcomes were determined at 18 months. We found the same results even after we removed data from these infants.

Özçalişkan, & Goldin-Meadow, 2008). In fact, drawing on a subsample of the 12-month-old infants in this study, Talbott et al. (2015a) found that mothers of unaffected high-risk infants produced significantly more total gestures than mothers of low-risk infants.

At 18 months, high-risk infants with and without ASD produced significantly fewer gestures than low risk infants. This finding is consistent with prior work that reported deficits in gesture production in high-risk infants (Cassel et al., 2007; Goldberg et al., 2005; Mitchell et al., 2006; Yirmiya et al., 2006). Notably, unaffected high-risk infants showed reduction in gesture production between 12 and 18 months, producing six fewer gestures, on average, at 18 months (Table 2.2). This substantial within-group variability may, again, highlight the heterogeneous profiles in early communicative skills of high-risk infants. Alternatively, this finding could suggest an atypical pattern of gesture development in unaffected high-risk infants, even though they did not eventually develop ASD. Taking the findings at 12 and 18 months together, there were significant differences in total gesture production among the three groups. Thus, these results suggest the need to go beyond the risk group comparisons, when possible, to study the specificity and generalizability of risk factors for ASD (Jones, Gliga, Bedford, Charman, & Johnson, 2014). Future studies may examine early communicative development of populations at risk for other neurodevelopmental disorders and infants at risk for ASD based on other definitions of risk (e.g., prematurity) and compare their development to that of high-risk infant siblings to address the issue of specificity.

While we found group differences in early gesture at 12 and 18 months, there was no group difference in overall gesture production at 24 months. This might be because typically developing children begin to reduce their gesture use and communicate using words around 2 years of age (Özçalışkan & Goldin-Meadow, 2009), whereas children with ASD may not yet replace gestures with words. While our findings are in line with several studies that used semi-structured assessments or parent report measures to study gesture in high-risk infants (Goldberg et al., 2005; Mitchell et al., 2006), they conflict with other previous findings that found group differences at 24 months (LeBarton & Iverson, 2016; Rozga et al., 2011). For example, LeBarton and Iverson (2016) reported that high-risk infants with ASD produced significantly fewer gestures than high-risk infants without ASD at 24 months (but not at 36 months) using a similar naturalistic observation method as the current study. The difference in findings may be attributed to methodological differences. For instance, the ASD diagnostic process was not the same between LeBarton and Iverson (2016) and the present study. Specifically, children's diagnostic outcomes were made at 36 months in LeBarton and Iverson (2016), whereas diagnostic outcomes were made at 18, 24, or 36 months, possibly leading to a less conservative sample in the current study. The difference could also be attributed to the fact that most of our high-risk infants came from relatively high socioeconomic families (Table 2.1) and ultimately had language scores within one standard deviation of the population mean (Table 2.7). Given the mixed findings in the infant sibling literature, future studies need to further explore the heterogeneity in early gesture production among high-risk infants using more diverse and larger longitudinal samples to depict a comprehensive picture of the developmental trajectory of gesture in high-risk infants.

When we broke down the total number of gestures into the number of gestures produced with or without speech, we found that at 12 months, the ASD outcome group integrated gestures with speech significantly less than high-risk infants without ASD diagnosis. At 18 months, the two high-risk groups produced a significantly fewer number of gesture–speech combinations, compared to low-risk infants. Similar to these findings, previous studies have reported that the ability to combine different communicative behaviors, such as gestures and vocalizations, might be impaired in high-risk infants, especially those who eventually receive an ASD diagnosis, in the first 2 years of life (Parladé & Iverson, 2015; Winder et al., 2013). When examining the number of gestures produced without speech, we found group differences only at 12 months, with high-risk infants with ASD and low-risk infants producing significantly fewer gestures alone than high-risk infants without ASD. As discussed above, this finding might be due in part to higher gesture production in caregivers of high-risk infants without ASD (Talbott et al. 2015a), which might have led to higher gesture production in their infants. Taken together, fewer gesture–speech combinations and gestures alone indicate that infants who later developed ASD communicated significantly less using gestures with their caregivers at 12 and 18 months than their typically developing peers.

After examining the quantity of gesture produced by infants, we examined the distribution of gesture categories each group produced. Consistent with prior literature (Özçalışkan et al., 2017), infants diagnosed with ASD did not differ in their proportional use of gesture categories from infants with no diagnosis. That is, infants of all three groups produced mostly deictic gestures between 12 and 24 months of age. The proportions of conventional and representational gestures were also comparable across the groups at three ages. Özçalışkan et al. (2017) suggested that the complexity of gestural representation may account for similar rates of different gesture categories across groups. For example, because a deictic gesture has a clearer mapping to its referent (e.g., pointing to a ball to indicate ball) and is less cognitively demanding to produce than a representational gesture (e.g., flapping arms to convey flying), young children may be more likely to produce deictic gestures than other gesture categories (see Özçalışkan et al. 2017 for detailed discussion). In summary, while we found group differences in the quantity of gestures, there was no qualitative difference in the distribution of gesture categories across the three groups. Notably, our coding of gesture categories (deictic, conventional, representational) is consistent with that of other studies (e.g., Rowe et al., 2008), but there are differences in how gestures are categorized in the extant literature. For example, Özçalışkan et al. (2017) distinguish giving gestures from deictic gestures, while the current study coded giving gestures as part of deictic gestures. Consistent and detailed coding of gestures in future studies can further refine our understanding of how groups resemble or differ from each other in their use of gestures.

Turning to the distribution of types of gesture–speech combinations, we found group differences at 18 and 24 months. At 12 months, all three groups produced a greater proportion of gestures with non-word vocalizations than other types, presumably because most children around this age do not have words yet and therefore depend on gestures and vocalizations to communicate (e.g., Winder et al. 2013). Compared to high- and low-risk infants without ASD, high-risk infants later diagnosed with ASD showed a trend toward a smaller proportion of reinforcing types and a significantly smaller proportion of disambiguating types at 18 and 24 months, respectively. This finding – high-risk infants with ASD producing a relatively lower proportion of developmentally advanced gesture–speech combinations than their peers with no ASD – suggests that infants with ASD might not have been advancing as quickly as nondiagnosed infants in the way that they combined gestures with words. In contrast, there was no significant group difference in the proportion of supplementary types at three ages. One possibility for the non-significant difference in supplementary types, in particular, is that the ability to convey a sentence-like meaning or create a two-unit construction through a supplementary type (e.g., point to cookie + "eat") may be equally variable or challenging for all groups, whereas reinforcing types (e.g., point to cookie + "cookie") and disambiguating types (e.g., point to cookie + "that") do not require a two-unit construction and may be easier to produce. Of note, it is important to highlight that our sample size is relatively small (although the number of HRA+ infants is larger than most infant sibling studies) and thus limits our ability to draw definitive conclusions. Also, a 10-min interaction might be too short a time period in which to capture children's use of different types of gesture–speech combinations. Hence, future research investigating specific types of gesture–speech combinations, using longer sampling of child communicative behaviors, could be informative in deepening our understanding of the development of gesture–speech integration in high-risk infants.

Caregiver Responsiveness to Infant Gesture

Given significant differences in early gesture profiles of infant groups, we sought to examine whether differences in infant gesture use affected immediate, contingent caregiver responsiveness to the gestures. As expected, there was a significant group difference in the total number of contingent responses that parents provided to their infants' gestures. That is, because high-risk infants with ASD gestured significantly less than their peers at 12 and 18 months, caregivers of high-risk infants with ASD consequently had fewer opportunities to provide contingent input to the infants' gestures. In other words, the differences in the sheer number of parental contingent responses were driven by the differences in the number of infant gestures. By implication, fewer infant gestures inherently limit the number of chances for parents to respond, which, in turn, may have cascading effects on children's language development (Leezenbaum et al. 2014). However, when we controlled for the differences in infant gestures and compared the response rates, we found that caregivers of all three groups provided high and comparable proportions of contingent responses to gestures – a pattern consistent with prior work (Dimitrova et al., 2016; Leezenbaum et al., 2014). Also, the proportions of contingent responses did not change with age, suggesting that parental responsiveness was high and stable over time in all three groups. These findings add to the broader literature that suggests minimal differences between mothers of high- and low-risk infants in response rates to their infant's communicative behaviors and play during dyadic interactions (Campbell, Leezenbaum, Mahoney, Day, & Schmidt, 2015; Leezenbaum et al., 2014; Talbott et al., 2016).

Early Gesture is Associated with Language and ASD Outcomes

Consistent with prior research (Rowe et al., 2008; Sauer, Levine, & Goldin-Meadow, 2010), we found that early gesture predicted later receptive language skills, even after controlling for covariates, in both typical and atypical development (Table 2.8). Our finding that 12-month gesture predicted later receptive language over and above 12-month word types suggests that early gesture may be a more sensitive indicator of potential language difficulties than early productive vocabulary (see also Rowe & Goldin-Meadow, 2009b). One possibility for the significant relation between gesture and receptive language is that infant gesture is related to parent gesture, which, in turn, may direct an infant's attention to objects and have an impact on child language (Rowe & Goldin-Meadow, 2009b).

While we found a significant relation between gesture and later receptive language, we found no such relation between gesture and later expressive language, as indicated by the lack of the significant correlation. Similar to our findings, Manwaring et al. (2017) and O'Neill and Chiat (2015) have reported significant associations between gesture and receptive language, but not expressive language, in children with ASD and children with language delay, respectively. In fact, expressive language skills have been reported to be less impaired than receptive language skills in children with ASD who acquire language before the age of five (Tager-Flusberg, 2016; Weismer, Lord, & Esler, 2010), which was the case for every child in the current study. Another explanation is that both early gesture use and receptive language skills may reflect an infant's ability to socially engage and interact with a caregiver or an experimenter and have less to do with language production abilities. A meta-analysis reported a stronger relation between pointing gestures and receptive language than expressive language in typical development (Colonnesi, Stams, Koster, & Noom, 2010), lending support to this explanation. Given that the implications of a significant relation between early gesture and language outcomes are important in creating targeted interventions, future studies should use experimental manipulation of gesture (e.g., LeBarton, Goldin-Meadow, & Raudenbush, 2015) to identify the precise mechanism(s) underlying the effect of gesture on children's receptive and expressive language skills in both typical and atypical development.

Unlike infant gesture, caregiver responsiveness to infant gesture was not associated with later language skills, when infant gesture was controlled. The fact that we did not find a relation between caregiver responsiveness and children's subsequent language skills was contrary to our hypothesis based on previous work (Dimitrova et al., 2016; Goldin-Meadow et al., 2007; Leezenbaum et al., 2014; McDuffie & Yoder, 2010). However, this finding likely reflects the differences in how responsiveness was defined and coded across the studies. The current study investigated overall responsiveness (i.e., did a caregiver provide an immediate, contingent response to child gesture?), while prior studies have examined specific types of parent verbal responses (e.g., translations, follow-in comments) in relation to child language outcomes. Thus, our follow-up work is currently examining type and modality of caregiver responses to address this limitation, with the goal of studying potential mechanism(s) underlying children's language learning process in high-risk infants.

Finally, we found that the total number of gestures at 12 months predicted which high-risk infants would likely receive an ASD diagnosis, even when controlling for early speech or language and demographic covariates[8]. This replicates previous work that found early gesture use was predictive of ASD outcomes (Chawarska et al., 2014; Colgan et al., 2006; Veness, Prior, Eadie, Bavin, & Reilly, 2014). By implication, careful monitoring of early communicative behaviors such as gestures may be important in differentiating infants who will eventually develop ASD from those who will not. However, it is important to keep in mind that although the effect was significant, it was small, and that gesture alone is not likely to be indicative of eventual ASD outcomes in clinical practice due to low specificity and sensitivity (Luyster, Seery, Talbott, & Tager-Flusberg, 2011). For example, gesture has been found to predict outcomes in other clinical populations (e.g., late talkers; Thal, Tobias, & Morrison, 1991), suggesting that atypicality in early gesture is not specific to ASD. Nevertheless, the current data indicates that early gestural abilities of high-risk infants should be closely monitored by primary care professionals, educators, and caregivers to ensure timely referral for intervention and access to services. Shire et al. (2018) reported that educational professionals could be reliably trained to assess nonverbal communicative skills and set appropriate intervention targets for children with ASD, showing the potential of training for stakeholders to facilitate earlier detection of risks and intervention.

One important limitation of the current study that warrants discussion is that the overall recurrence rate in our larger study was approximately 30%, which is higher than the expected rate reported in the prior literature (e.g., 18.7%; Ozonoff et al. 2011). This might be due to sampling bias; for example, mothers of high-risk infants who were concerned about the infant's

[8]Of note, caregiver education was also significantly and negatively associated with ASD diagnosis, such that infants whose parents had higher levels of education had a lower probability of receiving ASD diagnosis later. This finding, however, contrasts with previous findings that reported a positive association between maternal education and rates of ASD in the United States (e.g., Fountain, King, & Bearman, 2011), and is difficult to interpret considering that we have limited information on potential confounders of parental education and that parents of both HRA+ and HRA- infants had relatively high levels of education in the current study (Table 2.6). Further research may help elucidate potential mechanisms of association between parental education and ASD within a high-socioeconomic sample.

development (e.g., reduced gesture use) might have been more likely to enroll their infant in our study than those of high-risk infants who did not display atypicality in early development. In fact, a previous study using an overlapping sample as the current study found that mothers of high-risk infants reported significantly more concerns about infants' social communication within the first year of life, compared to mothers of low-risk infants (Talbott, Nelson, & Tager-Flusberg, 2015b). Considering this issue, our findings on infant gesture production may be biased and may not generalize to the larger population of high-risk infants, especially those who may not show atypicality in gesture use within the first year of life.

Conclusions

In summary, the current study provides a detailed description of gesture production in infants at high and low risk for ASD and caregiver responsiveness in relation to language or ASD outcomes between 12 and 24 months of age. Our findings indicate that low gesture use may be predictive of later developmental outcomes in high-risk infants. By implication, early gesture use should be closely monitored and assessed in high-risk infants to identify those who will have difficulties with language or ASD at a later age. Early identification of those at-risk children can lead to timely access to resources and intervention services that have been shown to promote positive outcomes for our children (Dawson, 2008; Kasari, Gulsrud, Freeman, Paparella, & Hellemann, 2012).

STUDY 3:

Reciprocal Influences Between Child and Parent Language in Dyads Involving High- and Low-risk Infants for Autism Spectrum Disorder[9]

Abstract

We examined input of parents of infants at high and low familial risk for autism spectrum disorder (ASD) and investigated reciprocal associations between parent input and child language skills in the first three years of life. Parent-infant dyads (high-risk: $n = 55$; low-risk: $n = 34$), 21 of whom included an infant later diagnosed with ASD, were videotaped during free play interactions at 12, 18, and 24 months. Measures of parent input were derived from parent-infant interactions. Children's language skills were assessed using Verbal Developmental Quotients (VDQ) from the Mullen Scales of Early Learning at 12, 18, 24, and 36 months. Results suggested that a) parents of high- and low-risk infants produced similar word tokens, word types, and proportions of contingent verbal responses, but parents of high-risk infants used shorter mean length of utterances (MLU) than parents of low-risk infants at 18 and 24 months; b) parents' MLU was positively associated with their infants' VDQ at the subsequent visit after six months, regardless of group; and c) infants' VDQ was positively associated with parents' MLU at the subsequent visit after six months in the high-risk group only. These findings contribute to our understanding of the mechanisms underlying early language learning of high-risk infants.

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[9]In preparation for publication

Background

According to social interactionist model of language development (e.g., Bruner, 1981; Vygotsky, 1978), children learn language from interactions with the environment. Parents, in particular, provide an important source of input during daily interactions with children in their early linguistic environment (Rowe, 2012; Tamis-LeMonda, Bornstein, & Baumwell, 2001). In addition to the important role that parent input plays in child language learning, a growing body of evidence suggests that children also contribute to their own language learning experiences, creating a bidirectional process between children and parents (Fusaroli, Weed, Fein, & Naigles, 2019; Sameroff, 2009; Song, Spier, & Tamis-Lemonda, 2014). While the importance of parent input is well documented in typical development, less is known about the role of parent input in child language skills (and vice versa) in the context of autism high-risk context. That is, infants who have an older sibling with autism spectrum disorder (ASD) are at high risk for ASD and its associated language deficits and delays (see Drumm & Brian, 2013 for review); yet, our understanding of factors that set the foundation for language learning in this high-risk population is relatively limited. In the current study, we examined the linguistic environment surrounding infants at high and low risk for ASD and reciprocal associations between parent input and child language development during the first three years of life.

Language Learning Environment for Infants at High Risk for ASD

ASD is characterized by persistent impairments in social communication and interaction and repetitive behaviors or restricted interests (American Psychiatric Association, 2013). In addition to these core features, many children with ASD experience atypical language development (see Tager-Flusberg, 2016 for review). Accordingly, many studies have focused on identifying factors that are related to language skills of children with ASD, especially ‘child-based' factors such as verbal and nonverbal abilities (Fusaroli et al., 2019). In addition, several studies have examined 'environmental' factors that are related to children's language skills, in particular, parent input. For example, Warren et al. (2010) found no significant group difference in the total number of words (word tokens) spoken by parents of children with ASD and those of age-matched typically developing children at 30 months. Swensen (2007) similarly reported that mothers of children with ASD (M_{age} = 33 months) produced a comparable number of different words (word types), as mothers of typically developing children matched on language production. In addition, Bang and Nadig (2015) reported no significant group differences in several input features including word tokens, word types, and mean length of utterances (MLU) between mothers of children with ASD (M_{age} = 61 months) and mothers of language-matched typically developing children. More recently, Fusaroli et al. (2019) found that word tokens and word types did not differ between parents of preschoolers with ASD (M_{age} = 33 months) and those of language-matched typically developing; however, parents of the ASD group produced significantly shorter MLU overall. Furthermore, several studies reported similar rates of verbal responses between caregivers of children with ASD and those of typically developing children (Bani Hani, Gonzalez-Barrero, & Nadig, 2013; Dimitrova, Özçalışkan, & Adamson, 2016; Siller & Sigman, 2002).

The findings above suggest that children with ASD and typically developing children are exposed to comparable linguistic environments regarding parent input in early childhood, but we know less about language learning environment available to infants at high risk for ASD. Talbott, Nelson, and Tager-Flusberg (2015) found no significant group differences in word tokens and word types among mothers of high-risk infants later diagnosed with ASD (HRA+), mothers of high-risk infants not diagnosed with ASD (HRA-), and mothers of low-risk comparison (LRC) infants at 12 months. Leezenbaum et al. (2014) reported similar proportions of contingent verbal responses to infants' communicative behaviors between mothers of high-risk infants and mothers of low-risk infants at 13 and 18 months. Similarly, Talbott et al. (2016) found no significant group difference in rates of maternal verbal responses to infants' vocalizations at 9 months between high- and low-risk groups. However, a comprehensive longitudinal picture of the linguistic environment of HRA+, HRA-, and LRC infants has not been published. A better understanding of the language learning environment during infancy, a period in which the brain is particularly receptive to environmental influences (e.g., caregiver input; Wade, Jenkins, Venkadasalam, Binnoon-Erez, & Ganea, 2018), may lead to the development of effective interventions for infants at risk for language deficits and delays later in life. Our first research goal was thus to contribute to this line of literature by providing a comprehensive picture of parent input measures such as word tokens, word types, MLU, and verbal responses to HRA+, HRA-, and LRC infants between 12 and 24 months, using a larger, longitudinal sample than in previous studies[10].

Role of Parent Input in Child Language Development

Links between parent input and children's language skills have been well established in typical development. Several seminal studies suggested that parents who spoke more words to their children had children with stronger language abilities, suggesting the important role of input quantity (Hart & Risley, 1995; Hoff, 2003; Huttenlocher, Haight, Bryk, Seltzer, & Lyons, 1991). Studies also have emphasized the contribution of input quality, or specific features of the input, in child language development (e.g., Cartmill et al., 2013; Hirsh-Pasek et al., 2015; Rowe, 2012).

[10]Of note, we used an overlapping sample as Talbott et al. (2015), who examined gesture and language (specifically, word tokens and word types) of mothers of high- and low-risk infants at 12 months. We built on the study by Talbott et al. (2015) by comparing multiple measures of parent input (i.e., word tokens, word types, MLU, contingent verbal responses) at multiple time points (i.e., 12, 18, and 24 months).

For example, parents' word types and MLU have been found predictive of children's vocabulary growth (Hoff & Naigles, 2002; Pan, Rowe, Singer, & Snow, 2005). In addition, parent verbal responsiveness, which reflects an interactional quality of parent-child interaction, has been shown to be important in facilitating communicative and language skills of typically developing children (Dunst, Gorman, & Hambly, 2010; Olson & Masur, 2015; Tamis-LeMonda, Kuchirko, & Song, 2014; Wu & Gros-Louis, 2014).

The role of parent input has also been examined in language development of children with ASD. For instance, Bang and Nadig (2015) found that parent MLU was significantly positively associated with later vocabulary size in children with ASD aged 50-85 months. Similarly, Fusaroli et al. (2019) reported that parent MLU predicted subsequent language production of preschoolers with ASD. Of note, these studies found that the relation between parent MLU and children's later language skills did not differ between dyads involving children with ASD and those involving typically developing children, suggesting that children with ASD benefit from parent input in the same way as their typically developing peers. Additionally, significant positive relations have been found between parent verbal responses that follow their child's attentional focus and language skills in children with ASD (Haebig, McDuffie, & Ellis Weismer, 2013a; Haebig, McDuffie, & Weismer, 2013b; McDuffie & Yoder, 2010; Siller & Sigman, 2002, 2008). Nevertheless, little is known regarding whether high-risk infants can also benefit from rich input environments; it is only known that their increased risk for ASD is associated with language deficits and delays (Drumm & Brian, 2013). Hence, our second research goal was to address this gap in the literature by investigating the role of parent input in language development of HRA+, HRA-, and LRC infants, while accounting for infants' ASD risk.

Role of Child Language Skills in Parent Input

While researchers have examined the role of parental input on child language development, the influence of the child on parents' language production has been less explored. This is surprising given that children and parents likely mutually influence each other (Sameroff, 2009). In fact, an emerging body of literature suggests reciprocal influences of communication and language between children and parents over time in typical development (Albert, Schwade, & Goldstein, 2018; Luo & Tamis-LeMonda, 2017; Vallotton, 2009). For example, Huttenlocher, Waterfall, Vasilyeva, Vevea, & Hedges (2010) found that children's word types predicted their parents' word types four months later. Song, Spier, and Tamis-Lemonda (2014) also found that children's cognitive scores at two years were related to mothers' word types one year later, suggesting bidirectionality of parent-child associations.

In the ASD literature, Fusaroli et al. (2019) reported that MLU and word types of children with ASD were associated with parents' later word types and MLU, respectively. In addition, Warlaumont et al. (2014) reported that infants' speech-related vocalizations such as babbling were more likely to elicit immediate parent responses, which, in turn, reinforced more speech-related vocalizations from infants, compared to non-speech-related vocalizations such as laughing. Collectively, these findings show that typically developing children and children with ASD contribute to their own linguistic environment through their influences on parents' input. One important limitation of prior research, however, is that these child-to-parent effects have not been thoroughly explored in the ASD high-risk population. Thus, our third research goal was to assess whether HRA+, HRA-, and LRC infants' language skills related to subsequent input measures of their caregivers.

The Present Study

In the current study, we examined a number of features of the linguistic environment of HRA+, HRA-, and LRC infants at 12, 18, and 24 months and reciprocal associations between parents' input and infants' language skills in the first three years of life. Multiple measures of parent input (i.e., word tokens, word types, MLU, and contingent verbal responses) were coded from parent-infant interactions in the lab at 12, 18, and 24 months. Children's language skills were assessed at 12, 18, 24, and 36 months using the Mullen Scales of Early Learning (MSEL; Mullen, 1995), and their ASD diagnostic outcomes were determined using the Autism Diagnostic Observation Scale (ADOS; Lord et al., 2000) and best clinical judgment between 18 and 36 months. We asked the following research questions:

1. Are there group differences in the measures of parent input (word tokens, word types, MLU, and contingent verbal responses) to HRA+, HRA-, and LRC infants at 12, 18, and 24 months?
2. Do the measures of parent input relate to language skills of infants at the subsequent visit?
3. Do infants' language skills relate to parents' later input, suggesting reciprocal influence between infants and parents?

Methods

Participants

The present study included 89 caregiver-infant dyads drawn from a prospective, longitudinal study of early development of high- and low-risk infants in the first three years of life. Infants were recruited at or before 12 months and drawn from two groups. The first group consisted of high-risk infants who had an older sibling with a community diagnosis of ASD based on parental report. The second group consisted of low-risk infants who had an older sibling and no immediate family history of ASD. ASD diagnosis (+/-) of older siblings were confirmed independently in the lab using the ADOS (Lord et al., 2000) and/or Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003).

For the current study, we included infants who had at least one free play interaction with their caregivers at 12, 18, or 24 months, had ASD outcomes determined at 18, 24, or 36 months (see the section 'ASD outcome classification' for details), and heard English as their primary language at home (> 80% of time). All infants were full-term, had no known prenatal or perinatal complications, and had no known genetic or neurologic disorders. Due to sample attrition (e.g., visits missed by families, technological error in recording during caregiver-infant interactions), data were available from 70 caregiver-infant dyads at 12 and 18 months and 69 dyads at 24 months. For three of our infants, either their mothers or fathers participated in caregiver-child interactions at 12, 18, and 24 months. For two of our infants, only fathers participated in caregiver-child interactions. Mothers participated in the rest of interactions.

For the purposes of data analyses, infants were categorized into one of three groups based on their risk for ASD (high or low) and diagnostic outcomes (ASD or no ASD): high-risk infants later diagnosed with ASD (HRA+), high-risk infants not diagnosed with ASD (HRA-), and low-risk comparison infants not diagnosed with ASD (LRC). Table 3.1 provides descriptive characteristics for each group. As can be seen in Table 3.1, the groups were similar in infant race and household income. However, the groups differed significantly in infant sex and caregiver education, $p = .038$; $\chi^2(2, N = 80) = 9.77$, $p = .008$, respectively. Post hoc pairwise comparisons revealed that the percentage of males was significantly higher in the HRA+ group than the HRA- group, $p = .013$, and that the level of parent education was significantly higher in the LRC group than the HRA+ group, $z = -3.35$, $p < .001$.

Table 3.1. Infant and parent demographic data ($N = 89$)

	HRA+	HRA-	LRC	p (3-group)
Sample size				
12 Months	17	25	28	
18 Months	16	25	29	
24 Months	15	25	29	
Child Characteristics				
Sex (% Female)	28.6% $N = 21$	64.7% $N = 34$	50.0% $N = 34$	.038*
Race/ethnicity (% White)	81.0% $N = 21$	94.1% $N = 34$	88.2% $N = 34$	.269
Parent Characteristics				
[a] Household Income	6.78 (2.26) $N = 18$	7.65 (1.05) $N = 31$	7.22 (1.83) $N = 27$	.306
[b] Caregiver Education	4.92 (1.73) $N = 19$	5.77 (1.71) $N = 31$	6.47 (1.01) $N = 30$	.008**

Note. Data are reported as group means with standard deviations in parentheses.
[a] Income was reported on an eight-point scale: (1) less than $15,000, (2) $15,000-$25,000, (3) $25,000-$35,000, (4) $35,000-$45,000, (5) $45,000-$55,000, (6) $55,000-$65,000, (7) $65,000-$75,000, (8) more than $75,000.
[b] Caregiver education was reported as the highest level attained on a nine-point scale: (1) some high school, (2) high school graduate, (3) some college, (4) community college/two-year degree, (5) four-year college degree, (6) some graduate school, (7) master's degree, (8) doctoral degree, (9) professional degree. For three of our infants, either their mothers or fathers participated in caregiver-child interactions at 12, 18, and 24 months; for them, parent education was calculated by averaging paternal and maternal education levels. For two of our infants, only fathers participated in caregiver-child interactions, and paternal education levels were used. Maternal education levels were used for the rest of the participants.
* $p < .05$, ** $p < .01$.

Procedure

The study was approved by the Institutional Review Boards at Boston Children's Hospital and Boston University. Written, informed consent was obtained from all families. At 12, 18, and 24 months, infants and their parents engaged in a free play interaction in the laboratory for a 10-minute period. Caregiver-infant interactions were videotaped for subsequent transcription and coding. At 12, 18, 24, and 36 months, children completed the MSEL(Mullen, 1995), which is a standardized cognitive assessment with five subscales – Gross Motor, Fine Motor, Visual Reception, Receptive Language, and Expressive Language – suitable for children between birth to 69 months of age. At the last visit to the laboratory, children were administered the ADOS (Lord et al., 2000), a standardized, semi-structured play assessment commonly used in ASD diagnosis.

Transcription

The videotaped sessions of caregiver-child interactions at 12, 18, and 24 months were transcribed verbatim following Codes for the Human Analysis of Transcripts (CHAT) conventions of the Child Language Data Exchange System (CHILDES; MacWhinney, 2000). Transcripts were verified by a second transcriber to ensure accuracy. Following previous work (e.g., Rowe, 2011), each session was transcribed at the level of utterance, which was defined as a sequence of a verbal utterance preceded and followed by a pause, a change in conversational turn, or a change in intonational pattern.

Coding and Measures

Parent input measures. Automated analyses of the transcripts were conducted using the Computerized Language ANalysis (CLAN) program (MacWhinney, 2000) to yield the total number of words (word tokens), number of different words (word types), and mean length of utterances (MLU) that parents produced during the interactions with their infants at 12, 18, and 24 months. These measures served as a measure of parents' input quantity, vocabulary diversity, and sentence complexity, respectively.

In addition, we reliably coded parents' responses to infants' communication. We first identified utterances in which infants' communicative behaviors occurred. Infants' gestures, communicative nonword vocalizations, and words were all counted as communicative behaviors. Infant hand or body movements that indicated objects, people, or locations in the environment (e.g., pointing), had culturally-established meanings with particular forms (e.g., nodding the head to convey *yes*), or recreated an aspect of the referent's shape or movement (e.g., flapping arms in the air to mean *flying)* were considered deictic, conventional, and representational gestures, respectively, based on previous work (Özçalışkan & Goldin-Meadow, 2009). Movements or actions that were not communicative in nature (e.g., manipulating an object) or were part of a ritualized game (e.g., itsy-bitsy-spider) were not considered gestures. Babbling was counted as a communicative nonword vocalization; in contrast, vegetative sounds, laughing, or crying were not counted. Dictionary words, onomatopoeic sounds (e.g., "meow"), and evaluative sounds (e.g., "oopsie") were counted as words.

After identifying the utterance in which the infant's communicative behavior occurred, we coded parent responses up to the two utterances following the infant communicative behavior. We then coded contingency and modality of parent responses (see Appendix D for coding flowchart). With regard to contingency, if a parental response followed the infant's attentional focus, it was determined as contingent. If a parent response redirected the infant's attention to a different object or topic, it was coded as non-contingent redirect response. If a parent did not produce any response, it was coded as no response. Contingent parent responses were further coded for modality: verbal, nonverbal (i.e., action or gesture), or both. For the current study, we focused on examining contingent verbal responses as prior research demonstrates their important role in promoting language development of typically developing children[11] (e.g., Tamis-LeMonda et al., 2001). If a contingent response was verbal only (e.g., saying ‘Do you want the cup?’) or both verbal and nonverbal (e.g., saying ‘Do you want the cup?’ and pointing to a cup simultaneously), it was counted as a verbal response in data analyses.

Child language skills. Children’s language skills were measured using the MSEL Verbal Developmental Quotients (VDQ) at 12, 18, 24, and 36 months. VDQ was calculated by dividing the average age-equivalent score from the MSEL Receptive Language and Expressive Language subscales by the child’s chronological age and multiplying by 100. The MSEL was selected as a measure of children’s language skills, as it spans the age range in our research questions and was administered by a researcher outside of caregiver-infant interactions, providing data that are independent from the interactions.

ASD outcome classification. Children’s final ASD diagnosis (+/-) was determined at their last visit to the lab (i.e., 18, 24, or 36 months) using both the ADOS and best clinical judgment by a licensed clinical psychologist. Research staff with extensive experience in testing children with developmental disorders administered and scored the ADOS. In addition, an ADOS-reliable researcher co-scored the ADOS via video recording. When children met criteria for ASD or came within three points of the cutoff score on the ADOS, a licensed clinical psychologist reviewed the ADOS scores along with behavioral assessment videos to determine final clinical judgment as ASD or no ASD. Final ASD outcomes were determined based on assessments at 18-month for four children ($n_{\text{HRA+}}$ = 3; $n_{\text{HRA-}}$ = 1; n_{LRC} = 0), based on

[11]In fact, our preliminary analyses suggested that only contingent verbal responses at each point in time were significantly correlated with child language skills at the following time, whereas contingent nonverbal responses and noncontingent/no responses were not significantly correlated with child language outcomes.

assessments at 24-month for ten children (n_{HRA+} = 2; n_{HRA-} = 8; n_{LRC} = 0), and based on assessments at 36-month for 75 children (n_{HRA+} = 16; n_{HRA-} = 25; n_{LRC} = 34). Of note, although most of our children had their diagnostic outcomes determined at 36 months (84%), there was a subset of the children who had their ASD outcomes made at 18 or 24 months due to sample attrition (16%). Given the diagnostic stability of ASD in high-risk infants between 18 and 36 months (Ozonoff et al., 2015; Zwaigenbaum et al., 2016), data from infants with ASD diagnoses made at the earlier time points were included to maximize sample size.

Data Analyses

To address our first research question on group differences in parent input at 12, 18, and 24 months between the HRA+, HRA-, and LRC groups, we converted parent word tokens, word types, and contingent verbal responses from raw numbers into rates per 10 minutes to control for the differences in lengths of caregiver-infant interactions[12]. In addition to the raw number of contingent verbal responses, proportions were calculated by dividing the number of contingent verbal responses by the number of possible chances the parent had to respond to. An arcsine transformation was applied to proportional data to examine group differences at each age. Of note, parent MLU was not converted into rate per 10 minutes, as MLU is already an average. Histograms and Shapiro-Wilk tests were examined for each parental measure to check for the normality assumption. One-way ANOVAs (for the measures that had normal distributions) and nonparametric tests (e.g., Kruskal-Wallis H and Mann-Whitney U tests; for the measures that had skewed distributions which violate the assumption of normality) were used to test group differences at each age. To address our second research question on the role of parent input in children's later language skills, we first conducted a series of correlations between parent input

[12]There was no group difference in mean lengths of caregiver-infant interaction videos (HRA+: M = 9.21, SD = 1.90; HRA-: M = 9.31, SD = 2.25; LRC: M = 9.77, SD = 2.04).

measures and children's subsequent language skills; all results were adjusted for multiple comparisons using Bonferroni adjustments. Using the information from the correlation analyses, we performed multiple regression analyses to determine the simultaneous effects of parent input and controls on subsequent child language skills. Finally, for our third research question, we used analogous analyses as those for the second research question, with child language skills as the predictor and parents' subsequent input measure as the outcome to examine the role of children's language skills in parents' later input.

Results

Group Differences in Parent Input to HRA+, HRA-, and LRC Infants

Prior to investigating parent input, we examined the total number of infants' communicative behaviors at 12, 18, and 24 months (Table 3.2). As the table shows, there were significant differences in the total number of infants' communicative behaviors across the three groups at each age. Specifically, at 12 months, HRA+ infants produced significantly fewer communicative behaviors than HRA- infants, $z = -2.35$, $p = .019$, $U = 121$. At 18 months, HRA+ infants produced significantly fewer communicative behaviors than LRC infants, $z = -2.63$, $p = .009$, $U = 121$. Finally, at 24 months, HRA+ infants produced significantly fewer communicative behaviors than LRC infants, $z = -2.74$, $p = .006$, $U = 107$. In sum, HRA+ infants produced significantly fewer communicative behaviors than HRA- and LRC infants in the first two years of life.

Table 3.2. Descriptive statistics (means, standard deviations, range, and Ns) for infant communicative behaviors (gestures, nonword vocalizations, words combined) at 12, 18, and 24 months, by group

Infant Communication	HRA+ Infants	HRA- Infants	LRC Infants
12 Months	29.52 (20.89) 5.69-78.31 *N* = 17	42.24 (16.37) 11.65-65.26 *N* = 25	37.25 (23.07) 8.17-111.00 *N* = 28
18 Months	29.08 (22.42) 2.80-71.92 *N* = 16	40.87 (19.16) 14.33-75.00 *N* = 25	50.83 (26.88) 7.37-134.62 *N* = 29
24 Months	60.21 (21.45) 30.86-115.31 *N* = 15	73.89 (30.05) 28.05-138.69 *N* = 25	85.93 (29.58) 32.13-158.32 *N* = 29

Next, we investigated group differences in measures of parent input at 12, 18, and 24 months (Table 3.3). At 12 months, there were no significant group differences in parent word tokens, word types, and MLU across the three groups. In contrast, there was a significant difference in the frequency of parents' contingent verbal responses, $\chi^2(2, N = 70) = 7.51$, $p = .023$. Post hoc pairwise comparisons revealed that parents of HRA+ infants provided significantly fewer contingent verbal responses than parents of HRA- infants, $z = -2.81$, $p = .005$, $U = 103$. However, parents of the three groups did not differ in the proportion of parents' contingent verbal responses.

At 18 months, there were no significant group differences in parent word tokens and types. However, parents of the three groups differed significantly in MLU, $F(2, 67) = 9.88$, $p < .001$. Post hoc pairwise comparisons suggested that parents of HRA+ and HRA- infants produced significantly shorter MLU, compared to parents of LRC infants, $t = 4.35$, $p < .001$; $t = 2.61$, $p = .030$, respectively. In addition, there was a significant group difference in the frequency of contingent verbal responses, $\chi^2(2, N = 70) = 7.95$, $p = .019$. Specifically, parents of HRA+ infants showed significantly fewer contingent verbal responses than parents of HRA- and LRC infants, $z = -2.09$, $p = .037$, $U = 122$; $z = -2.63$, $p = .009$, $U = 121$, respectively. Importantly though, when the proportion of the responses was compared, the three groups did not differ from one another.

At 24 months, there was, again, no significant group difference in parent word tokens and types. On the other hand, there was a significant group difference in parent MLU, $F(2, 66) = 6.57$, $p = .003$. Post hoc comparisons revealed that HRA+ and HRA- parents produced significantly shorter MLU than LRC parents, $t = 3.02$, $p = .010$; $t = 3.04$, $p = .009$, respectively. Finally, there was a significant group difference in the frequency of contingent verbal responses

Table 3.3. Descriptive statistics (means, standard deviations, range, and Ns) for parent input at 12, 18, and 24 months, by group

	HRA+ Parents	HRA- Parents	LRC Parents
12 Months			
Word Tokens	464.01 (219.06) 106.04-924.86 *N* = 17	580.16 (199.23) 222.04-1055.31 *N* = 25	544.05 (226.88) 169.50-992.69 *N* = 28
Word Types	135.54 (54.31) 57.10-235.23 *N* = 17	168.03 (62.82) 75.18-328 *N* = 25	154.8 (50.06) 89.07-245.23 *N* = 28
MLU	3.14 (0.65) 1.78-3.99 *N* = 17	3.07 (0.53) 2.07-3.89 *N* = 25	3.33 (0.51) 2.48-4.75 *N* = 28
Contingent Verbal Responses (Freq.)	29.90 (23.10) 5.21-81.62 *N* = 17	48.06 (19.71) 17.48-91.06 *N* = 25	41.62 (27.40) 5.08-123 *N* = 28
Contingent Verbal Responses (Prop.)	0.68 (0.18) 0.33-1.00 *N* = 17	0.76 (0.12) 0.50-0.93 *N* = 25	0.73 (0.19) 0.29-1.00 *N* = 28
18 Months			
Word Tokens	538.35 (166.10) 327.68-1021.25 *N* = 16	616.42 (169.13) 329.82-1039.56 *N* = 25	639.85 (186.75) 312.36-1005.69 *N* = 29
Word Types	149.86 (37.49) 106.38-238.24 *N* = 16	175.89 (40.57) 108.27-241.43 *N* = 25	173.03 (43.26) 110.41-264.77 *N* = 29
MLU	2.82 (0.38) 2.31-3.44 *N* = 16	3.10 (0.48) 2.19-4.11 *N* = 25	3.42 (0.44) 2.69-4.47 *N* = 29
Contingent Verbal Responses (Freq.)	35.44 (26.97) 2.80-94.64 *N* = 16	51.55 (22.65) 11.97-87.14 *N* = 25	62.91 (33.57) 8.19-185.58 *N* = 29
Contingent Verbal Responses (Prop.)	0.83 (0.14) 0.47-1.00 *N* = 16	0.83 (0.10) 0.59-0.96 *N* = 25	0.84 (0.11) 0.54-1.00 *N* = 29

Table 3.3. Descriptive statistics (means, standard deviations, range, and Ns) for parent input at 12, 18, and 24 months, by group (continued)

	HRA+ Parents	HRA- Parents	LRC Parents
24 Months			
Word Tokens	640.82 (170.11) 341.11-901.84 *N* = 15	607.98 (173.51) 373.24-1078.47 *N* = 25	683.09 (207.44) 270.41-1059.95 *N* = 29
Word Types	176.10 (28.35) 124.31-219.38 *N* = 15	171.89 (32.81) 116.74-260.06 *N* = 25	188.68 (41.05) 100-263.49 *N* = 29
MLU	3.40 (0.56) 2.67-4.32 *N* = 15	3.46 (0.46) 2.56-4.23 *N* = 25	3.86 (0.47) 2.96-4.98 *N* = 29
Contingent Verbal Responses (Freq.)	71.48 (26.15) 34.29-126.56 *N* = 15	82.51 (31.35) 37.82-149.51 *N* = 25	96.91 (32.84) 39.80-172.71 *N* = 29
Contingent Verbal Responses (Prop.)	0.83 (0.09) 0.60-0.95 *N* = 15	0.79 (0.08) 0.59 (0.96) *N* = 25	0.81 (0.11) 0.44-0.93 *N* = 29

Note. For proportions of contingent verbal responses, untransformed data are reported in Table.

at 24 months, $\chi^2(2, N = 69) = 6.51$, $p = .039$. Post hoc comparisons revealed that parents of HRA+ infants produced a significantly smaller number of contingent verbal responses than parents of LRC infants, $z = -2.44$, $p = .015$, $U = 119$. In contrast, there was no significant group difference in the proportion of the responses.

Taken together, parents of HRA+, HRA-, and LRC infants were comparable in word tokens and types during 10-minute interactions with their infants at 12, 18, and 24 months. However, parents of HRA+ and HRA- produced shorter MLU than LRC parents at 18 and 24 months. Also, parents of HRA+ infants showed fewer contingent verbal responses at 12, 18, and 24 months; however, when the proportion of contingent verbal responses was compared to account for the chances that parents had to respond to infant communicative behaviors, the three groups of parents were similarly responsive.

Relations between Parent Input and Children's Later Language Skills

To study the relations between parent input and children's subsequent language skills, we first examined zero-order correlations between input measures and children's MSEL VDQ at the subsequent visit (Table 3.4). The results suggested that at 12 months, parents' contingent verbal responses (frequency) were significantly positively correlated with children's VDQ at six months later. At 18 months, parents' word tokens, word types, MLU, and contingent verbal responses (frequency) were all significantly positively related to children's VDQ at six months later. At 24 months, parents' MLU and contingent verbal responses (frequency) were correlated with children's VDQ one year later. In the next step, we examined partial correlations between each of the parent input measures and subsequent child language, controlling for parent education and earlier child language (VDQ), which have been reported to be predictive of child language (e.g., Hoff, 2003; Hoff & Naigles, 2002; Rowe, 2012). The partial correlations are presented in

Table 3.4. Zero-order correlations between parent input measures and children's VDQ at the subsequent time

	MSEL VDQ		
	18 months (N = 68)	24 months (N = 65)	36 months (N = 56)
Word tokens at the previous visit	0.16	0.33**	0.06
Word types at the previous visit	0.15	0.40**	0.23~
MLU at the previous visit	-0.08	0.46***	0.42***
Contingent verbal responses (freq.) at the previous visit	0.38**	0.35**	0.29*
Contingent verbal responses (prop.) at the previous visit	0.19	0.12	-0.08

Note. * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 3.5. As Table 3.5 shows, parent MLU at 18 months was significantly related to child language skills at 24 months, with parent education and previous child language skills controlled. There were no other significant correlations.

Using the information from the partial correlation analyses, we conducted multiple regression analyses to determine the simultaneous effects of parent input (specifically, 18-month MLU) and controls on subsequent child language skills. We built our regression-models in the following steps. First, we began with a control model with parent education and previous child language skills. Second, we added our question predictor, parent MLU, to the model with controls. Third, we included children's risk for ASD in the model to determine whether the relation between parent MLU and children's language skills held even when controlling for children's ASD risk. Finally, we tested an interaction effect of parent MLU and child ASD risk to determine whether the relation between parent MLU and children's later language skills differed between high- and low-risk groups. The results of the regression models are presented in Table 3.6 and are summarized below.

In Table 3.6, Model 1a shows that parent education was a significant positive predictor of 24-month VDQ and explains approximately 7% of the variance in the outcome. When 18-month VDQ was added (Model 1b), it explained an additional 31% of the variance in 24-month VDQ. When 18-month parent MLU was added to the controls (Model 2), it was a significant positive predictor and explained an additional 14% of the variation in 24-month VDQ. When ASD risk was included (Model 3), it was not a significant predictor, but the direction of the effect was in the expected direction and resulted in a slight increase in the R^2 statistic ($\Delta R^2 = 2\%$). Finally, we found that the interaction term between parent MLU and ASD risk was not significant (not shown), suggesting that the relation between 18-month parent MLU and 24-month child VDQ

Table 3.5. Partial correlations between parent input measures and children's language skills at the subsequent visit, controlling for parent education and previous child language skills

	MSEL VDQ		
	18 months	24 months	36 months
Word tokens at the previous visit	0.03	0.11	-0.05
Word types at the previous visit	0.00	0.17	0.09
MLU at the previous visit	-0.21	0.51***	0.15
Contingent verbal responses (freq.) at the previous visit	0.24~	0.15	0.12
Contingent verbal responses (prop.) at the previous visit	0.02	0.04	0.01

Note. The partial correlations with 18-month VDQ control for parent education and child VDQ at 12 months. The partial correlations with 24-month VDQ control for parent education and child VDQ at 18 months. The partial correlations with 36-month VDQ control for parent education and child VDQ at 24 months. MSEL VDQ: Mullen Scales of Early Learning Verbal Developmental Quotient.
~$p < .1$, *** $p < .001$.

Table 3.6. Multiple regression models predicting child language skills at 24 months

	Child VDQ (24mo)			
	Model 1a	Model 1b	Model 2	Model 3
Intercept	96.52*** (6.53)	59.14*** (8.62)	30.56** (11.08)	42.90** (13.79)
Parent education	2.51* (1.09)	0.93 (1.04)	0.12 (1.10)	-0.32 (1.12)
Previous child VDQ (18mo)		0.44*** (0.08)	0.36*** (0.08)	0.35*** (0.08)
Parent MLU (18mo)			12.90*** (3.04)	11.03** (3.26)
Child ASD risk				-5.09 (3.45)
N	73	68	56	56
R^2 (%)	6.9	37.9	51.4	53.4

Note. Data are reported as unstandardized coefficients with standard errors in parentheses. Child ASD risk was coded as low-risk = 0, high-risk = 1. VDQ: Verbal Developmental Quotient; MLU: Mean Length of Utterances; ASD: Autism Spectrum Disorder.

did not differ by ASD risk. In sum, our final model (Model 3) suggests that parents who used longer utterances with their 18-month-olds had children with higher language skills 6 months later, controlling for parent education, children's earlier language skills, and ASD risk.

Relations between Child Language Skills and Subsequent Parent Input

We used the same analytic approach as above to study associations between child language skills and subsequent parent input. First, the results of the zero-order correlations (Table 3.7) showed that there were significant positive correlations between children's 12-month VDQ and parent word types and contingent verbal responses (frequency) at six months later. Also, children's 18-month VDQ were significantly positively correlated with parent word types MLU, and contingent verbal responses (frequency) at six months later. Next, the partial correlations between child language and parents' later input, controlling for parent education and earlier measure of parent input, suggested that the only significant correlation was found between children's 18-month VDQ and parents' 24-month MLU (Table 3.7). Using the correlations in Table 3.7, we built the regression models to determine the simultaneous effects of child language and controls on subsequent parent input (Table 3.8).

Model 1a in Table 3.8 shows that parent education was a significant positive predictor of MLU and explained approximately 7% of the variation in 24-month MLU. When 18-month MLU was added to the model to control for earlier parent MLU (Model 1b), it also was a significant predictor and explained an additional 22% of the variation in 24-month MLU. When child VDQ at 18 months (Model 2) and ASD risk (Model 3) were added to the model with the controls, they were not significant predictors of parent MLU. However, when the interaction term between child language and ASD risk was included to test whether the relation between child language and parents' subsequent MLU differed based on ASD risk (Model 4), it was a

Table 3.7. Zero-order/partial correlations between child language and parent input at the subsequent time

		Parent Input Measures at Six Months Later				
		Word Tokens	Word Types	MLU	Contingent Verbal Responses (Freq.)	Contingent Verbal Responses (Prop.)
Child VDQ	12 months	.20~/.15	.27*/.23~	.19/.15	0.38**/0.11	0.20~/0.17
	18 months	.19/.11	.28*/.13	.41***/.27*	0.34**/0.07	0.00/0.00

Note. Zero-order correlations are shown before a slash sign (/). Partial correlations appear after a slash sign (/). The partial correlations control for parent education and earlier parent input.
~ $p < .1$, * $p < .05$, ** $p < .01$, *** $p < .001$.

Table 3.8. Multiple regression models predicting parent MLU at 24 months

	Parent MLU (24mo)				
	Model 1a	Model 1b	Model 2	Model 3	Model 4
Intercept	3.11*** (0.26)	1.80*** (0.45)	1.43* (0.53)	2.02** (0.61)	4.10*** (0.92)
Parent education	0.09* (0.04)	0.07 (0.05)	0.05 (0.05)	0.03 (0.05)	0.02 (0.05)
Previous parent MLU (18mo)		0.45** (0.14)	0.42** (0.14)	0.34* (0.15)	0.19 (0.14)
Child VDQ (18mo)			0.01 (0.00)	0.01 (0.00)	-0.01 (0.01)
Child ASD risk				-0.27~ (0.15)	-2.57** (0.82)
Interaction (VDQ x ASD risk)					0.02** (0.01)
N	60	45	44	44	44
R^2 (%)	7.4	29.2	31.7	36.7	47.9

Note. Data are reported as unstandardized coefficients with standard errors (SE) in parentheses. Child ASD risk was coded as low-risk = 0, high-risk = 1. VDQ: Verbal Developmental Quotient; MLU: Mean Length of Utterances; ASD: Autism Spectrum Disorder.

significant predictor of parent MLU, and this model explained approximately 48% of the variation in parent MLU at 24 months. Post-hoc analyses suggested that even when controlling for parent education and 18-month MLU, child 18-month VDQ was significantly positively associated with parent 24-month MLU in the high-risk group, $b = 0.01$, $p < .01$. However, child VDQ was not significantly associated with parent later MLU in the low-risk group, $b = -0.01$, $p = .18$ (Figure 3.1). In sum, these results suggest that the relation between child language skills at 18 months and parent MLU at 24 months differed in high- and low-risk dyads.

Discussion

The current study examined the language learning environment of high- and low-risk infants, some of whom were later diagnosed with ASD, and associations between parents' input and infants' language skills in the first three years of life. Our key findings were that (1) parents used similar word tokens, word types, and proportions of contingent verbal responses, but parents of high-risk infants produced significantly shorter MLU than parents of low-risk infants at 18 and 24 months; (2) parents' MLU at 18 months was significantly associated with children's language skills at 24 months, controlling for parent education, earlier child language skills, and ASD risk; and (3) children's language skills at 18 months were significantly associated with their parents' MLU at 24 months in the high-risk group, but not in the low-risk group, when controlling for parent education and earlier parent MLU.

Parents of two high-risk groups produced significantly shorter MLU, compared to that produced by parents of low-risk infants, at 18 and 24 months. One explanation for this finding is that parents may be sensitive to their children's language skills and fine-tune the sentence complexity of their input accordingly. In fact, our analyses showed that high-risk children had significantly lower VDQ than low-risk children at 18 and 24 months, $F(1, 81) = 5.71$, $p = .019$;

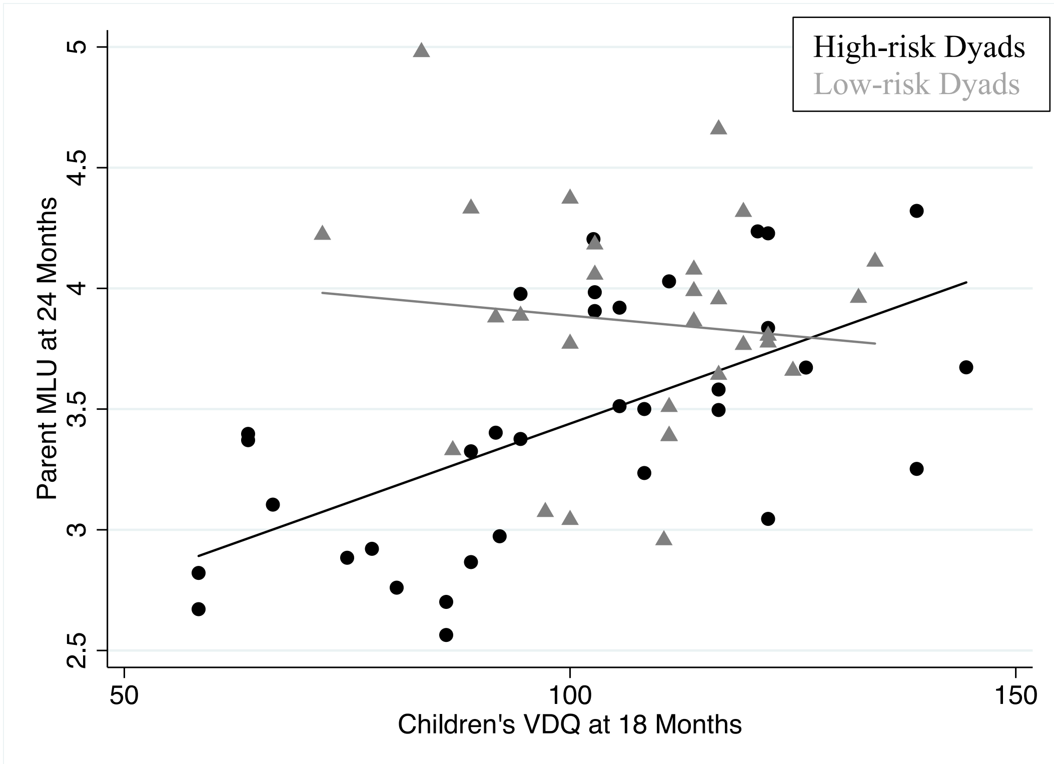

Figure 3.1. Scatterplot showing relations between children's Verbal Developmental Quotients (VDQ) on the Mullen Scales of Early Learning at 18 months and the respective parent's mean length of utterances (MLU) at 24 months. Black line and dots represent data for high-risk dyads, and grey line and dots show data for low-risk dyads. Best fit lines show a significant positive relation between children's VDQ and parents' subsequent MLU in high-risk dyads and no relation in low-risk dyads.

$F(1, 79) = 7.01$, $p = .010$, respectively, lending support to this explanation. Another possibility is that parents of high-risk infants, who have an older child diagnosed with ASD, may be exposed to intervention approaches that promote the use of simplified language for children with ASD (e.g., Lovaas, 2003; Rogers & Dawson, 2010). While our study did not collect detailed information about the nature of early intervention services that infants and their parents were exposed to, future research can examine how parents may adapt input depending on the strategies they learn from early interventions. Of note, it is important to keep in mind that we did not match infants on language abilities in the current study as in some of previous studies (e.g., Bang & Nadig, 2015; Fusaroli et al., 2019). Rather, we compared naturalistic language data from parents at each chronological age of infants. Thus, the differences in parent MLU between high- and low-risk groups should be interpreted with caution.

Parents of HRA+ infants provided a significantly smaller number of contingent verbal responses than parents of HRA- and LRC infants at 12, 18, and 24 months. However, when proportions of contingent verbal responses were compared across the groups, there was no group difference, suggesting that the group differences in the sheer number of parents' contingent verbal responses were attributed to the differences in the number of chances that parents had to respond to infants' communicative behaviors. In other words, when infants produced fewer communicative behaviors, parents consequently had fewer opportunities to contingently verbally respond to their infants. In addition to this non-significant group difference in the proportion of contingent verbal responses, parent word tokens and word types were also comparable across the groups at 12, 18, and 24 months. Taking these findings together, parents did not differ in the rate of contingent verbal responses, the total number of words, and the number of different words they used with their children at 12, 18, and 24 months. Our finding that the measures of parent input (except MLU) did not differ based on infants' ASD risk and diagnostic outcomes are consistent with previous findings (Bang & Nadig, 2015; Fusaroli et al., 2019; Leezenbaum, Campbell, Butler, & Iverson, 2014).

Overall, the only difference we found in parent input was a difference in MLU at 18 and 24 months, with parents of high-risk infants using shorter utterances than parents of low-risk infants, which possibly reflects that parents adapt their input based on language abilities of their child and/or intervention approaches they have been exposed to. We did not find any other differences in the input measures such as word tokens, word types, and proportions of contingent verbal responses for parents of HRA+, HRA-, and LRC infants. Hence, infants are exposed to similarly rich linguistic input environment regardless of their ASD risk status and diagnostic outcomes.

After we examined whether parent input differed for groups, we investigated the role of input as a predictor of children's language development. Parent MLU at 18 months was significantly positively associated with children's language skills at six months later, controlling for parent education, children's earlier language skills, and ASD risk. Thus, parents who used longer utterances with their children at 18 months had children with stronger language skills at 24 months, compared to those who used shorter utterances. Moreover, the finding that the relation between parent MLU and children's subsequent language skills did not differ between high- and low-risk groups, as indicated by the lack of the interaction effect, suggests that parents' grammatical input, as measured by MLU, seems to play a similar role in language learning for high- and low-risk infants. Our finding adds to a growing number of studies that documented a positive predictive relation between parents' MLU and later language outcomes in children with ASD and typically developing children (Bang & Nadig, 2015; Fusaroli et al., 2019; Sandbank &

Yoder, 2016) with a sample of younger ASD high-risk children. Taken together, the emerging body of the literature provides suggestive evidence that longer parental utterances may provide children with more linguistic cues that children can use to acquire language rules and subsequently develop stronger language skills (Sandbank & Yoder, 2016; Venker et al., 2015).

By implication, it may be helpful for parents to use long, grammatically complete utterances to promote positive language outcomes of children (Rowe, Levine, Fisher, & Goldin-Meadow, 2009; Sandbank & Yoder, 2016; Venker et al., 2015). Considering that high-risk infants have an elevated risk for language delays and deficits (Drumm & Brian, 2013), providing grammatically rich input may especially be helpful in lessening such risk and enhancing the early language learning environment for high-risk infants. Regarding intervention practices, our findings did not find support for some approaches that promote use of simplified input or telegraphic speech with children with ASD. While more research is needed to understand *for whom* long utterances benefit the most (e.g., what are the language and/or cognitive abilities of children for whom parent MLU is beneficial) and *how* (i.e., underlying mechanisms that facilitate language learning in high-risk children), our findings point to the importance of grammatically rich input in supporting language development of high-risk infants, as it does for other clinical populations (see Rowe et al., 2009 for early brain injury; see Sandbank & Yoder, 2016 and van Kleeck et al., 2010 for reviews on other developmental disabilities). Relatedly, examining the role of grammatical (vs. telegraphic) input in language development of children with or at risk for ASD will be an important avenue for future intervention research.

Thus far, we found that the differences in parent MLU were associated with differences in subsequent language outcomes of high- and low-risk infants alike. But did child language skills predict parents' language production in a reciprocal fashion? The answer seems to be positive based on the findings in this study. Specifically, we found that children's language skills at 18 months were significantly positively associated with parental MLU at 24 months, controlling for parent education and earlier child language skills, in high-risk dyads, but not in low-risk dyads. In other words, the relation between children's language skills and parents' subsequent MLU differed between high- and low-risk groups. Specifically, in high-risk infants, the higher the language skills at 18 months, the longer the parent MLU at the subsequent visit; however, in low-risk infants, there was no relation between children's language skills and parents' later MLU. These results suggest that parents of high-risk infants may be more sensitive to their infants' earlier language abilities as they adapt their own grammatical input. In contrast, parents of low-risk infants may not perceive a need to adjust their length of utterances to their infant's earlier ability, as they may be less concerned about the development of their infants (Talbott et al., 2015). This finding is consistent with previous findings that suggested that children may contribute to their own language learning by affecting the language of their parents (Fusaroli et al., 2019; Huttenlocher et al., 2010; Warlaumont et al., 2014; Wu & Gros-Louis, 2014). Furthermore, our findings provide more evidence to support a transactional model of development (Sameroff, 2009) in that there are bidirectional influences between children and parents that mutually promote language development.

Conclusions

Overall, the findings described here depict a comprehensive picture of parent input to high- and low-risk infants across the first three years of life and demonstrate that parents and high-risk infants collectively cultivate the interactional language environment. These findings contribute to a growing body of the literature that examine environmental factors that relate to language development of children with ASD. A better understanding of risk and protective factors that shape language learning in ASD – the genes, brains, behaviors, environment, and interactions among these factors – will help facilitate timely identification of children with potential language delays and develop effective interventions that can help all children reach their full potential.

GENERAL CONCLUSIONS

Language ability is a robust predictor of positive long-term outcomes of children with typical and atypical development, including ASD (Durand et al., 2013; Howlin et al., 2004). Finding reliable predictors of early language skills can be useful in maximizing the potential of all children. The present dissertation contributes three studies that identify fine motor skills, gestures, and parent input as early behavioral and environmental factors that predate and predict later language skills of ASD high- and low-risk infants. Given the right timing and opportunities, atypical communicative and language trajectories of high-risk infants could be altered in early childhood and lead to optimal language and long-term outcomes of children. In this chapter, I discuss implications of the main findings and limitations from this dissertation.

Implications

Findings from this dissertation show that (1) developmental trajectories of fine motor skills predict subsequent expressive language skills; (2) early gesture is associated with later receptive language and ASD outcomes; and (3) parent input, particularly MLU, predicts later language skills and vice versa in the ASD high-risk context. Taken together, these findings suggest that not only child-based behaviors, but also environmental factors contribute to early language learning of high-risk infants. By implication, promoting early fine motor skills, gesture use, and reciprocity in parent-infant dyads may facilitate language development of high-risk infants, who are at elevated risk for future language deficits and delays. A recent gesture intervention that provided parents with a 5-minute video, emphasizing the importance of pointing, found increases in use of pointing gestures in both parents and their typically developing toddlers (Rowe & Leech, 2018). Given the promising results of a brief intervention program, future research could conduct a similar intervention study with ASD high-risk infants.

If a brief training program were found to be effective in the high-risk population, it could lead to efficacious and cost-effective intervention practices, capable of reaching wide dissemination. Importantly, while many ASD interventions focus on enhancing parent-child interactions, it has not been established what the most effective targets – what researchers call 'active ingredients' – of interventions are (Zwaigenbaum et al., 2015). Thus, future research should evaluate the effects of individual components of existing interventions to determine which component(s) may be most effective in promoting optimal language development in children. Given the increasing number of intervention studies in the ASD field over the past several years (French & Kennedy, 2018), a meta-analysis, for example, may be particularly useful in integrating and evaluating the findings from intervention studies. Such approach could lead to the development of more targeted and cost-effective interventions and be successful in reaching more families, especially those who have limited resources to fully participate in currently available intensive interventions.

Limitations

Findings of this dissertation should be interpreted in light of several limitations. First, although each of the three studies examined the contribution of one specific factor (i.e., fine motor skills, gestures, and parent input) to language outcomes, the *interplay* between these factors was not examined; however, a combination of multiple factors likely shapes language development of children. Thus, future research should examine how different factors may relate to each other and uniquely and/or simultaneously affect language learning in high-risk infants. Relatedly, it would be important to investigate more genetic, neurophysiological, behavioral, and environmental factors that relate to language development of high-risk infants, beyond the ones studied in this dissertation. Identification of multiple risk factors for language impairment will help enhance the predictive value for early detection of infants who are vulnerable to future language difficulties. For example, Chawarska et al. (2014) found that the combination of multiple behavioral features such as gestures, eye contact, and pretend play allowed the prediction of ASD with higher accuracy at 83%, compared to using one behavioral feature alone. A similar cumulative risk approach might also be helpful in prediction of language outcomes of high-risk infants.

Next, our infants in high- and low-risk groups had language scores in the typical range (i.e., above or below one standard deviation of the mean), suggesting that our sample is not likely to be representative of the larger ASD high- and low-risk populations. Relatedly, our sample was skewed with respect to the levels of parent education and household income. Therefore, the findings from this dissertation clearly merit replication with more representative and more diverse samples. If these results were replicated in larger, more diverse samples from multi-site autism research networks such as the Baby Siblings Research Consortium and Infant Brain Imaging Study (whose samples would be more representative of the population), they would have significant implications for mitigating or preventing future language difficulties in high-risk infants.

Summary

In sum, this dissertation presents an investigation of the early behavioral and environmental factors that predate and predict language development in infants at high and low risk for ASD and expands on prior work by using both risk for and diagnosis of ASD to classify infants and integrating data from multiple time points. Also, this dissertation focuses on a prediction of later language skills based on information from as early as infancy, which could allow earlier detection of and interventions for those at risk for language impairment.

Findings show that (1) infants diagnosed with ASD show slower developmental trajectories of fine motor skills than typically developing peers, and these differences in early fine motor skills are associated with subsequent language skills; (2) early gesture is related to later language skills and diagnostic outcomes; and (3) parents' grammatical input is associated with subsequent child language skills and vice versa. These findings have implications for facilitating early identification of infants who need language interventions and informing the development of effective interventions that can improve language and long-term outcomes of children.

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Appendix A

Equation for the Final HLM Model in Study 1

Level 1:

$$Y_{ti} = \pi_{0i} + \pi_{1i}(age_{ti} - 6) + \pi_{2i}(age_{ti} - 6)^2 + e_{ti}, \qquad e_{ti} \sim N(0, \sigma_t^2)$$

Level 2:

$$\pi_{0i} = \gamma_{00} + \gamma_{01}(group_i) + u_{0i}$$

$$\pi_{1i} = \gamma_{10} + \gamma_{11}(group_i) + u_{1i}$$

$$\pi_{2i} = \gamma_{20} + u_{2i}$$

$$u_i \overset{iid}{\sim} N(0, \square^2)$$

In the Level 1 equation, the growth parameter π_{0i} represents the predicted level of fine motor skills of child *I* at 6 months. The parameter π_{1i} represents the predicted linear rate of fine motor growth for child *i.* The parameter π_{2i} represents the non-linear acceleration/deceleration in fine motor growth for each child over time. As is standard with these types of models, we assume an error structure where each e_{ti} is normally distributed with mean of zero and variance σ_t^2. In the Level 2 equation, π_{0i}, π_{1i}, and π_{2i} represent the growth parameters from the Level 1 model. γ_{p0} , $\gamma_{p1}$and γ_{p2} are linear regression coefficients. The coefficient on the term *group* is of main interest to the study. Finally, u_{0i}, u_{1i}, and u_{2i} represent random effects, each with a mean of 0. The set of three random effects for child *i* are assumed multivariate normally distributed with full covariance matrix, T, dimensioned a 3x3 matrix.

$$T = \begin{bmatrix} \tau_{00} & & \\ \tau_{10} & \tau_{11} & \\ \tau_{20} & \tau_{21} & \tau_{22} \end{bmatrix} = \begin{bmatrix} Var(\pi_{0i}) & & \\ Cov(\pi_{1i}, \pi_{0i}) & Var(\pi_{1i}) & \\ Cov(\pi_{2i}, \pi_{0i}) & Cov(\pi_{2i}, \pi_{1i}) & Var(\pi_{2i}) \end{bmatrix}$$

Appendix B

Equation for the Linear Model Predicting 36-Month Expressive Language in Study 1

Similar to the methodological approach used by Rowe, Raudenbush, and Goldin-Meadow (2012), we assumed a linear prediction model for later expressive language as:

$$E(W_i|\pi_{0i}, \pi_{1i}, \pi_{2i}) = \alpha + \gamma_0\pi_{0i} + \gamma_1\pi_{1i} + \gamma_2\pi_{2i} + y_3X_i$$

- W_i represents expressive language skills at 36 months
- γ_0, γ_1 and γ_2 tells us how child i's predicted fine motor skills (status, velocity, and acceleration) at age 6 months, that is, how π_{0i}, π_{1i}, and π_{2i}, contributes to W_i, controlling for background covariate X_i (i.e., MSEL Visual Reception scores, sex, and SES).

The equation above represents our hypothesis that a child's status, velocity and acceleration in fine motor skills at age 6 months help us predict 36-month expressive language, W_i, controlling for nonverbal cognition, sex, and SES. Since we cannot directly observe $\pi_{0i}, \pi_{1i,}$and π_{2i}, we estimated these unknowns using the Empirical Bayes' predictions from the models to determine how expressive language changes as a function of these estimates.

Appendix C

Equations for Calculating the Estimated Probabilities of ASD Diagnosis in Study 2

Below we have written out the prediction equation, which comes directly from Model 4 in Table 2.9:

$$\widehat{ASD} = \frac{1}{1+e^{-(4.41+(-0.17)(gesture)+0.57(word\ types)+(-1.78)(sex)+(-0.57)(caregiver\ education)}}$$

Below we describe the prototypical values we selected for illustrative purposes:

- Gesture: The 10th percentile corresponds to 2.3 gestures, and the 90th percentile corresponds to 21.05 gestures
- Word types: We chose to hold word types constant at the sample mean of 1.05
- Sex: Infant sex was dummy coded such that male = 0 and female = 1. We decided to calculate the probabilities for male infants (sex = 0)
- Caregiver education: We chose to hold education constant at the sample mean of 5.24

Finally, we have written out the regression equations, with prototypical values substituted in:

- For a male infant whose gesture was at the <u>10th percentile</u> and had mean word types and caregiver education:
    - $$\widehat{ASD} = \frac{1}{1+e^{-(4.41+(-0.17)(2.3)+0.57(1.05)+(-1.78)(0)+(-0.57)(5.24)}} = 83.6\%$$
- For a male infant whose gesture was at the <u>90th percentile</u> and had mean word types and caregiver education:

$$\widehat{ASD} = \frac{1}{1+e^{-(4.41+(-0.17)(21.05)+0.57(1.05)+(-1.78)(0)+(-0.57)(5.24)}} = 17.4\%$$

Appendix D

Coding Flowchart and Examples in Study 3