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Language Development in Emerging Autism: Neural and Behavioral Mechanisms of Risk and Resilience

Author

Cohenour, Torrey Lynn

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A dissertation submitted in partial satisfaction

of the requirements for the degree Doctor of Philosophy

in Education

by

Torrey Lynn Cohenour

2024

ABSTRACT OF THE DISSERTATION

Language Development in Emerging Autism:
Neural and Behavioral Mechanisms of Risk and Resilience

by

Torrey Lynn Cohenour
Doctor of Philosophy in Education
University of California, Los Angeles, 2024
Professor Connie L. Kasari, Chair

Autism spectrum disorder (autism) is a heterogeneous, highly heritable neurodevelopmental condition. Language delays are highly prevalent among children with autism or with an elevated likelihood of autism, and delays in spoken language development are often the earliest concerns reported by parents of autistic children. However, there is remarkable heterogeneity in language skills and trajectories among autistic children. There is thus intense interest in identifying early markers that may shed light on language variability in autism. This dissertation sought to fill these gaps by studying individual variability in receptive and expressive language abilities, cross-sectionally and longitudinally, among community-referred 12- to 23-month-olds with autism symptoms. The studies reported here utilized a multimodal approach to identify behavioral and neural mechanisms associated with variability in language abilities in emerging autism.

Study 1 examined receptive-expressive language phenotypes (i.e., the extent to which receptive and expressive language abilities were of a similar developmental level). Nearly half of children exhibited an atypical “expressive advantage” language profile characterized by stronger expressive language skills than receptive language skills. Contrary to hypotheses, there was no evidence for significant concurrent associations between receptive-expressive language phenotypes and proposed demographic, cognitive, social communication, and behavioral predictors. However, receptive-expressive language phenotype at T1 did significantly predict rate of expressive language growth: children with a greater expressive language advantage (i.e., a greater delay in receptive language relative to their own expressive language level) exhibited significantly slower expressive language growth over 12 months than children with a receptive language level more similar to or exceeding their own expressive language level at T1.

Leveraging task-free electroencephalography (EEG) data acquired at T1, Study 2 examined EEG correlates of concurrent receptive-expressive language phenotypes and individual differences in receptive and expressive language growth. Data-driven analyses revealed significant, positive associations between spontaneous theta (3-6 Hz) power and receptive-expressive phenotypes and significant associations between spontaneous alpha power (6-9 Hz) and rate of both receptive language and expressive language growth.

These findings suggest that early receptive-expressive language profiles are a meaningful prognostic marker of language delay, and EEG-based metrics may be sensitive to individual differences in neurocognitive mechanisms that shape language growth.

The dissertation of Torrey Lynn Cohenour is approved.

Jennie Katharine Grammer

Sandra H. Graham

Helen Tager-Flusberg

Connie L. Kasari, Committee Chair

University of California, Los Angeles

2024

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VITA

Academic Degrees

2018 M.A. in Education (Human Development and Psychology)
University of California, Los Angeles
Los Angeles, CA

2012 B.A. in Psychology
Emory University
Atlanta, GA

Academic Positions

2018 – 2023 Graduate Student Researcher
Semel Institute for Neuroscience and Human Behavior
University of California, Los Angeles
Los Angeles, CA

Fall 2020 Teaching Assistant
Department of Education
University of California, Los Angeles
Los Angeles, CA

2016 – 2018 Research Specialist
Marcus Autism Center
Emory University School of Medicine
Atlanta, GA

Awards and Scholarships

2022 – 2023 Dr. Ursula Mandel Scholarship Award (UCLA)
2021 Graduate Summer Research Mentorship Fellowship (UCLA)
2021 International Society for Autism Research Travel Award
2018 – 2023 Wasserman Dean's Scholar Award (UCLA)

Publications

Cohenour, T., Dickinson, A., Jeste, S.S., Gulsrud, A. & Kasari, C. (*under review*). Patterns of spontaneous neural activity associated with social communication abilities in infants and toddlers showing signs of autism.

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Peer-Reviewed Presentations

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Cohenour, T., Gulsrud, A., Kasari, C. (2021, May 3 – 5). E*ffects of mechanism of genetic transmission of autism on clinical characteristics of infants and toddlers with emerging autism symptoms*. International Society for Autism Research Annual Meeting (*virtual*).

Cohenour, T., Gulsrud, A., Kasari, C. (2021, April 5 – 8). *Familial autism risk and the emerging autism phenotype: A comparison of toddlers from simplex and multiplex families.* Gatlinburg Conference on Research and Theory in Intellectual and Developmental Disabilities (*virtual*).

Cohenour, T., Libster, N., Gulsrud, A. & Kasari, C. (2020, May). *Spontaneous imitation and the emerging autism phenotype in at-risk infants.* International Society for Autism Research Annual Meeting (*cancelled*).

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Cohenour, T., Gillespie, S., Jones, W., Shultz, S., (2018, June 30 – July 3). *Smiling in newborns: A longitudinal study from birth to 4 months*. International Conference on Infant Studies, Philadelphia, PA.

Invited Oral Presentations

"*Supporting Children with Intellectual and Developmental Disabilities in Schools*", (2020, November 29). Guest lecture, University of California, Los Angeles.

"*Developing an In-Home Device to Capture Rapid Developmental Change in Infant Behavior*", (2017, February 21). Department of Research Technology Development, Children's Healthcare of Atlanta.

Professional Service

2022 – 2024	Student Representative, Educational Neuroscience Faculty Search Committee University of California, Los Angeles
2022 – present	Associate Faculty Member, Faculty Opinions Psychology

GENERAL INTRODUCTION

Autism spectrum disorder (autism) is an early-emerging, highly prevalent neurodevelopmental condition characterized by persistent difficulties in social communication and restricted interests or repetitive behaviors (American Psychiatric Association, 2013; Maenner et al., 2020). Autism diagnosis is considered stable and reliable as early as 18 to 24 months of age (Barbaro & Dissanayake, 2017; Ozonoff et al., 2015), though early behavioral signs of autism are often evident far earlier (e.g., Sacrey et al., 2015; Zwaigenbaum et al., 2021). However, most children with autism in the United States are not diagnosed until after their fourth birthday (Maenner et al., 2023). Evidence suggests that earlier initiation of behavioral intervention is associated with more favorable intervention response and improved child outcomes (Flanagan, Perry, & Freeman, 2012; Granpeesheh, Dixon, Tarbox, Kaplan, & Wilke, 2009; Rogers et al., 2012; Vivanti, Dissanayake, & The Victorian ASELCC Team, 2016), perhaps due to the remarkable neuroplasticity of the birth- to 36-month period (Klin et al., 2020). Thus, developing biomarkers and tools to improve early detection and identification of children with or at risk of autism remains a high priority.

Recent years have seen a surge in research using neuroimaging, electroencephalographic (EEG), and behavioral methodologies to identify “pre-symptomatic” markers of autism; that is, markers that can identify infants who will later receive an autism diagnosis (Grzadzinski et al., 2021). These studies primarily include infants recruited from the first months of life who are known to have a greater chance of receiving an autism diagnosis by virtue of having a sibling with the condition (i.e., infants with an elevated familial likelihood of autism, EL). While these studies have provided key insight into autism pathogenesis, pre-symptomatic markers that can be used to identify individual infants with autism before symptom emergence remain far from a clinical reality (Dawson, Rieder, & Johnson, 2023). It is also unclear whether markers identified among EL infants later diagnosed with autism generalize to infants from the general population, most of whom have no family history of autism. Moreover,

pre-symptomatic identification of autism is complicated by practical and ethical questions, given the current lack of evidence-based interventions designed for young infants who present with no overt signs of delay or appreciable autism features.

A more promising approach with more near-term implications may involve identifying neural and behavioral *prognostic* markers (i.e., markers predictive of later developmental outcomes within a given population) among infants and toddlers already exhibiting early signs of autism. Relative to EL infants, less is known about infants and toddlers showing early signs of autism sampled from the general population, nor about neural and behavioral mechanisms linked with specific social capacities disrupted from very early in autism. Identifying features of functional brain development that contribute to variability in early language skills among young children with autism symptoms, for example, could provide critical insight into neural mechanisms contributing to heterogeneity within the emerging autism phenotype. Addressing this gap in our understanding of the mechanisms that shape social development during the "pre-diagnostic" period in the second year of life (i.e., when markers of autism first become apparent and can be intervened upon with targeted intervention) has the potential to improve access to personalized interventions among infants first showing signs of autism. For instance, identifying prognostic markers using EEG to predict which symptomatic infants are also at the highest risk of language delay could facilitate earlier identification of infants who may benefit from targeted language intervention. Moreover, understanding the behavioral, environmental, and neural mechanisms that shape language development in the context of emerging autism could provide insight into treatment mechanisms or specific targets most likely to deliver the greatest benefit to child language outcomes. Given that language delays are among the earliest concerns expressed by parents of children with autism (Herlihy, Knoch, Vibert, & Fein, 2015; Karp, Ibañez, Warren, & Stone, 2017; McMahon, Malesa, Yoder, & Stone, 2007; Ramsey et al., 2018; Sacrey et al., 2015; Talbott, Nelson, & Tager-Flusberg, 2015), and early language abilities are predictive of a wide range of developmental and functional outcomes (Bal, Kim, Cheong, &

Lord, 2015; Bennett et al., 2008; Gillespie-Lynch et al., 2012; Howlin, Mawhood, & Rutter, 2000; Howlin, Moss, Savage, & Rutter, 2013; Kim, Bal, & Lord, 2018; Szatmari, Bryson, Boyle, Streiner, & Duku, 2003), it is increasingly evident that identifying markers that can shed light on individual differences in language development and predict language outcomes in emerging autism may have real clinical and practical value.

Autism as an Adaptive Alternate Developmental Trajectory

Recent frameworks for understanding functional brain development in the context of emerging social and cognitive competencies stress the dynamic, bidirectional relationships between genes, brain, and experience that together cultivate the optimal state for learning and development. For example, the "neuroconstructivist" framework (e.g., Karmiloff-Smith, 2009) assumes that the developing brain is self-organizing, exquisitely attuned to the learning opportunities offered in the environment, and will direct resources (e.g., attention) to maximize learning. Under the neuroconstructivist framework, *ontogenetic adaption* is the process by which infants adapt to the features of their environment and intrinsic factors (e.g., genetics) endowed from birth (Johnson, 2015). Adaptations necessarily shape experiences in the environment and shape what infants are prepared to learn and what information is most "learnable." Under species-expectant environmental conditions and against a typical genetic background, ontogenetic adaptation allows for the establishment of neural infrastructure needed for the emergence of increasingly complex social and cognitive skills, resulting in a "neurotypical" developmental trajectory and outcome. However, adaptations in response to atypical intrinsic (e.g., genetic anomalies) or environmental conditions (e.g., early deprivation or neglect) may result in disrupted, or alternative, developmental trajectories and outcomes.

Disruptions to typical brain-behavior development seen in autism may be attributable, in part, to underlying genetic factors. For example, there is evidence for overlap between autism-associated genetic variants and genes implicated in prenatal brain development and activity-dependent synaptic function (Ruzzo et al., 2019), suggesting that genetic mechanisms that

confer autism risk may also influence synaptic plasticity and brain development from very early. Indeed, familial genetic risk of autism is associated with altered trajectories of structural (Hazlett et al., 2017; Shen et al., 2017; Wolff et al., 2015; Wolff et al., 2012) and functional brain development in infancy (Dickinson et al., 2021; Dickinson, Varcin, Sahin, Nelson, & Jeste, 2019; Gabard-Durnam et al., 2019; Orekhova et al., 2014). Behavioral and cognitive features of autism may reflect adaptations in response to neuromaturational constraints and cumulative experiences within the environment: for instance, children with autism tend to have stronger local information processing capacity than neurotypical children (Guy, Mottron, Berthiaume, & Bertone, 2019), show heightened sensitivity to subtle physical contingencies that neurotypical children fail to detect (Klin, Lin, Gorrindo, Ramsay, & Jones, 2009), and spend more time exclusively attending to objects during free-play interactions with caregivers (Adamson, Bakeman, Deckner, & Romski, 2009), reflecting an early preference for and growing expertise in non-social aspects of the environment. Thus, atypical neurocognitive development in autism may reflect an *adaptive* response to underlying genetic and environmental influences that ultimately lead children to privilege elements of their environment that are most "learnable".

The ontogenetic adaptation hypothesis suggests that individual differences in brain maturation may also help explain variability in language development in autism. While it is well-established that enriching experiences within the social context (e.g., dyadic social interaction) are critical for the acquisition of skills like language (Kuhl, 2011; Swanson et al., 2019), evidence suggests that intrinsic maturational factors, like brain development, constrain infants' ability to learn from these social encounters. The impact of maturational constraints on development has been demonstrated in studies of healthy preterm infants, who have additional postnatal experience relative to full-term infants of the same postconceptional age. Studies suggest the extra experience afforded to preterm infants provides little benefit, if not detriment, in the development of more complex social and cognitive milestones, such as speech and language acquisition (Bosseler et al., 2013; Jansson-Verkasalo et al., 2010; Peña, Pittaluga, &

Mehler, 2010; Peña, Werker, & Dehaene-Lambertz, 2012). Although postconceptional age-matched preterm infants have weeks more postnatal experience than full-term infants, studies find little evidence that preterm infants achieve language milestones earlier. Furthermore, many preterm-born children tend to lag behind full-term peers in cognitive (Kerr-Wilson, Mackay, Smith, & Pell, 2012), language (Jansson-Verkasalo et al., 2010; van Noort-van der Spek, Franken, & Weisglas-Kuperus, 2012), and social development (Crnic, Ragozin, Greenberg, Robinson, & Basham, 1983) – an effect that is not fully explained by perinatal neurological insult or injury. One possible explanation is a "mismatch" between preterm infants' biological maturational status and environmental demands – that is, the brain is not yet equipped to learn from experiences or exposures in the postnatal environment.

This framework points to the potential utility of identifying neural and behavioral metrics of "readiness" for language acquisition (e.g., metrics of functional brain maturity and pre-linguistic communication skills) in autism, which could, in turn, provide meaningful prognostic insight. Such findings may provide an initial jumping-off point for rigorous testing of candidate prognostic and predictive biomarkers (FDA-NIH Biomarker Working Group, 2020) that can facilitate clinical decision-making, including individualizing intervention approaches among infants/toddlers developing autism identified as being at the highest risk of language delay.

Overview of Studies

Study 1: Receptive-Expressive Language Phenotypes and Language Growth in Emerging Autism

Children diagnosed with autism are more likely than children with neurotypical development or those with non-autism developmental differences to present with a language profile characterized by stronger expressive language abilities relative to their receptive language level (Chawarska, MacAri, & Shic, 2012; Davidson & Ellis Weismer, 2017; Ellis Weismer et al., 2010; Luyster et al., 2008; McDaniel, Yoder, Woynaroski, & Watson, 2018; Swanson et al., 2017). Whether receptive-expressive phenotypes (the extent to which receptive

and expressive language skills are of a similar developmental level) are associated with co-occurring cognitive or social communication strengths or weaknesses among infants and toddlers exhibiting early signs of autism has yet to be established. Crucially, the causes and longer-term consequences of early atypical receptive-expressive profiles have yet to be explored systematically among community-referred, racially and ethnically diverse infants and toddlers at "high clinical risk" of autism. To address these gaps, Study 1 aimed to characterize early receptive-expressive phenotypes (capturing *within-individual* variability in language abilities) among 12- to 23-month-old infants and toddlers with autism symptoms. Study 1 further aimed to test whether receptive-expressive language phenotypes were linked with concurrent behavioral characteristics and predictive of receptive and expressive language growth over 12 months.

Study 2: Neural Mechanisms Associated with Language Heterogeneity in Emerging Autism

Building on behavioral findings from Study 1, Study 2 tested whether electroencephalography (EEG) measures of endogenous oscillatory activity in the developing brain predict individual differences in language development. Using a data-driven analytical approach, Study 2 tested whether spectral power in two empirically and theoretically motivated frequency bands, theta (3-6 Hz) and alpha (6-9 Hz), is predictive of concurrent receptive-expressive language phenotypes and rate of receptive and expressive language growth among infants and toddlers with autism symptoms.

By investigating behavioral and neural mechanisms that shape language growth in the second year among children developing autism, these findings can set the stage for future research integrating neural and behavioral data to develop prognostic and predictive biomarkers to facilitate early identification, and personalized, adaptive interventions tailored to infants' brain-behavioral phenotypic characteristics.

STUDY 1

Receptive-Expressive Language Phenotypes in Emerging Autism

Abstract

Evidence suggests a significant proportion of children diagnosed with autism spectrum disorder (autism) exhibit expressive language skills that are more developmentally advanced than would be expected relative to their receptive language skill level. Whether atypical receptive-expressive language profiles are present among infants and toddlers showing early signs of autism remains unclear. Crucially, the causes and developmental consequences of early disruptions to typical receptive-expressive language development in autism are not well understood. The objective of Study 1 was to characterize variation in language abilities among 70 infants and toddlers with early signs of autism by examining receptive-expressive language profiles (i.e., discrepancies between receptive and expressive language levels) and trajectories of language growth.

While there was marked heterogeneity in the magnitude of receptive-expressive language discrepancies, the proportion of children who presented with "atypical" language profiles (i.e., an expressive advantage [41.4%] or a receptive advantage [34.3%]) far exceeded the proportion of children with balanced receptive and expressive language levels (24%). Contrary to hypotheses, there were no significant associations between receptive-expressive language phenotype (measured dimensionally or categorically) and concurrent chronological age, cognitive functioning, autism symptom levels, or joint attention skills. Hierarchical linear modeling revealed significant associations between initial receptive-expressive profiles and trajectories of expressive language growth, such that children with an expressive language “advantage” (i.e., language production skills that exceed comprehension skills, as measured on a standardized developmental assessment) showed significantly slower expressive language growth over 12 months. Together, these findings suggest that relative weakness in language comprehension may stall growth in language production among children with autism, consistent

with many models of neurotypical language acquisition. Early receptive-expressive profiles may serve as prognostic markers of expressive language growth in infants and toddlers developing autism.

Receptive-Expressive Language Phenotypes in Emerging Autism

Acquisition of spoken language early in development is a key predictor of longer-term developmental outcomes among children with autism, including academic achievement, social competence, and quality of life decades later in adulthood (Anderson, Liang, & Lord, 2014; Bal, Kim, Cheong, & Lord, 2015; Gillespie-Lynch et al., 2012; Kim, Bal, & Lord, 2018). Language abilities are highly heterogeneous among children with autism but also appear highly malleable, particularly before age six (Pickles, Anderson, & Lord, 2014). For this reason, early interventions for infants/toddlers with autism or autism features often focus on bolstering communication and language skills (Schreibman et al., 2015). Despite the importance of language skills, there is still a lack of clarity as to which clinical, behavioral, environmental, or biological factors are most predictive of language abilities and language growth, and which variables may predict language improvement in response to early interventions. In addition to experiencing a higher rate of language delays, children with autism are also more likely to present with atypical receptive-expressive language phenotypes characterized by atypically strong expressive language skills relative to receptive language skill level. The mechanisms that give rise to atypical receptive-expressive phenotypes in autism and the longer-term consequences of atypical language profiles very early in development remain unclear. Despite the importance of early language skills in neurotypical development and autism, we know very little about the intrinsic or environmental mechanisms that may explain the remarkable variability in language outcomes and language trajectories among community-referred infants and toddlers exhibiting early autism symptoms.

Language Development in Autism

Prospective longitudinal studies of infants with an older autistic sibling (who thus have an elevated likelihood of developing autism themselves; EL) have provided unprecedented insight into autism emergence, given that approximately 15-20% of these infants will go on to develop autism themselves by toddlerhood (Ozonoff et al., 2011). These studies have provided

opportunities to identify the earliest markers of autism risk and insight into how early variability in cognitive and behavioral development within the first two years of life maps onto later outcomes.

Earlier theories of autism (e.g., Fein et al., 1986) hypothesized that social and language difficulties associated with autism arose from abnormalities or the outright absence of endogenous mechanisms of socially adaptive behavior normally intact at birth (e.g., preference for faces exhibiting directed gaze versus averted gaze, preference for infant-directed speech versus adult-directed speech; Batki et al., 2000; Farroni et al., 2002; Johnson, 2005; Pegg et al., 1992). Given that these capacities, coupled with early experiences, facilitate the development of children's understanding of others' communicative cues and their ability to initiate and maintain contingent social interactions, it was hypothesized that early disruptions to these mechanisms resulted in the observed social communication features of autism first evident around 12 months of age. However, evidence from prospective studies of EL infants later diagnosed with autism suggests that many social adaptive mechanisms are, indeed, intact in the first year of life, including attention to others' eyes (Elsabbagh et al., 2012; Jones & Klin, 2013), gaze-following (a precursor to joint attention; Bedford et al., 2012; Thorup et al., 2018), and perceptual narrowing to non-native phonemes (Seery, Vogel-Farley, Tager-Flusberg, & Nelson, 2013). These findings are remarkable given that atypical eye contact, joint attention difficulties, and spoken language delays or deficits in toddlerhood are considered cardinal features of the condition.

There is also evidence that EL infants later diagnosed with autism are similar to neurotypical infants in early communication skills prior to the 9 to 12-month window, including in the use of directed gaze and social smiles during interactions with caregivers (e.g., Filliter et al., 2015; Gangi et al., 2021; Ozonoff et al., 2010; Rozga et al., 2011), and vocalizations (Northrup & Iverson, 2015; Paul, Fuerst, Ramsay, Chawarska, & Klin, 2011; Plate et al., 2021; Talbott, Nelson, & Tager-Flusberg, 2015). Studies using standardized developmental assessments

(e.g., Mullen Scales of Early Learning; Mullen, 1996) similarly find little evidence for differences before 12 months in receptive and expressive communication between infants with or without autism, with differences only emerging at or shortly after 12 months of age (Bussu et al., 2018; Estes et al., 2015; Iverson et al., 2018; Landa, Gross, Stuart, & Faherty, 2013; Landa, Holman, & Garrett-Mayer, 2007; Levin, Varcin, O'Leary, Tager-Flusberg, & Nelson, 2017; Ozonoff et al., 2010, 2014; Paterson et al., 2019; Swanson, 2020; Swanson et al., 2017).

By 12 months of age, infants later diagnosed with autism begin to diverge substantially from non-autistic peers in language acquisition and early language milestones, and language differences between children with or without later autism grow more dramatic across the second and third years of life. While most autistic infants and toddlers show gains in language skills over time, EL infants later diagnosed with autism show significantly slower language growth than non-autistic EL infants and infants with no family history of autism, including those with non-autism language delays (e.g., Iverson et al., 2018), resulting in a growing disparity between groups in receptive and expressive abilities over the second year (Anderson et al., 2007; Bussu et al., 2018; Franchini et al., 2018; Ozonoff et al., 2010). Marked delays are also evident in the acquisition of early language milestones, including production of first words (Harrop et al., 2021; Howlin, 2003; Kover, Edmunds, & Ellis Weismer, 2016; Mayo, Chlebowski, Fein, & Eigsti, 2013; Ohashi et al., 2012; Pickles et al., 2022) and first multi-word phrases (Harrop et al., 2021; Howlin, 2003; Kover et al., 2016; Ohashi et al., 2012; Pickles et al., 2022). Perhaps as striking as the magnitude of such delays is the vast variability within groups of children with autism in age at skill acquisition: for instance, Mayo et al. (2013) report that the average age at first words in their sample of 98 autistic toddlers was approximately 19.5 months. However, estimates ranged from as low as seven months to as high as 37 months within their sample.

Receptive-Expressive Phenotypes in Autism

Though neural and behavioral substrates of language comprehension and production emerge simultaneously over the first year of life, language comprehension skills (i.e., receptive

language skill) mature earlier than production skills (i.e., expressive language) in neurotypical and non-autistic developmentally-delayed children (Ellis Weismer et al. 2010; Seol et al., 2014), such that the number of words understood almost always exceeds the number of words produced (Bornstein & Hendricks, 2012). In contrast, the "comprehension precedes production" adage does not appear to be universally true among children with autism.

Evidence suggests that a large proportion of children with autism have stronger expressive language skills than would be expected from their receptive language abilities. However, there are inconsistencies regarding how common receptive-expressive language skill discrepancies are and whether they are linked to other demographic or behavioral characteristics, perhaps due to differences in measuring language abilities and in sample chronological ages across studies.

Generally, evidence for stronger expressive language skills relative to receptive language skills is more consistent in studies of toddler- and preschool-aged children (Chawarska, MacAri, & Shic, 2012; Davidson & Ellis Weismer, 2017; Ellis Weismer et al., 2010; Luyster et al., 2008; McDaniel, Yoder, Woynaroski, & Watson, 2018; Swanson et al., 2017), and studies using clinician-administered measures of language abilities or caregiver-report measures of vocabulary (Charman et al., 2003; Davidson & Ellis Weismer, 2017; Ellis Weismer et al., 2010; Hudry et al., 2010; Luyster et al., 2008; Maljaars, Noens, Scholte, & Berckelaer-Onnes, 2012; McDaniel et al., 2018; Nevill et al., 2019; Reinhartsen et al., 2019; Seol et al., 2014; Swanson et al., 2017; Volden et al., 2011). In contrast, there is little evidence to suggest infants later diagnosed with autism show atypical receptive-expressive profiles (that is, a discrepancy between receptive and expressive skill levels) prior to 12 months, and results are inconsistent in studies of school-age children with autism (Arutiunian et al., 2021; Kjelgaard & Tager-Flusberg, 2001; Kover, McDuffie, Hagerman, & Abbeduto, 2013; Maljaars et al., 2012). Further, several studies report cross-sectional or longitudinal evidence to suggest the prevalence of expressive-dominant profiles (i.e., language profiles characterized by stronger

expressive than receptive skills) declines with increasing chronological age across toddlerhood and the preschool years (Davidson & Ellis Weismer, 2017; Reinhartsen et al., 2019; Seol et al., 2014), and autistic children with stronger nonverbal cognitive ability tend to have receptive-expressive language profiles more similar to those exhibited by neurotypical children (Kover et al., 2013; Nevill et al., 2019; Reinhartsen et al., 2019; Volden et al., 2011; though see Hudry et al., 2010). Moreover, a large longitudinal study of children referred for possible autism at 24 months identified distinct trajectories of language development across 2 to 19 years of age, finding that children who showed expressive language gains also tended to make gains in receptive language, but expressive gains tended to exceed receptive (Pickles et al., 2014).

Quantifying Receptive-Expressive Language Discrepancies and Profiles

One challenge in characterizing receptive-expressive language profiles among children with autism symptoms is identifying the best approach for quantifying differences between receptive and expressive language levels and translating quantitative differences into discrete categories (e.g., typical or atypical profiles; receptive- or expressive-dominant profiles). This is particularly challenging given the lack of guidance for drawing such comparisons across language domains and what constitutes a clinically meaningful discrepancy. For example, the manual for the Mullen Scales of Early Learning (Mullen, 1996), which is one of the most frequently used measures of cognitive and language ability in studies of infant/toddler-age children with autism, does not provide explicit guidance for comparing scores across domains, nor is there established guidelines for what constitutes a statistically- or clinically-significant difference in between receptive and expressive language scale scores.

Studies using the Mullen or other clinician-administered norm-referenced assessments to examine receptive-expressive profiles have primarily used three approaches to quantify receptive-expressive discrepancy: (1) comparing domain scores statistically via hypothesis testing; (2) computing receptive-expressive difference scores from age equivalent (AE) scores (Hudry et al., 2014; Swanson et al., 2017), raw scores (Prescott & Ellis Weismer, 2022),

standard scores (Davidson & Ellis Weismer, 2017), or DQ scores (Chawarska et al., 2012); or (3) computing receptive-expressive ratio scores (i.e., receptive language AE divided by expressive language AE score; Reinhartsen et al., 2019; Seol et al., 2014). While it is generally agreed upon that a language profile characterized by stronger expressive language skills relative to receptive language skills is "atypical," what constitutes a sufficiently large discrepancy to be considered atypical varies across studies. For instance, using Mullen AE scores, Swanson et al. (2017) argued that a positive receptive-expressive difference score (i.e., receptive scores higher than expressive scores) reflects a more "normative" profile than a difference score of zero, citing evidence that neurotypical infant and toddler-aged samples show higher mean receptive language than expressive language T-scores (Longard et al., 2017; Mitchell et al., 2006; Plate et al., 2021; Toth et al., 2007; Yankowitz et al., 2022), raw scores (Ozonoff et al., 2010) and age equivalent scores (Reinhartsen et al., 2019). However, other large studies of prospectively-followed EL infant siblings (e.g., Hatch et al., 2021) and community-referred samples (e.g., Pierce et al., 2023) report similar mean receptive and expressive language T-scores within neurotypical groups (suggesting a difference score of '0' is still "normative").

Criteria for translating continuous metrics of receptive-expressive language abilities into categorical language profiles are also variable. In a large multisite case-control study of 30- to 68-month-old children with autism (n = 695, mean age = 59.3 months), non-autism developmental delay (n = 987, mean age = 59.5 months), and children sampled from the general population (n = 889, mean age = 59.4 months), Reinhartsen et al. (2019) calculated receptive-expressive ratio scores (receptive language AE divided by expressive language AE). Using the distribution of ratio scores in the general population "control" group, they then identified cut-off ratio scores corresponding with the mean (1.04) ± one standard deviation (0.13). Those within one standard deviation of the mean were classified as having balanced or "non-dominant" receptive-expressive language profiles, whereas those one standard deviation above or below the mean were classified as having "receptive dominant" and "expressive

dominant" profiles, respectively. Among children with autism, 46.6% had a non-dominant profile (relative to 74% of the general population sample), 29.8% had a receptive-dominant profile (relative to 15.6% of the general population sample), and 23.6% had an expressive-dominant profile (relative to 10.8% of the general population sample), largely consistent with evidence for an increased prevalence of atypical language profiles in autism. In a younger sample of children diagnosed with autism (mean age = 35.7 months, range = 20 to 50 months), Seol et al. (2014) similarly computed ratio scores using receptive and expressive AE scores, then classified children into categorical profiles using pre-specified ratio score cut-offs. Children with ratio scores below 0.9 were classified as "expressive dominant" (42.7% of the autistic sample), those with scores above 1.1 were classified as "receptive dominant" (30.1% of the autistic sample), and the remaining children were classified as "non-dominant" (27.2% of the autistic sample). The distribution of participants across the three language profiles differs starkly between the toddler-aged sample described in Seol et al. (2014) and the older, preschool- to early school-aged sample described in Reinhartsen et al. (2019), despite the fact that both groups included children with confirmed autism spectrum disorder diagnoses.

Demographic and Behavioral Correlates of Receptive-Expressive Discrepancies

Inconsistent findings regarding the magnitude of receptive-expressive differences in autism, the prevalence of atypical ("unbalanced") profiles, and whether receptive-expressive profiles are linked with other demographic or behavioral variables may reflect variability across studies in approaches to quantify receptive-expressive discrepancies (notwithstanding differences in chronological and mental ages, ascertainment strategy, and autism genetic risk across samples). The association between early receptive-expressive language profiles and concurrent social communication skills and cognitive functioning among children with autism also remains elusive. While there is some inconsistent evidence for concurrent associations between receptive-expressive language discrepancies in autism and nonverbal cognitive functioning (e.g., Hudry et al., 2010; Nevill et al., 2019; Volden et al., 2011), autism symptom

levels (e.g., Hudry et al., 2010; Reinhartsen et al., 2019), and chronological age (e.g., Davidson & Ellis Weismer, 2017; Seol et al., 2014) the direction of these associations is inconsistent across studies. Moreover, whether receptive-expressive language profiles are associated with social communication skills known to play a crucial role in language acquisition (e.g., joint attention) remains unclear. It should also be noted that no known study to date has attempted to characterize receptive-expressive language profiles among community-referred "pre-diagnostic" infants and toddlers who are showing early behavioral signs of autism. Characterizing emerging language skills in this population during this window of development may help shed light on the early origins of social communication and language heterogeneity in autism and the potential consequences of typical or atypical receptive-expressive language profiles on other facets of social and cognitive functioning.

Behavioral Predictors of Language Development in Autism

Numerous studies of autistic children of varying chronological ages and language levels have sought to identify concurrent and longitudinal links between language skills and behavioral, demographic, and clinical variables. However, there remains little consensus as to which variables are most strongly linked with language outcomes at a given age. Among the most consistent findings, nonverbal cognitive ability is a robust predictor of receptive and expressive language ability among children with autism and EL infant siblings (Anderson et al., 2007; Bedford, Pickles, & Lord, 2016; Brignell et al., 2018; Ellis Weismer & Kover, 2015; Ellis Weismer et al., 2010; Huberty et al., 2023; Hudry et al., 2010; Nevill et al., 2019; Norrelgen et al., 2015; Thurm, Lord, Lee, & Newschaffer, 2007; Thurm, Manwaring, Swineford, & Farmer, 2015), predicting both concurrent language skills (e.g., Ellis Weismer et al., 2010), later outcomes (e.g., D. K. Anderson et al., 2007; though see Charman et al., 2003; Mundy et al., 1990), and growth over development (e.g., Bedford et al., 2016; Huberty et al., 2023). In contrast, associations between language skills and other variables, including autism symptom severity (Bacon, Osuna, Courchesne, & Pierce, 2018; Bopp & Mirenda, 2011; Bopp, Mirenda, &

Zumbo, 2009; Chenausky, Norton, Tager-Flusberg, & Schlaug, 2018; Ellis Weismer & Kover, 2015; Nevill et al., 2019), gross and fine motor skills (Bedford et al., 2016; Choi, Leech, Tager-Flusberg, & Nelson, 2018; Lebarton & Iverson, 2013; Leonard, Bedford, Pickles, Hill, & BASIS Team, 2015; Wickstrom et al., 2021), joint attention (Anderson et al., 2007; Bono, Daley, & Sigman, 2004; Bottema-Beutel, 2016; Charman et al., 2003; Edmunds, Ibañez, Warren, Messinger, & Stone, 2017; Gillespie-Lynch et al., 2015; Malesa et al., 2013; Mundy et al., 1990; Nevill et al., 2019; Smith, Mirenda, & Zaidman-Zait, 2007; Toth et al., 2006; Yoder, Watson, & Lambert, 2015), play skills (Bopp & Mirenda, 2011; Ellis Weismer et al., 2010; Smith et al., 2007; Toth et al., 2006), age at first words (Kenworthy et al., 2012; Kover et al., 2016; Mayo et al., 2013), history of language regression (Norrelgen et al., 2015; Pickles et al., 2022) and hours of intervention (Bono et al., 2004; Stone & Yoder, 2001) are more variable. Thus, there is currently a lack of consensus on the characteristics and early skills most strongly linked with later language outcomes or language growth in the second year of life among children with autism or those with autism features. Moreover, many studies have focused on predicting later outcomes at a fixed timepoint rather than predicting the rate of growth (two related but distinct constructs with differing clinical implications).

In the context of intervention, compelling evidence exists for positive effects of early behavioral interventions on language abilities among children with autism (Fuller & Kaiser, 2020; Sandbank et al., 2020), including naturalistic developmental behavioral interventions (NDBIs) delivered to young children of varying cognitive and language levels in a variety of settings (e.g., Y.-C. Chang et al., 2016; Dawson et al., 2010; Hardan et al., 2015; Kasari et al., 2008, 2012). However, at the individual level, as many as 50% of autistic children show little improvement in spoken language even when receiving early intensive behavioral intervention coupled with speech/language therapy (e.g., Frazier et al., 2021) or high-quality, targeted evidence-based intervention (e.g., Panganiban & Kasari, 2022). Attempts to identify pre-treatment predictors of language gains have yet to reveal a consistent set of clinical, behavioral,

or demographic variables that predict language growth at the aggregate group or individual level. Some studies report that younger chronological age at intervention start is associated with greater cognitive or language gains in response to intervention (e.g., Frazier et al., 2021; Kasari et al., 2012; Lombardo et al., 2021), while others fail to find an effect of age at initiation of intervention (Contaldo, Colombi, Pierotti, Masoni, & Muratori, 2020; Green et al., 2010; Tiura, Kim, Detmers, & Baldi, 2017). Similarly, evidence is somewhat mixed on whether beginning intervention with stronger language skills is associated with a larger intervention effect on language outcomes. While some naturalistic developmental behavioral intervention (NDBI) studies report greater gains among children with stronger language abilities at baseline (e.g., Kasari et al., 2008), others find no moderating effect of baseline language scores (Green et al., 2010; Hardan et al., 2015) on intervention-induced language gains. Indeed, while a large meta-analysis of the effects of non-pharmacological interventions on language skills of autistic young children found stronger language at baseline (but not intervention style, dosage, chronological age, or symptom severity) was associated with larger treatment effects (Sandbank et al., 2020), a meta-analysis of NDBIs specifically found neither chronological age nor language ability at baseline moderated intervention effects on language ability (Crank et al., 2021). As in studies examining predictors of language development in autism broadly, behavioral variables predictive of language gains in response to NDBIs are also mixed. For instance, some studies find stronger baseline cognitive abilities predict greater growth in response to intervention (e.g., Hardan et al., 2015), while others find no such effects (e.g., Green et al., 2010; Rogers et al., 2021). However, there is consistent evidence that in the context of NDBIs, baseline autism symptom severity does not moderate the effect of intervention on language gains (Green et al., 2010; Rogers et al., 2021).

Associations Between Early Language Profiles and Language Growth

The potential role of early receptive-expressive language profiles in predicting subsequent trajectories of language growth has received less attention. While most neurotypical

models of language development (which posit language comprehension drives language production (e.g., Bornstein & Hendricks, 2012; Goldin-Meadow, Seligman, & Gelman, 1976; though see Bauer, Goldfield, & Reznick, 2002) would suggest that children with a relative receptive language advantage should exhibit greater (or faster) language growth, evidence from both observational and intervention studies suggest this relationship may be altered in autism.

Longitudinal studies examining receptive and expressive vocabulary among young children with and without autism report stronger associations between early expressive vocabulary and later receptive language vocabulary than between early receptive and later expressive vocabulary (Bottema-Beutel et al., 2019; Woynaroski, Yoder, & Watson, 2016). This relationship between receptive and expressive language skills appears to be specific to autism, given evidence that these cross-modal vocabulary associations differ significantly between children diagnosed with autism and language- and mental age-matched neurotypical children (Bottema-Beutel et al., 2019).

Studies examining receptive-expressive (i.e., cross-modal) generalization in the context of language instruction have also provided evidence contrary to what would be suggested by neurotypical language acquisition. For instance, evidence from single-case studies suggests children with autism more readily generalize language initially taught expressively than language initially taught receptively – that is, a higher proportion of children demonstrate successful expressive-to-receptive generalization of word learning than demonstrate successful receptive-to-expressive generalization (Bao, Sweatt, Lechago, & Antal, 2017; Su, Castle, & Camarata, 2019; Wynn & Smith, 2003). Intriguingly, there is some limited evidence that a similar pattern of superior expressive-to-receptive generalization is evident in the context of manual signed language instruction in children with autism (Watters, Wheeler, & Watters, 1981), suggesting that this atypical receptive-expressive association may be rooted in something fundamentally social cognitive rather than an artifact of disruptions to neuromotor systems underpinning speech production, for instance.

Clinically, understanding the association between initial receptive-expressive phenotypes and subsequent trajectories of language growth could provide important insight into potential prognostic markers that could facilitate the early identification of children who may be at greatest risk of poorer language growth, as well as initial insight into mechanisms that may contribute to heterogeneity and plasticity in language growth across the second and third years of life among children with autism.

The Present Study

The objective of Study 1 is to describe within-individual variability in language skills among infants and toddlers showing early signs of autism and test whether individual differences in receptive-expressive language phenotypes are associated with concurrent behavioral characteristics and predictive of language growth.

It was hypothesized the proportion of infants and toddlers who present with marked discrepancies between their receptive and expressive language levels would exceed estimates derived from samples of neurotypical children (e.g., Reinhartsen et al., 2019) and children with non-autism developmental language delays (e.g., Seol et al., 2014). Given evidence from the extant literature that lower nonverbal cognitive ability is associated with atypical receptive-expressive language discrepancies among children with autism (e.g., Volden et al., 2011), it was hypothesized that children who exhibit a larger discrepancy between receptive and expressive language abilities will have poorer nonverbal cognitive functioning. Further, given the reciprocal associations between early social communication skills (e.g., RJA) and receptive language ability (Frost, Pomales-Ramos, & Ingersoll, 2022) and the possibility that stronger receptive language skills allow children to both initiate and maintain dyadic social interactions more readily and glean more from these interactions, one possible hypothesis is that an "atypical" expressive advantage, or a larger receptive-expressive discrepancy overall, would be associated with poorer concurrent social communication skills, and slower language growth over time. Poorer receptive language skills may impede children's ability to learn from their

environment (specifically, linguistic input from their environment) and disrupt or interfere with children's ability to establish and maintain reciprocal social interactions. However, the reverse could also be true: relative deficits in receptive language could arise as a result of disruptions to fundamental social communication skills, such as responsiveness to joint attention, that emerge early in development and support social learning. Though the present study is not designed to address the directionality of the relationship between social communication and language profiles, both of these possibilities would suggest that a more atypical receptive-expressive profile would be associated with poorer concurrent social communication functioning (i.e., poorer verbal cognitive ability overall, poorer performance on response to joint attention [RJA] tasks, and higher levels of autism symptoms), and slower language growth. On the contrary, it is also possible that atypical language profiles may reflect some "compensatory" mechanism in autism (in which case more atypical profiles may be more prominent among children with stronger cognitive skills and those acquiring language at a pace similar to neurotypical children). Study 1 will provide needed insight into these relationships, potentially identifying behavioral markers of both risk for atypical receptive-expressive development as well as markers of resilience (i.e., compensatory mechanisms).

Study 1 Aims

Aim 1a: Quantify receptive-expressive language abilities (i.e., the discrepancy between receptive and expressive skill level) at baseline (T1) using a standardized, clinician-administered developmental assessment, and estimate the prevalence of Receptive Advantage (RA; receptive language > expressive language), Expressive Advantage (EA; expressive language > receptive language), and Balanced (receptive language ≈ expressive language) profiles among infants and toddlers with autism symptoms.

Hypothesis 1a: Infants and toddlers will present with discrepancies in receptive and expressive language skill levels, though the magnitude and direction of these differences will vary markedly

between individuals. The proportion of children with EA profiles will be greater than the proportion of children with RA profiles.

Aim 1b: Test for associations between baseline receptive-expressive language phenotypes and concurrent chronological age, autism symptom level, cognitive functioning, and joint attention skills.

Hypothesis 1b: Children with a smaller discrepancy between receptive and expressive language levels will exhibit lower levels of autism symptoms, stronger cognitive abilities, and stronger social communication skills than those exhibiting larger discrepancies between language domains.

Aim 2a: Map trajectories of receptive and expressive language growth over 12 months.

Aim 2b: Test whether initial receptive-expressive language phenotype is predictive of rate receptive language growth and expressive language growth over 12 months.

Hypothesis 2: Children with a smaller discrepancy between receptive and expressive language will show faster receptive and expressive language growth than children with a larger discrepancy between receptive and expressive skill levels.

Method

Participants

Participants are infants and toddlers between 12 and 23 months of age drawn from a larger randomized controlled trial of a caregiver-mediated intervention for infants and toddlers with autism symptoms. Children were eligible for participation if they were (1) between 12 and 24 months of age, (2) had scores on the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2) Toddler Module (Lord, Luyster, Gotham, & Guthrie, 2012) consistent with Mild-to-Moderate-Concern range or higher, and (3) had autism-specific clinical concerns from a healthcare provider, psychologist or other professional. Exclusionary criteria included: (1) the presence of co-occurring neurological conditions (e.g., uncontrolled seizure activity), (2) known genetic conditions (e.g., tuberous sclerosis complex), or (3) major physical or sensory

impairments (e.g., cerebral palsy, blindness). Given that this study focuses on young children showing early autism symptoms before the typical age of diagnosis, children were not required to have a formal autism diagnosis to participate. Recruitment efforts focused primarily on community healthcare providers (e.g., pediatrician offices) and autism diagnostic or early intervention service providers. Online advertisements were also used to recruit families directly.

A total of 108 infants and toddlers were referred to the intervention trial and screened for eligibility by trained clinicians with expertise in the differential diagnosis of autism in young children. Ten families dropped from the study immediately following screening and were not randomized to intervention. An additional five infants and toddlers were ineligible due to the presence of a known genetic condition. Thirteen children were deemed ineligible for participation due to insufficient evidence of autism symptoms (i.e., ADOS-2 scores below the eligibility cut-off and few or no autism-specific concerns from study clinicians). The remaining 80 eligible infants and toddlers were enrolled and randomly assigned to the experimental (Baby JASPER) or active control (Standard Baby) interventions. Of those participants, 70 consented to and completed all measures at the first timepoint (T1). The final sample includes 70 infants and toddlers (Baby JASPER n = 37; Standard Baby n = 33). See **Table 1.1** for participant demographic characteristics across the total sample and by intervention assignment.

Table 1.1. *Participant Demographic Characteristics*

Variable	Total *N* = 70		Baby JASPER *n* = 37		Standard Baby *n* = 33	
	M	SD	*M*	SD	*M*	SD
Chronological age, months	18.07	2.39	18.10	3.19	18.03	2.65
Nonverbal mental age	15.41	3.16	15.07	2.97	15.80	3.36
ADOS-2 Total Score	17.90	4.72	18.57	4.67	17.15	4.74
	N	%	*N*	%	*N*	%
Sex, female/male	14/56	20/80	8/29	21.62/78.38	6/27	18.18/81.82
Race and ethnicity						
African American or Black	3	4.29	2	5.41	1	3.03
Asian	6	8.57	3	8.11	3	9.09
Hispanic or Latin origin	8	11.43	3	8.11	5	15.15
White	30	42.86	17	45.95	13	39.39
Other	4	5.71	2	5.41	2	6.06
More than one race	15	21.43	8	21.62	7	21.21
Not reported	4	5.71	2	5.41	2	6.06
Familial history of autism						
≥ 1 sibling with autism	19	27.14	6	16.22	13	39.39
Parental education						
≥ 1 parent with college degree	56	80.00	26	70.27	30	90.91
No parent with college degree	11	15.71	8	21.62	3	9.09
Not reported	3	4.29	3	8.11	0	0.00
Household income						
$100 000 or less	29	41.43	16	43.24	13	39.39
Above $100 000	34	48.57	16	43.24	18	54.55
Not reported/refused	7	10.00	5	13.51	2	6.06

Note. Mullen visual reception age equivalent scores were used as a proxy for nonverbal mental age. ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition.

Intervention

An independent statistical group was responsible for randomizing eligible participants to two intervention conditions, Baby JASPER (experimental treatment) or Standard Baby (active control), for the larger intervention study. Briefly, both groups received eight weeks of intervention, which included two 2.5-hour sessions per week. These biweekly intervention sessions included one hour of direct parent education or coaching and two hours of group-based activities. The Standard Baby intervention included one hour of direct parent education and used group-based activities targeting various developmental domains (e.g., cognitive, motor, daily living skills) based on the Assessment, Evaluation, and Programming System for Infants and Children, Second Edition (AEPS; Bricker, Pretti-Frontczak, Johnson, & Straka, 2002). The Baby JASPER intervention included one hour of Joint Attention Symbolic Play

Engagement and Regulation intervention (JASPER; Kasari et al., 2022) and utilized group activities that specifically targeted social communication and dyadic engagement. Thus, the Standard Baby classroom took a more "domain-general" approach, whereas the Baby JASPER classroom focused more explicitly on social communication skills that are disrupted from very early in autism symptom development. Both interventions are manualized and equivalent in contact and intensity. These interventions are described in detail elsewhere (Gulsrud et al., *under review*; Sterrett, Magaña, Gulsrud, Paparella, & Kasari, 2022).

Behavioral Measures

This study uses a subset of behavioral outcome measures administered as part of a larger randomized controlled trial of an early intervention for infants and toddlers with autism symptoms. Participating infants and toddlers completed behavioral assessments at three timepoints: T1 (baseline, pre-intervention), two months later at T2 (exit, immediate post-intervention), and 12 months after T1 at T3 (follow-up). Participants were 18.07 months old on average at T1 (SD = 2.93), 20.74 months old at T2 (SD = 2.88), and 31.29 months old at T3 (SD = 2.55). The distribution of chronological ages across enrollment (stratified by participant) is displayed in **Figure S1.1**. On average, participants completed the T2 visit 2.77 months after T1 (SD = 0.66) and completed the T3 visit 12.95 months after T1 (SD = 0.64).

Demographic Form. Participating families completed a demographic questionnaire at T1. The questionnaire included items designed to gather information about child and family characteristics.

Autism Diagnostic Observation Schedule, Second Edition (ADOS-2). Infants and toddlers referred for participation were screened for eligibility with the ADOS-2 Toddler Module (Lord et al., 2012), administered by trained independent clinicians from a specialized clinic. The ADOS-2 is an autism diagnostic instrument for children and adults of varying language levels. The Toddler Module is designed specifically for children between 12 and 30 months of age. The ADOS-2 measures core autism symptoms, including social communication impairments (Social

Affect domain) and restricted/repetitive behaviors (RRB domain). Domain scores are summed to generate an Overall Total score. The ADOS-2 Toddler Module scoring algorithm provides guidance for mapping Overall Total scores onto three categories reflecting the level of clinical concern (Little-to-No Concern, Mild-to-Moderate Concern, and Moderate-to-Severe Concern).

Mullen Scales of Early Learning (Mullen). The Mullen Scales of Early Learning (Mullen, 1996) is a standardized developmental assessment of cognitive and motor development for children up to 68 months of age. The Mullen was administered to participants by research-reliable, independent evaluators. The Mullen assesses skills across five domains: gross motor, fine motor, visual reception, receptive language, and expressive language. Raw scores, age equivalent scores, and T-scores are provided for each subscale. The Mullen has been used extensively in infants and toddlers with autism or other developmental disabilities in research settings (Belteki, Lumbreras, Fico, Haman, & Junge, 2022), and evidence for construct, convergent and divergent validity of the Mullen in children with autism has been established (Swineford, Guthrie, & Thurm, 2015). Nonverbal and verbal developmental quotient (DQ) scores were computed to index cognitive functioning relative to chronological age expectations. Nonverbal DQ (NVDQ) scores are calculated by dividing the average of visual reception and fine motor scale AE scores by the child's chronological age and multiplying the results by 100. The same procedure is used to compute Verbal DQ (VDQ) scores, though using the average AE from the receptive language and expressive language scales. The purpose of using DQ scores, as is common in studies of infants and toddlers with or at increased likelihood of autism, is to avoid possible floor effects associated with T-scores while providing a metric quantifying functioning *relative to chronological age expectations* that captures variability in cognitive functioning even among children with the most profound developmental delays (Lord et al., 2006; Munson et al., 2008).

Continuous measures of receptive-expressive phenotype and language profiles (**Aim 1**) were derived from receptive and expressive language scale AE scores from the T1 Mullen

administration. To map trajectories of language growth (**Aim 2**), receptive and expressive language age equivalent scores (AE) from T1, T2, and T3 were used.

Early Social Communication Scales (ESCS). The Early Social Communication Scales (ESCS; Mundy et al., 2003) is a structured, observational measure designed to elicit early social communication behaviors, including child initiations of joint attention (IJA) and responsiveness to others' bids for joint attention (RJA). The assessment is approximately 15 to 20 minutes in duration and is video-recorded for later coding offline. IJA is quantified as the frequency with which a child *spontaneously* uses gaze, language/communicative vocalizations, or gestures to initiate shared attention with the assessor. IJA behaviors are distinct from other social communication behaviors (e.g., child-initiated requests) in that the underlying intent is to direct the assessor's attention to share an experience. Overtures involving multiple combined skills are counted as one instance of IJA (e.g., a child-initiated point paired with eye contact is scored as one instance of IJA). RJA was assessed during a shared book-reading task and gaze-following task. The assessment typically involves a total of 14 RJA probes, or opportunities, for the child to respond to the assessor's bid for joint attention. RJA is quantified as the total number of child responses divided by the total number of opportunities for response. A trained independent assessor administered the ESCS, and independent coders blind to intervention assignment and timepoint scored the video-recorded assessments. Coders maintained reliability of at least 80%, assessed by intraclass correlation coefficients.

Analysis Strategy

Aim 1a: Characterizing Receptive-Expressive Phenotypes

To clarify inconsistencies in the extant literature on receptive-expressive language profiles among children with autism (and whether atypical profiles are more common among children with or developing autism than in the general population), receptive-expressive language discrepancies and profiles were quantified using three approaches: (1) receptive-expressive **Difference Scores** (as in Swanson et al., 2017), (2) receptive-expressive **Ratio**

Scores (as in Reinhartsen et al., 2019; Seol et al., 2014), and (3) using published receptive-expressive ratio score cut-offs (Seol et al., 2014) to classify children into three discrete language profiles. Language profiles included **Receptive Advantage** (**RA**; receptive language level > expressive language level), **Expressive Advantage** (**EA**; expressive language level > receptive language), and **Balanced** (receptive language level ~ expressive language level) profiles. Thus, these three approaches yield two continuous metrics of receptive-expressive discrepancy and one categorical metric describing the strength of receptive versus expressive language skills.

Aim 1b: Concurrent Behavioral Correlates of Receptive-Expressive Phenotypes

To examine the association between continuous metrics of receptive-expressive language ability (Difference and Ratio Scores) and the behavioral variables of interest (chronological age, autism symptoms, cognitive ability, and joint attention skills), Spearman's rank-order correlations (r_s) were computed. The present sample of $N = 70$ provided 80% power to detect a medium effect (i.e., $|r_s| = .35$) at an alpha-level = .05. One-way ANOVA was used to test whether children with EA, RA, or Balanced language profiles differed significantly on the behavioral variables of interest. The present sample size of $N = 70$ provided 80% power to detect a medium-to-large effect (Cohen's $f = 0.37$) of language profile on the behavioral variables of interest.

Aim 2: Receptive and Expressive Language Trajectories

Hierarchical linear modeling (HLM) was used to model change across the 12-month study period in receptive and expressive language ability. Models were computed separately for receptive and expressive language. The HLM approach for studying longitudinal change has several desirable characteristics particularly well-suited to the present dataset: HLM readily accommodates missing observations (e.g., in cases of attrition) and allows time to be modeled in a flexible manner (e.g., as a function of chronological age, time elapsed since the first measurement occasion; Singer & Willett, 2003).

To address the research aims, unconditional means and unconditional growth models were fit to the language data in order to characterize group mean trajectories of language growth (fixed effects), variability in initial status and rate of growth (level-1 and level-2 residual variance components), and the extent to which initial status was related to rate of change over time. With only three measurement occasions, modeling options are limited. While curvilinear (e.g., decelerating quadratic) or piece-wise linear models may fit the data better than a linear specification, these models require more measurement occasions (perhaps as many as five or more per participant; Raudenbush & Bryk, 2005) to capture individual differences in rates of growth with sufficient precision. As the primary objective of Aim 1 is to capture individual differences in language abilities and growth, a linear growth model was proposed with random participant-level intercepts and slopes.

Given the current longitudinal design, there were a number of ways that time (i.e., the level-1 predictor) could be conceptualized, including child chronological age, timepoint (i.e., Entry, Exit, Follow-Up), or its time-structured analog (i.e., target data collection timeline; Month 0, Month 2, Month 12), or actual days, week, or months elapsed since the first measurement occasion. Given between-participant variability in the spacing of assessments (e.g., some children completed T3 assessments precisely 12 months after T1, whereas others completed T3 assessments at a delay), both categorical and time-structured variants of timepoint were quickly eliminated. Given the broad age range covered at each measurement occasion (e.g., children were as young as 12 months or as old as 23 months at the first measurement occasion; see **Figure S1.1.**) and relatively sparse sampling across the measurement period, age (either centered or raw) was also eliminated.

I chose to model time as months elapsed since baseline (*Time*) given that this metric is readily interpretable with respect to intercept (i.e., the intercept is the estimated score at T1), and rate of change, given the dependent variables (age equivalent scores) approximate child performance using "age" in months. This interpretation of linear slope also provides useful

insight into the extent to which language growth, on average, is outpacing what would be expected for a given period of time (e.g., slope < 1 suggests slower growth relative to normative development, whereas slope > 1 suggests language skills are growing at a faster rate than what would be expected in normative development). Moreover, given the significant share of participants who completed fewer than three timepoints and the relatively sparse sampling of language over the 12 months, the variability in temporal spacing of measurement occasions is beneficial for estimating fixed effects (i.e., group mean trajectories) in the presence of missing and unbalanced data (Singer & Willet, 2003).

To test whether initial receptive-expressive phenotype was predictive of the rate of language growth (**Aim 2b**), T1 receptive-expressive language profile was added to the unconditional growth models as a predictor of initial status and rate of linear growth. Intervention assignment was then added to the subsequent model, allowing me to evaluate the effects of language profiles on growth trajectories after statistically controlling for intervention assignment. Sensitivity analyses were conducted using T1 Difference Scores to evaluate whether observed effects were consistent across receptive-expressive language metrics. While I had proposed examining the several T1 child demographic and behavioral predictors of language trajectories, it quickly became clear that the present sample size (N = 70, n = 168 measurement occasions) is insufficient for testing a large number of predictors simultaneously (including testing whether initial language phenotypes are predictive of language growth above and beyond the effects of other T1 predictors). This decision-making process is discussed in detail in the Results section.

Results

Aim 1a: Cross-Sectional Receptive-Expressive Language Phenotypes

Quantifying Receptive-Expressive Language Phenotypes at T1

Difference Scores and Ratio Scores were computed as previously described. The distribution of Difference and Ratio scores within the present sample (see **Table 1.2**, **Figure 1.1**) suggests that, on average, infants and toddlers had relatively balanced receptive and

expressive language abilities. However, there was remarkable variability within the sample (recall Difference Scores of 0 and Ratio Scores of 1 reflect equivalent receptive and expressive abilities, respectively). Difference Scores appear approximately normally distributed upon visual inspection, consistent with the results of the Shapiro-Wilk test (W = 0.966, p = .055). Skew and kurtosis were acceptable. No outliers were detected (i.e., all observed values fell within three standard deviations of the mean). In contrast, visual inspection of Ratio Scores (Figure 1.1) suggests the presence of potential outliers and deviation from the normal distribution. As expected, Difference Scores and Ratio Scores are highly correlated (r_s = 0.975, p <.001).

Three groups reflecting receptive-expressive language profiles were formed using Ratio Score cut-offs described in Seol et al. (2014). EA profiles were the most prevalent, as nearly half (n = 29, 41.4%) of infants and toddlers met criteria for an expressive advantage profile. Of the remaining children, 24 had Ratio Scores consistent with an RA profile (34.3%) and 17 (24.3%) had Ratio Scores consistent with a Balanced receptive-expressive language profile.

Table 1.2. *Descriptive Statistics for Metrics of Receptive-Expressive Language Phenotypes*

Metric	**Computation**	**Descriptives**		
		M	SD	Min, Max
Difference Score	Receptive AE – Expressive AE	0.30	3.76	[-7, 11]
Ratio Score	Receptive AE ÷ Expressive AE	1.09	0.53	[0.14, 3.25]
Language Profile		*N*	%	
Expressive Advantage	Ratio Score < 0.90	29	41.43%	
Receptive Advantage	Ratio Score > 1.10	24	34.29%	
Balanced	1.10 ≥ Ratio Score ≥ 0.90	17	24.29%	

Note. AE = age equivalent score.

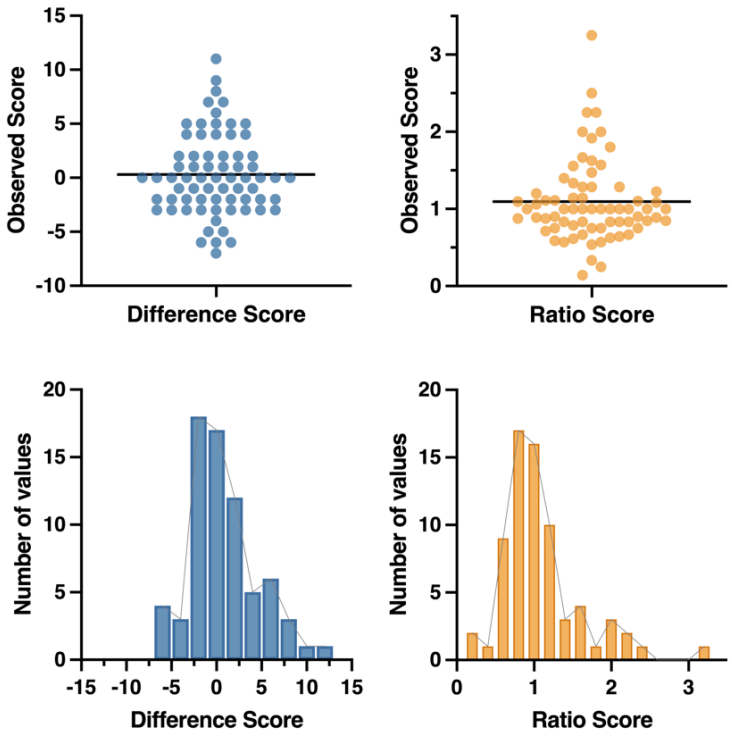

Figure 1.1. *Distribution of receptive-expressive Difference Scores and Ratio Scores.*

Aim 1b: Cross-Sectional Associations with Receptive-Expressive Phenotypes

Preliminary Analyses

Following computation of language metrics, preliminary analyses were undertaken to examine whether there was an association between the three receptive-expressive language profile metrics (Difference Scores, Ratio Scores, and Language Profiles) and select demographic variables: sex at birth, family history of autism (dummy coded, such that 1 = at least one autistic sibling per parent report, 0 = no autistic siblings or not reported), parental education (1 = at least one parent obtained a college or graduate degree, 0 = no parents with a college or not reported), and race/ethnicity. Given the group-level sample sizes were relatively small for those who reported a racial/ethnic identity other than White (see Table 1.1), for statistical analyses, groups were collapsed to ensure cell sizes were sufficiently large to satisfy assumptions of chi-square tests. Racial/ethnic identity groups were collapsed into three groups:

White (the most-frequently-endorsed identity; *n* = 30), more than one race/ethnicity (the second most-frequency endorsed category, *n* = 15), and others (Hispanic/Latin origin, *n* = 8; Asian *n* = 6; African American or Black, *n* = 3; Other, *n* = 4; not reported/refused, *n* = 4). While traditional significance could not be carried out without combining racial/ethnic groups due to small expected cell counts, the distribution of Difference Scores, Ratio Scores, and Language Profile membership across each race/ethnic group is displayed in **Figure S1.2.** for descriptive purposes. Note that the variables tested here are not the primary variables of interest but rather background variables to include as potential covariates in later analyses when indicated. Thus, *p*-values have not been adjusted for multiple comparisons.

Nonparametric Mann-Whitney tests were implemented for preliminary analyses examining associations between background demographic variables and Difference and Ratio Scores. Note that while Difference Scores satisfied assumptions of independent samples *t*-test, Ratio Scores did not. Mann-Whitney tests are reported for both variables in the interest of consistency. There were no significant differences between males and females in Difference Scores (U = 380, z = -0.18, p = .864) or Ratio Scores (U = 379.5, z = -0.18, p = .859). There were also no differences in Difference Scores (U = 504.5, z = 0.27, p = .791) or Ratio Scores (U = 524.50, z = 0.53, p = .596) as a function of family history of autism. There was no effect of parental educational attainment on Difference Scores (U = 398.00, z = 0.09, p = .929) or Ratio Scores (U = 376.50, z = -0.23, p = .820). For tests of race/ethnicity, nonparametric rank-based one-way ANOVA was used (Kruskal-Wallis H). Results indicate no significant differences in Difference Scores (H = 0.96, df = 2, p = .620) or Ratio Scores (H = 1.00, df = 2, p = .605) across racial/ethnic groups.

For preliminary analyses of categorical language profiles, traditional 3x2 chi-square analyses were not possible due to an excessive number of cells with expected counts below 5 for sex at birth, family history of autism, and parental education. However, the distribution of males and females appeared similar across groups (20.7%, 20.8%, and 17.6% of participants

assigned female at birth for EA, RA, and Balanced groups, respectively). The proportion of children with at least one autistic sibling was also similar across groups (24.1% of EA group, 29.2% of RA group, and 29.4% of Balanced group), as was the proportion of children with at least one parent who earned a college or graduate degree (82.4% of EA group, 82.8% of RA group, and 75.0% of Balanced group). Chi-squared tests failed to detect significant associations between Language Profile membership and race/ethnic identity ($\chi^2(4) = 4.10$, $p = .398$).

Correlates of Receptive-Expressive Difference and Ratio Scores

Spearman's nonparametric correlation analyses were used to identify associations between continuous measures of receptive-expressive language discrepancy and hypothesized demographic and behavioral predictors. Briefly, analyses revealed no significant associations between Difference Scores and child chronological age ($p = .227$), ADOS-2 Total score ($p = .164$), NVDQ ($p = .352$), VDQ ($p = .356$), RJA ($p = .120$) or IJA ($p = .932$). This pattern was consistent with the results for Ratio Scores (see **Table 1.3.**).

Table 1.3*. Correlational Analyses of Receptive-Expressive Language Discrepancy Scores and Primary Behavioral Variables*

				Correlation with Difference Score		**Correlation with Ratio Score**	
Variable	*N*	*M*	*SD*	r_s	*p*	r_s	*p*
Chronological age	70	18.10	2.93	.15	.227	.10	.405
Nonverbal DQ	70	86.26	16.17	.11	.352	.14	.243
Verbal DQ	70	58.25	22.59	.11	.356	.12	.306
ADOS-2 Total Score	70	17.90	4.72	-.17	.164	-.19	.123
RJA	67	34.60%	24.01%	.19	.120	.17	.180
IJA	67	11.05	9.86	.01	.932	.05	.686

Note. ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition; DQ = developmental quotient; IJA = initiations of joint attention; RJA = response to joint attention.

Considering these findings, more granular exploratory follow-up analyses were conducted to evaluate whether there were associations between Difference and Ratio scores and (1) ADOS-2 domain-level scores, and (2) Mullen scale-level scores for all five scales (rather than nonverbal and verbal scores, which aggregate across multiple scales). Given the large number of correlation coefficients calculated in these follow-up analyses, Bonferroni adjustment was applied to *p*-values computed for ADOS-2 domain scores (adjusting for two tests) and

Mullen scale scores (adjusting for five tests). Bonferroni adjustment was carried out separately for Difference Scores and Ratio Scores.

The results of follow-up analyses are displayed in **Table 1.4.** For Difference Scores and Ratio Scores, receptive language AE scores were the only significant associations following Bonferroni correction ($p_{adj} < .001$). The direction of this positive association suggests a greater receptive advantage is associated with stronger receptive skills overall (recall that Difference Scores alone provide no information about language level, but rather, the difference between language domains)). While the associations with expressive language did not survive Bonferroni correction, the correlation coefficients suggest that an increasing expressive advantage is associated with stronger expressive language skills.

Table 1.4. *Follow-up Correlation Analyses of ADOS-2 Domain and Mullen Scale Scores*

				Correlation with Difference Score		**Correlation with Ratio Score**	
Variable	*N*	*M*	*SD*	r_s	*p*	r_s	*p*
ADOS-2 Domain							
Social Affect	70	14.94	3.89	-.16	.179	-.19	.115
RRB	70	2.96	1.62	-.03	.834	-.02	.848
Mullen Scale AE							
Gross Motor	69	15.51	2.39	.19	.111	.19	.120
Visual Reception	70	14.67	3.94	.20	.100	.21	.082
Fine Motor	70	16.16	3.13	.07	.542	.08	.501
Receptive Language	70	10.57	5.21	.52	<.001	.53	<.001
Expressive Language	70	10.27	4.32	-.26	.033[a]	-.25	.041[a]

Note. ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition; AE = age equivalent score; DQ = developmental quotient; RRB = restricted/repetitive behaviors. [a]No longer significant following Bonferroni correction.

Associations Between Language Profiles and Behavioral Variables

The within-groups assumption of normality was not satisfied for nearly all the dependent variables of interest (i.e., the distribution of the dependent variables was non-normal within at least one of the language profile groups, per visual inspection and Shapiro-Wilk test), with the exception of NVDQ. Thus, for all dependent variables other than NVDQ, a robust variation of traditional one-way ANOVA using 10% trimmed means was employed using the *WRS2* package (Mair & Wilcox, 2020) available in *R* (R Core Team, 2021). The robust test statistic, F_t, is a generalization of Welch's *F* (Field & Wilcox, 2017; Wilcox, 2023). Post-hoc pairwise

comparisons and corresponding effect sizes are computed using 10% trimmed means. The effect sizes, d_t, are a robust version of Cohen's *d* (Algina, Keselman, & Penfield, 2005) and may be interpreted similarly (i.e., a standardized mean difference between groups).

Groups did not differ significantly in age ($F_t(2, 33.61) = 1.39$, $p = .264$), ADOS-2 Total Score ($F_t(2, 34.22) = 0.790$, $p = .462$), NVDQ ($F(2, 67) = 0.71$, $p = .497$), VDQ ($F_t(2, 32.52) = 0.47$, p = .628), IJA ($F_t(2, 30.55) = 0.85$, $p = .437$), or RJA ($F_t(2, 29.29) = 0.240$, $p = .788$). Figure 1.3 depicts the distribution of demographic and behavioral variables across language profile groups.

As with correlational analyses, granular ADOS-2 domain-level and Mullen scale-level follow-up analyses were conducted. There were no group differences in ADOS-2 Social Affect domain scores ($F_t(2, 33.79) = 0.59$, p = .560) or RRB domain scores ($F_t(2, 34.35) = 1.31$, $p = .283$). Groups also did not differ significantly in gross motor ($F_t(2, 32.7) = 0.36$, $p = .703$), or visual reception ($F_t(2,32.13) = 2.06$, $p = .143$). The tests of fine motor ($F_t(2, 35.10) = 3.51$, $p = .066$) and expressive language scales $F_t(2, 31.89) = 2.96$, $p = .066$) approached significance. The test of receptive language AE scores was significant ($F_t(2, 30.62) = 6.65$, $p = .004$), such that mean receptive language AE scores were significantly lower in the EA group relative to the Balanced group ($p = .008$, $d_t = -.82$) and relative to the RA group ($p < .001$, $d_t = -0.89$). Pairwise group differences remained significant following Bonferroni correction. The discrepancy between groups in receptive language scores, and lack thereof for other Mullen scale scores, is evident in **Figure 1.3.**

Aim 1 Summary

Although receptive and expressive language levels appear relatively balanced at the aggregate sample level, examining individual-level discrepancies in between language domains made clear that there are substantial individual differences in receptive-expressive phenotypes across children A larger proportion of children exhibited atypical language profiles characterized by an imbalance between receptive and expressive language skill levels. Contrary to

hypotheses, receptive-expressive phenotypes, whether quantified using Difference Scores, Ratio Scores, or categorical language profiles, were not significantly associated with child chronological age, autism symptom levels, cognitive ability, motor functioning, or joint attention abilities in the present sample. Rather, the only significant association across all three receptive-expressive metrics was with receptive language level, such that children with stronger expressive language skills than receptive language skills tended to exhibit poorer concurrent receptive language abilities overall.

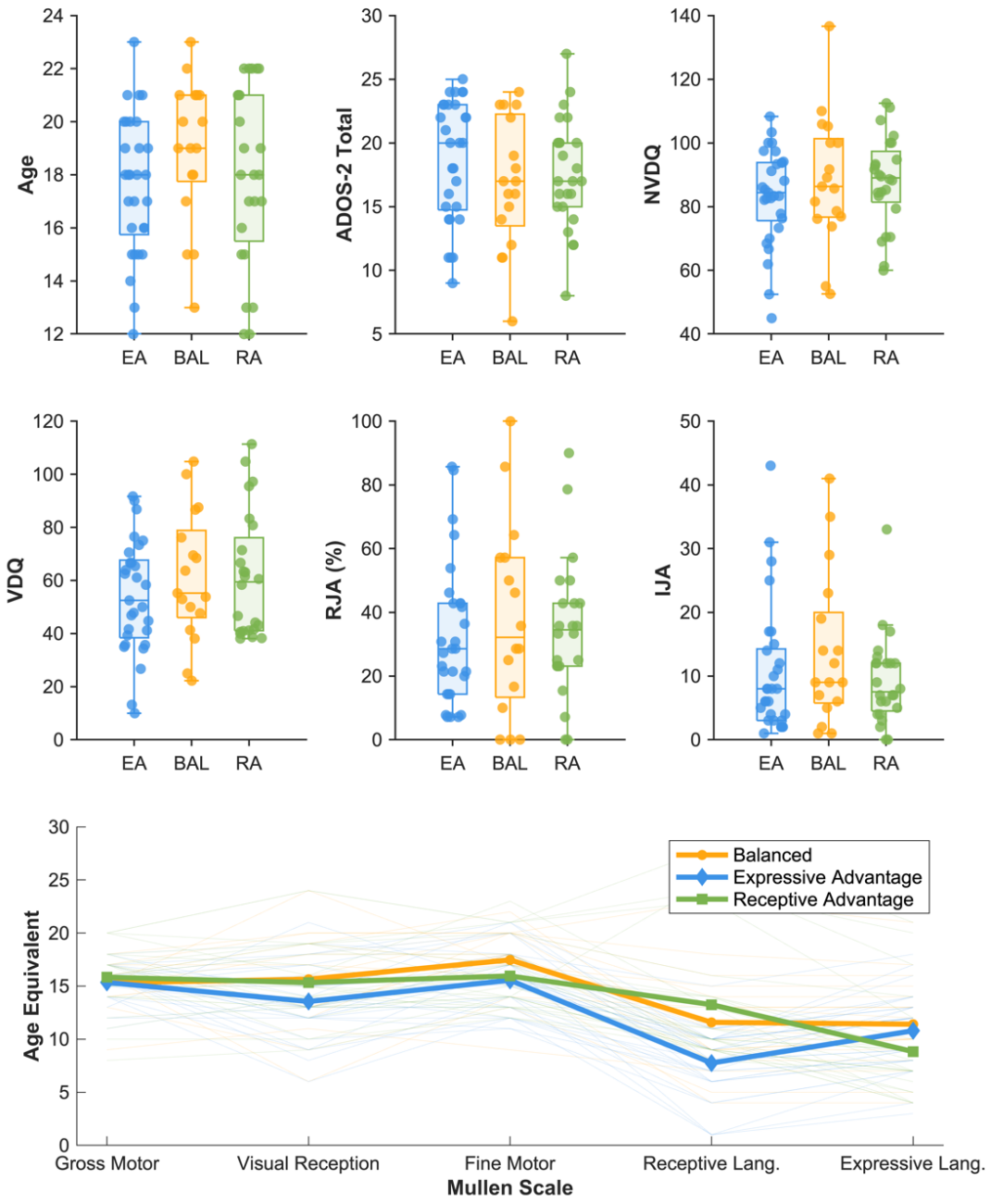

Figure 1.2. *Distribution of child-level behavioral and demographic characteristics by language profile. BAL = balanced profile, EA = expressive advantage profile, RA = receptive advantage profile. NVDQ = nonverbal developmental quotient; VDQ = verbal developmental quotient.*

Aim 2: Receptive-Expressive Language Phenotypes and Language Growth

Preliminary Analyses: Missing Data

As is common in longitudinal studies, not all participants contributed language data at all three timepoints. Language data was available for 70 participants at T1 (100% of the sample), 57 participants at T2 (81.4%), and 40 participants at T3 (57.1%). In total, 38 children (54.3% of the sample) contributed language data at all three timepoints, 21 contributed data at two timepoints (i.e., either T1 and T2 only [27.1%], or T1 and T3 only [2.9%]), and 11 children contributed data at only one timepoint (i.e., T1, 15.7%). Data loss was largely due to attrition, though there were a few instances when data loss was due to non-compliance (n = 2 children missed the T2 visit but completed the T3 visit; n = 3 children attended the T3 visit but did not complete the Mullen). T**able S1.1** summarizes demographic information and descriptive statistics for behavioral variables (measured at T1) stratified by the number of timepoints completed. Briefly, there were no differences between children who contributed three, two, or one timepoint in male-to-female sex ratio, autism family history, parental educational attainment, or household income (as reported at T1). Groups also did not differ significantly in chronological age, receptive language AE score, expressive language AE score, visual reception AE score, or ADOS-2 Total scores at T1.

Mapping Trajectories of Language Growth

Cross-sectional descriptive statistics for language age equivalent scores, chronological age, and time elapsed are shown in Table 1.5. Prior to fitting growth trajectories, an unconditional means model was fit to examine variance components for receptive and expressive language models separately. Next, the unconditional linear growth models were fit with random intercept and linear slope parameters to allow initial status (i.e., language scores at T1) and rates of change to vary across participants, thereby providing a means to capture individual differences in language development.

Table 1.5. *Cross-Sectional Descriptive Statistics for Key Child-Level Variables*

	T1 *N* = 70	**T2** *N* = 57	**T3** *N* = 40
	M (SD)	*M* (SD)	*M* (SD)
Chronological age, months	18.07 (2.93)	20.74 (2.88)	31.29 (2.55)
Receptive Language AE	10.57 (5.20)	15.47 (6.28)	26.80 (8.82)
Expressive Language AE	10.27 (4.32)	14.60 (5.11)	25.63 (8.81)
NVMA (Visual Reception AE)	14.67 (3.94)	–	–
ADOS-2 Total Score	17.90 (4.72)	–	–
Time since T1, months	0	2.77 (0.66)	12.95 (0.62)

Note. AE = age equivalent; ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition; AE = age equivalent; NVMA = nonverbal mental age.

The following section describes the results of fitting unconditional means (Model 0) and unconditional growth (Model 1) models to receptive and expressive language AE scores. Receptive and expressive language models are summarized in **Tables 1.6** and **1.7**, respectively.

Aim 2a: Mapping Longitudinal Trajectories of Receptive and Expressive Language

Estimates of fixed effects, variance components, and goodness-of-fit indices for unconditional means (Model 0) and unconditional growth (Model 1) models of receptive and expressive language are displayed in Tables 1.6 and 1.7.

Model 0, Unconditional Means Model

The variance estimates derived from the unconditional means models indicate that average receptive language scores vary significantly over time (level-1 variance; σ_e^2 = 68.22, p<.001), and average receptive language scores vary significantly between individuals (level-2 variance in initial status; σ_0^2 = 15.27, p < .001). The intraclass correlation coefficient (ICC) computed from the estimated level-1 and level-2 variance parameters indicate that approximately 17.7% of the variance in receptive language outcomes lies “between” individuals (ICC = 0.177); that is, nearly 20% of the variation in receptive language ability is attributable to difference *among* children. Findings were similar for the expressive language unconditional means model (level-1 σ_e^2 = 62.69, p < .001; level-2 variance in initial status σ_0^2 = 8.72, p < .001), such that average language scores vary significantly over time, and average expressive

language scores differ between individuals. Approximately 12% (ICC = 0.116) of the variance in expressive language outcomes is attributable to differences among children

Model 1, Unconditional Linear Growth Model

Model 1 added *Time* (quantified as months since T1) as a level-1 predictor. Models included random intercepts and slopes. Fixed effects for the receptive language model indicate the estimated population mean receptive language AE score at T1 is approximately 11 AE "months" (γ_{00} = 11.14, F(1,69.37) = 319.11, p < .001), and on average, children's receptive language AE scores increase approximately by 1.2 AE "months" each month (γ_{10} = 1.17, 95% CI [1.01, 1.33], F(1, 42.65) = 215.33, p < .001). The level-1 variance component (σ_e^2 = 12.16, p < .001) declined by 82.18% with the addition of *Time* to the model, suggesting that approximately 82% of the within-individual variation in receptive language is systematically associated with linear time (Singer & Willett, 2003). Estimated level-2 variance components describe the unpredicted variability in individual growth parameters that remains after adding *Time* to the model. Variance in initial status (σ_0^2 =18.69, p < .001) and in rate of change (σ_1^2 =0.135, p = .02) both differ significantly from zero, suggesting the addition of level-2 (between-child) predictors to the model may help explain heterogeneity. Notably, the estimated correlation between level-2 residuals (indexing the extent to which receptive language abilities at T1 are related to the rate of growth in receptive language skills over time) approached statistical significance ($\hat{\rho}_{01}$ = 0.340, p = .076), suggesting there is a non-significant positive association between level of receptive language abilities at T1 and rate of growth over time.

Fixed effects for the expressive language model indicate that the average expressive language AE score at T1 is approximately 10.5 AE "months" (γ_{00}= 10.62, 95% CI [9.58, 11.66], F(1,69.41) = 417.32, p < .001), and on average, AE scores increase by approximately 1.1 AE "months" for every month since T1 (γ_{10}= 1.10, 95% CI [0.93, 1.26], F(1,48.86) = 178.17, p < .001). All level-1 and level-2 variance components differed significantly from 0, suggesting

significant unpredicted variability in individual growth parameters remains. Level-1 residuals declined by approximately 87.54% compared to the unconditional means model, indicating that most within-individual variance in expressive language is systematically associated with linear *Time.* Notably, the correlation between level-2 residuals was not significantly different from 0 ($\hat{\rho}_{01}$ = 0.265, p = .095), though there was a trending positive association such that stronger expressive language skills at T1 was associated with faster growth.

After fitting the unconditional growth models, assumptions of normality were assessed graphically with normal probability plots of raw level-1 and level-2 residuals and scatterplots of standardized level-1 and level-2 residuals by participant ID number. The homoscedasticity assumption was evaluated graphically by plotting level-1 residuals against *Time* (i.e., the level-1 predictor). Following guidelines outlined by Singer and Willett (2003), it was determined that there was sufficient evidence that the models' basic assumptions were met.

Observed trajectories of receptive and expressive language with estimated population mean trajectories derived from unconditional growth models are displayed in **Figure 1.3**.

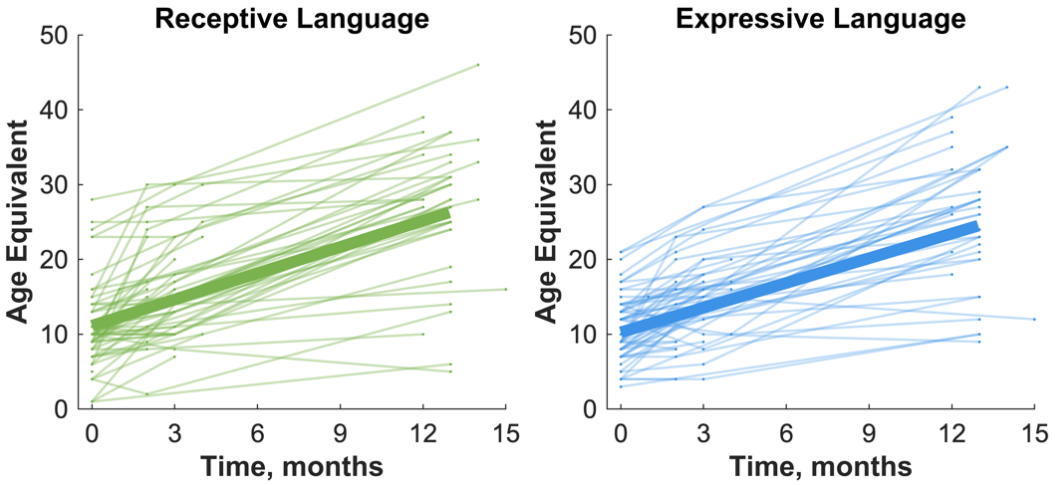

Figure 1.3*. Empirical growth charts of observed receptive and expressive language scores and prototypical growth trajectories from unconditional growth models.*

Aim 2b: Receptive-Expressive Phenotypes as Predictors of Language Trajectories

Model-Building Strategy

The proposal for this dissertation included an analysis plan aimed at identifying T1 predictors of language growth, including initial receptive-expressive language profile, chronological age, nonverbal cognitive ability, ADOS-2 Total scores, joint attention skills, demographic variables (i.e., socioeconomic status), and intervention assignment. However, it quickly became clear that the present sample size (N = 70 children, with n = 168 total measurement occasions) is likely underpowered for this approach. Given these constraints, the analysis plan was modified to focus on the T1 receptive-expressive phenotype as a predictor of language growth.

Notably, preliminary analyses (not shown) were conducted to test the effects of T1 predictors of language growth originally proposed as control variables (that is, variables not of substantive interest that may be associated with language growth, based on existing evidence). Child sex at birth, parental educational attainment (at least one parent completed college versus no parent completed college or no response), annual household income (above $100,000 versus below $100,000 or refused/no response), home language exposure (as reported on the demographic questionnaire at T1; more than one language versus one language or no response) were not significant predictors of initial status or growth for receptive or expressive language and were thus not considered for inclusion in any subsequent models.

Further, preliminary analyses with intervention assignment as a level-2 predictor of initial status and growth found no significant effect of intervention assignment on language growth (i.e., the *Time* by intervention assignment interaction term was not significant). This is consistent with preliminary results from the larger randomized controlled trial, which found no significant treatment effect on receptive language or expressive language scores (Gulsrud et al., *in preparation*). However, both models indicated that intervention assignment was a predictor of *initial* language status. Here, "initial status" corresponds with estimated language abilities prior to random assignment to intervention (recall that *Time* was coded such that the first measurement occasion was set to equal 0). Thus, these significant effects are likely a reflection

of *chance* rather than anything systematic associated with intervention: children who were eventually randomly assigned to the Standard Baby group tended to have stronger language skills on average than those randomly assigned to the Baby JASPER condition. This raises important questions about the value of including intervention assignments in these models, particularly in light of the limitations already imposed by this relatively small sample size. In the presence of a larger sample with more densely sampled language data across the measurement period, the most conservative approach would be to retain intervention assignment as a control variable in all analyses, regardless of whether its effects on initial status or rate of change are statistically significant. However, this decision is less straightforward in the presence of sample size limitations.

In light of these preliminary analyses, the following analysis plan was formulated. As a first step (Model 2), T1 receptive-expressive language profile (*Profile*) would be added as a level-2 predictor to the unconditional growth models, providing a means to test whether T1 *Profile* was associated with average initial status or rate of growth. For analyses, T1 *Profile* was dichotomized into EA profile versus RA or Balanced profiles (1 = EA, 0 = RA or Balanced). This decision was partly hypothesis-driven based on Aim 1 findings, and also an effort to reduce the number of parameters estimated in the growth models. Results from Model 2 are thus interpreted as "uncontrolled" effects of T1 *Profile* on growth parameters, given that intervention assignment is not included in the model (Singer & Willett, 2003). To test whether T1 *Profile* is predictive of initial status and rate of growth *after* statistically controlling for intervention assignment, Model 3 adds intervention assignment (*Tx*) as a control variable (1 = Baby JASPER, 0 = Standard Baby). Future work with a larger sample size will explore whether receptive-expressive profile is predictive of language growth above and beyond the effects of other child-level characteristics (e.g., nonverbal cognitive ability, autism symptom levels) and whether these early language profiles are associated with variability in intervention response.

Note for Models 2 and 3, fixed effects parameter estimates are of primary interest.

Model 2, Uncontrolled Effects of T1 Language Profile on Language Trajectories

Adding *Profile* to unconditional growth models improved model fit for both receptive language (Δ -2 Log Likelihood [-2LL] = 12.58, *df* = 2, *p* = .002) and expressive language (Δ -2 LL = 7.47, *df* = 2, *p* = .024). *Profile* was a significant predictor of initial receptive language status (*p* < .001) but not a significant predictor of linear growth in receptive language (*p* = .745). Having an EA profile at T1 was associated with markedly lower estimated initial receptive language scores. *Profile* was predictive of linear growth in expressive language (*p* = .009) but not of initial expressive language ability. Having an EA profile at T1 was associated with significantly slower linear growth (see **Table 1.8**).

Model 3, Effects of T1 Language Profile on Language Trajectories, Controlling for Intervention Assignment

The addition of intervention assignment (*Tx*) as a predictor of initial status and linear growth of receptive language did not appreciably alter parameter estimates for the effect *Profile* on initial receptive language status (*p* < .001) or linear growth in receptive language (*p* = .878). This is consistent with findings for expressive language growth: *Profile* remained a significant predictor of linear growth in expressive language (*p* = .008) but was not predictive of initial expressive language status (*p* = .254). Notably, in both models, intervention assignment was a significant predictor of initial language status (i.e., estimated language scores at T1) but not of estimated rate of language growth. As previously outlined, this likely is a reflection of differences between intervention groups due to chance rather than a systematic effect of intervention, given children were randomly assigned to intervention groups *after* T1 language assessments were administered. See **Table 1.9** for parameter estimates of fixed effects.

Sensitivity Analysis: Converging Evidence Across Unique Measures of T1 Receptive-Expressive Phenotypes

The analyses testing the uncontrolled (Model 2, not shown) and controlled (Model 3; see Table **1.10**) effects of receptive-expressive language phenotype of language growth were

repeated using T1 Differences Scores. The results were largely consistent with those obtained using a categorical measure of receptive-expressive profile: T1 receptive-expressive Difference Scores significantly predicted initial receptive language status and expressive language growth. After controlling for intervention assignment, the effect of T1 Difference Score on initial expressive language status was also significant.

Aim 2 Summary

Infants and toddlers with autism symptoms showed substantial gains in language skills over 12 months. Growth trajectories suggest that on average, children's language skills grew at a rate similar to what would be expected in neurotypical development. There was a trending, though non-significant, positive association between estimated initial status and estimated rate of change for both receptive and expressive language models; the true nature of this association may be clearer when re-evaluated in a larger sample.

Initial receptive-expressive language phenotype as measured at T1 was a significant predictor of expressive language growth, such that having a greater expressive language advantage (or put otherwise, a greater receptive disadvantage) at T1 was associated with slower growth over the 12-month measurement period. Notably, this effect was consistent when using categorical language profiles and a dimensional measure of receptive-expressive phenotype.

Discussion

The present study examined receptive-expressive language phenotypes among infants and toddlers showing early signs of autism spectrum disorder and tested the extent to which early language phenotypes were associated with other domains of social, cognitive, and motor development. This study further evaluated whether initial receptive-expressive language phenotypes were predictive of subsequent receptive and expressive language growth.

Receptive-Expressive Language Phenotypes

The distribution of Difference and Ratio Scores in the present sample suggests that while children had, on average, relatively balanced receptive and expressive language skills, there were substantial individual differences in the extent to which receptive level differed from expressive skill level. Moreover, when categorizing children into discrete language profiles using published Ratio Score cut-scores, it became apparent that children with relatively equal receptive and expressive language levels were, in fact, in the minority. In contrast, EA profiles were the most prevalent in the present sample. Notably, the distribution of language profiles in the present sample of children with autism symptoms is remarkably consistent with that reported in the toddler-age group of children diagnosed with autism described by Seol et al. (2014), which used the same Ratio Score cut-points to create language profile groups. Specifically, they report 42.7% of autistic children presented with an Expressive Advantage profile, 30.1% presented with a Receptive Advantage profile, and the remaining 27.2% had Balanced profiles.

The strong prevalence of EA profiles in the present sample is consistent with evidence from older children indicating that children with autism may be more likely than children with neurotypical development or non-autism developmental delays to show atypically advanced expressive language abilities relative what would be expected based on their receptive language level (Chawarska et al., 2012; Davidson & Ellis Weismer, 2017; Ellis Weismer et al., 2010; Hudry et al., 2010; Luyster et al., 2008; Maljaars et al., 2012; McDaniel et al., 2018; Reinhartsen et al., 2019; Swanson et al., 2017; Volden et al., 2011).

Contrary to hypotheses, there was no evidence to suggest receptive-expressive language phenotypes – whether defined using Difference Scores, Ratio Scores, or discrete language profiles – are linked with chronological age, autism symptom levels, or even cognitive ability. This finding is in contrast with previous work suggestive of a decline in receptive-expressive discrepancy with increasing chronological age (e.g., Davidson & Ellis Weismer, 2017; Seol et al., 2014, though see Hudry et al., 2010; Kover et al., 2013), and some work indicating an association between nonverbal cognitive ability and discrepant language profiles

(though notably, the direction of this association varies across studies; Hudry et al., 2010; Nevill et al., 2019; Volden et al., 2011). There was also no association between levels of autism symptoms and receptive-expressive language discrepancy, which is consistent with some research on school-age autistic children (Kover et al., 2013; though see Reinhartsen et al., 2019) but not with other studies of preschool-age autistic children that report positive associations between level of autism symptoms and degree of receptive advantage (Hudry et al., 2010). Furthermore, contrary to hypotheses, there was no evidence for an association between joint attention skills and receptive-expressive discrepancies.

It is important to highlight that the present sample represents a population that differs from the populations typically sampled from in extant research on receptive-expressive profiles, both with respect to chronological age as well as diagnostic status. Here, I report on a sample of children who are significantly younger on average (many of whom are younger than 18 months, the age at which autism diagnosis is considered reliable; Ozonoff et al., 2015) and who also have not yet received a formal autism diagnosis, in part owing to their young age. This may, in part, account for discrepant findings.

Receptive and Expressive Language Growth

Somewhat consistent with hypotheses, results of longitudinal hierarchical linear growth models suggest that early receptive-expressive language phenotype may be a candidate marker of risk for poorer language growth. These findings were specific to expressive language, such that children who had weaker receptive language skills relative to their own expressive skill level (i.e., an expressive advantage) tended to show slower expressive language growth. While these findings should be replicated in a larger sample, this preliminary evidence suggests that relative weakness in language comprehension may stall growth in language production, whereas comprehension-production discrepancy is less important for growth in language comprehension.

The slowed expressive language growth among children with a relative receptive language delay (expressive advantage) is consistent with neurotypical models of language development, in which language comprehension skills are said to drive language production (Bornstein & Hendricks, 2012). However, the dampening effect of receptive "disadvantage" on expressive language growth and lack of significant association between receptive-expressive discrepancy and receptive language growth is in contrast with evidence from preverbal preschool-age autistic children. Recent studies examining longitudinal associations between receptive and expressive vocabulary suggest that links between *early* expressive vocabulary and *later* receptive vocabulary may be stronger than the association between early receptive and later expressive vocabulary, specifically among children with autism (Bottema-Beutel et al., 2019; Woynaroski et al., 2016). However, it is possible that this discrepancy is a reflection of differences in the measures used to index language performance and differences in sample characteristics (e.g., in chronological age, autism diagnostic status). For instance, while the recent studies reporting atypical associations between early expressive and later receptive language examined receptive and productive *vocabulary*, the present study utilized the Mullen receptive and expressive language subscales, which provide a more holistic measure of receptive and expressive communication.

Why might children with an expressive language advantage (or, put otherwise, a receptive language *disadvantage*) show slower expressive language growth? One possibility is that difficulties with language comprehension have far-reaching consequences for social functioning and communication development. For instance, comprehension delays may interfere with children's ability to engage in meaningful contingent social interactions, which play a crucial role in scaffolding language acquisition, particularly among children with autism (Adamson, Bakeman, Deckner, & Romski, 2009; Adamson, Bakeman, Suma, & Robins, 2019; Bottema-Beutel, Lloyd, Watson, & Yoder, 2018; Kuhl, 2011). Difficulties with receptive language may emerge as a result of disruptions to neurocognitive mechanisms that support children's ability to

effectively and efficiently process and make meaning of linguistic input in their environment. Studies of EL infants suggest that disruptions to mechanisms that underpin adaptive social attention are present even before autism symptoms emerge (e.g., Hatch et al., 2021; Jones & Klin, 2013; Pierce et al., 2023); thus, early receptive language delays, and dampening of expressive language growth, may be a consequence of very early differences in more domain-general cognitive capacities. This hypothesis is supported by recent work demonstrating that levels of attention to a speaker (measured behaviorally) are predictive of receptive-expressive vocabulary discrepancy, such that preverbal autistic toddlers and preschoolers who spent more time attending to a speaker had more typical receptive-expressive vocabulary discrepancies (McDaniel, Yoder, Woynaroski, & Watson, 2018). In Study 2, I explore this possibility by testing whether patterns of functional brain activity are associated with early receptive-expressive language phenotypes and language growth, focusing on electroencephalography (EEG) metrics known to be associated with cognitive and social skills in infancy and early childhood.

It is worth noting that the relative disadvantage in language comprehension may also manifest later in development in other facets of language functioning among children with autism. For instance, on average, children with autism show relative weakness in meaning-related emergent literacy skills (i.e., comprehension) relative to decoding-related skills (Davidson & Ellis Weismer, 2014; Westerveld et al., 2017). Moreover, consistent with the elevated prevalence of receptive-expressive oral language discrepancy among children with autism, the prevalence of hyperlexia (typically defined as a marked discrepancy in decoding skills relative to comprehension and often, very early acquisition of reading skills without explicit instruction) is elevated among children with autism relative to those with other neurodevelopmental conditions (Grigorenko et al., 2002; Ostrolenk, Forgeot d'Arc, Jelenic, Samson, & Mottron, 2017). This is suggestive of continuity between early language profiles and language functioning across multiple modalities (e.g., spoken, written) and raises further

questions about the extent to which early language profiles are predictive of growth in other facets of language functioning.

Strengths and Limitations

The results reported in Study 1 should be interpreted in light of several methodological considerations. First, it is essential to underscore that this sample includes children who are showing clear, elevated symptoms of autism spectrum disorder who have not necessarily met clinical diagnostic criteria for autism. This sampling approach was motivated by evidence that very young “pre-diagnostic” infants and toddlers later diagnosed with autism show clear delays in social communication development well before autism diagnosis is considered reliable and stable, and often many years before children receive a comprehensive diagnostic evaluation in the community. As such, there is a clear need to develop interventions that can address these early vulnerabilities before the time at which diagnostic evaluation may be performed (or accessed) in the community clinical setting. Thus, these findings are specific to children exhibiting the emerging autism phenotype, who may or may not go on to meet diagnostic criteria. While this sampling strategy somewhat limits the generalizability of findings to other populations (e.g., elevated likelihood infants, children with community autism diagnoses), there are significant benefits to this approach: enrolling pre-diagnostic infants/toddlers with autism symptoms provides an opportunity to leverage the remarkable neuroplasticity of this period and deliver intervention when the brain may be in an optimal state for learning. Furthermore, this largely “pre-diagnostic” infant/toddler sample is likely more reflective of the clinical population that community-based providers (e.g., pediatricians, early intervention service providers) regularly encounter in their clinical practice.

Although the Mullen is one of the most frequently used measures of language ability and has been used extensively in cross-sectional and longitudinal studies of language development in infants, toddlers, and preschoolers with autism (e.g., Anderson et al., 2007; Bono, Daley, & Sigman, 2004; Bruyneel, Demurie, Zink, Warreyn, & Roeyers, 2019; Fusaroli, Weed, Fein, &

Naigles, 2019; Iverson et al., 2018; Lebarton & Iverson, 2013; Longard et al., 2017; Mitchell et al., 2006; Swanson et al., 2017; Toth et al., 2007), it provides a more "holistic" assay of communication ability and thus may fail to capture important nuances that naturalistic language samples, for example, may capture. However, given the sample age and anticipated rate of language delays, a more holistic measure of receptive and expressive communication ability (i.e., measuring preverbal and verbal skills) may be more meaningful in this population than a measure of vocabulary, for example. The fact that the Mullen is clinician-administered is also a strength, given parent-report measures of language abilities (e.g., Vineland, MCDI) may provide biased estimates of language skills. Examining receptive-expressive discrepancies using alternative standardized and/or naturalistic measures of language competence may be highly informative.

Statistical power is rarely addressed in studies of brain and behavioral development among infants with or at elevated likelihood of autism, despite the fact that small sample sizes have long been a limitation in the field. The present study of N = 70 children was powered to detect moderate effects for correlational analyses and moderate-to-large effects for omnibus comparisons across categorical language profile groups. Thus, it's possible that the present study lacks sufficient statistical power to detect associations or group differences that were smaller in magnitude.

As previously discussed, the present sample size, coupled with a relatively sparse sampling of language abilities over the 12-month measurement period, were also limitations to longitudinal analyses of language growth. Increasing the number of measurement occasions would provide a means to examine possible curvilinear (e.g., quadratic) trajectories and also would allow for modeling of discontinuous trajectories (for instance, using separate slope parameters to estimate growth during the intervention period and after the withdrawal of intervention). Further, future work with larger sampled sizes and more densely sampled observations of language abilities would allow us to test whether receptive-expressive language

phenotypes are predictive of language growth, above and beyond the effects of other child-level characteristics, and whether receptive-expressive language profile moderates the effect of a social communication-focused intervention on child social, cognitive, and language outcomes.

Conclusions

This study provides evidence in support of an increased prevalence of atypical receptive-expressive language profiles among young children showing early behavioral signs of autism. While previous research in older autistic children has provided evidence to suggest that receptive-expressive phenotype may be associated with other demographic or behavioral characteristics, no such associations were identified in this sample of symptomatic infants and toddlers. However, exploratory longitudinal analyses indicate that initial receptive-expressive language phenotype, measured in terms of categorical language profiles or dimensionally, were predictive of expressive language growth, such that children with an atypical expressive language advantage were predicted to show slower language growth. These findings suggest that measures of early receptive-expressive language phenotypes may serve as clinically meaningful markers of increased risk for stalled language growth over the second and third years of life.

Table 1.6. *Receptive Language Unconditional Means and Unconditional Growth Models*

	Model 0 *Unconditional Means*					**Model 1** *Unconditional Growth*				
Fixed Effects	Est.	SE	*t*	*df*	*p*	Est.	SE	*t*	*df*	*p*
Initial Status										
Intercept, γ_{00}	15.85	.80	68.50	19.93	<.001	11.14	0.62	69.36	17.86	<.001
Linear Growth										
Time, γ_{10}						1.17	0.08	42.65	14.67	<.001
Variance	Est.	SE	*z*	*p*		Est.	SE	*z*	*p*	
Level-1, σ_e^2	68.20	9.51	7.17	<.001		12.16	2.36	5.16	<.001	
Intercept σ_0^2	14.65	8.04	1.82	.034		18.69	4.89	3.82	<.001	
Slope, σ_1^2						0.14	0.07	2.05	.020	
Correlation, ρ_{01}						0.35	0.29	1.20	.115	
Goodness-of-Fit										
-2 LL	1207.63					1032.71				
AIC	1213.63					1044.71				

Note. Results of hierarchical linear growth modeling for receptive language age equivalent scores, with estimates of fixed effects, random effects, and goodness-of-fit indices -2LL = -2 Log Likelihood; AIC = Akaike information criterion.

Table 1.7. *Expressive Language Unconditional Means and Unconditional Growth Models*

	Model 0 *Unconditional Means*					**Model 1** *Unconditional Growth*				
Fixed Effects	Est.	SE	*t*	*df*	*p*	Est.	SE	*t*	*df*	*p*
Initial Status										
Intercept, γ_{00}	15.23	0.71	65.60	21.50	<.001	10.62	0.52	69.40	20.43	<.001
Linear Growth										
Time, γ_{10}						1.10	0.08	48.86	13.35	<.001
Variance	Est.	SE	*z*	*p*		Est.	SE	*z*	*p*	
Level-1, σ_e^2	62.68	8.80	7.12	<.001		7.81	1.49	5.26	<.001	
Intercept σ_0^2	8.22	6.72	1.22	.110		13.38	3.37	3.97	<.001	
Slope, σ_1^2						0.21	0.06	3.25	.001	
Correlation, ρ_{01}						0.27	0.22	1.23	.220	
Goodness-of-Fit										
-2 LL	1183.84					986.93				
AIC	1189.84					998.93				

Note. Results of hierarchical linear growth modeling for expressive language age equivalent scores, with estimates of fixed effects, random effects, and goodness-of-fit indices -2LL = -2 Log Likelihood; AIC = Akaike information criterion.

Table 1.8. *Parameter Estimates for Models Predicting Language Growth from T1 Language Profile (**Model 2**)*

Receptive Language						
Fixed Effects	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	12.91	0.75	70.17	17.25	<.001	[11.42, 14.41]
Profile, γ_{01}	-4.22	1.16	68.54	-3.65	<.001	[-6.52, -1.91]
Linear Growth						
Time, γ_{10}	1.20	0.11	41.94	11.11	<.001	[0.98, 1.42]
*Time*Profile,* γ_{11}	-0.05	0.16	42.69	-0.33	.745	[-0.38, 0.27]
Goodness-of-Fit						
-2 LL	1020.13					
AIC	1036.13					

Expressive Language						
Fixed Effects	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	10.17	0.68	70.42	14.99	<.001	[8.81, 11.52]
Profile, γ_{01}	1.09	1.05	69.12	1.04	.300	[-1, 3.19]
Linear Growth						
Time, γ_{10}	1.29	0.10	46.28	12.50	<.001	[1.08, 1.49]
*Time*Profile,* γ_{11}	-0.41	0.15	47.21	-2.71	.009	[-0.72, -0.11]
Goodness-of-Fit						
-2 LL	979.46					
AIC	995.46					

Notes. Profile refers to receptive-expressive language profile at T1 (0 = RA or Balanced, 1 = EA). Time was parameterized as months since T1, thus, estimates of initial status are estimates of language scores at T1. -2 LL = -2 Log Likelihood; AIC = Akaike information criterion; EA = expressive advantage; RA = receptive advantage.

Table 1.9. *Parameter Estimates for Models Predicting Language Growth from T1 Language Profile, Controlling for Intervention Assignment (**Model 3**)*

Receptive Language						
Fixed Effects	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	14.34	0.91	70.25	15.71	<.001	[12.52, 16.16]
Profile, γ_{01}	-4.14	1.10	67.39	-3.75	<.001	[-6.34, -1.94]
Tx, γ_{02}	-2.73	1.09	68.06	-2.50	.015	[-4.9, -0.55]
Linear Growth						
Time, γ_{10}	1.19	0.13	40.69	9.27	<.001	[0.93, 1.45]
*Time*Profile,* γ_{11}	-0.06	0.16	42.53	-0.35	.725	[-0.38, 0.27]
*Time*Tx*, γ_{12}	0.02	0.16	42.56	0.15	.878	[-0.3, 0.35]
Goodness-of-Fit						
-2 LL	1014.18					
AIC	1034.18					

Expressive Language						
Fixed Effects	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	11.39	0.83	70.67	13.69	<.001	[9.73, 13.05]
Profile, γ_{01}	1.16	1.01	68.48	1.15	.254	[-0.85, 3.17]
Tx, γ_{02}	-2.31	1.00	69.03	-2.32	.023	[-4.3, -0.32]
Linear Growth						
Time, γ_{10}	1.39	0.12	44.20	11.58	<.001	[1.15, 1.64]
*Time*Profile,* γ_{11}	-0.42	0.15	46.74	-2.79	.008	[-0.72, -0.12]
*Time*Tx*, γ_{12}	-0.20	0.15	46.84	-1.34	.186	[-0.5, 0.10]
Goodness-of Fit						
-2 LL	972.11					
AIC	992.11					

Note. Profile refers to receptive-expressive language profile at T1 (0 = RA or Balanced, 1 = EA). Tx refers to intervention assignment (1 = Baby JASPER, 0 = Standard Baby). Time was parameterized as months since T1, thus, estimates of initial status are estimates of language scores at T1. -2 LL = -2 Log Likelihood; AIC = Akaike information criterion; EA = expressive advantage; RA = receptive advantage.

Table 1.10. *Parameter Estimates for Models Predicting Language Growth from T1 Difference Scores, Controlling for Intervention Assignment*

Receptive Language

	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	12.18	0.77	69.68	15.87	<.001	[10.65, 13.71]
Difference Score, γ_{01}	0.68	0.14	70.64	4.80	<.001	[0.4, 0.96]
Tx, γ_{02}	-2.27	1.05	69.20	-2.17	.034	[-4.37, -0.18]
Linear Growth						
Time, γ_{10}	1.17	0.11	42.29	10.53	<.001	[0.95, 1.4]
*Time*Difference Score,* γ_{11}	-0.02	0.02	44.27	-0.86	.397	[-0.06, 0.03]
*Time*Tx*, γ_{12}	0.02	0.16	43.11	0.09	.925	[-0.31, 0.34]
Goodness-of-Fit						
-2 LL	1007.17					
AIC	1027.17					

Expressive Language

	Est.	SE	*df*	*t*	*p*	95% CI
Initial Status						
Intercept, γ_{00}	12.09	0.71	69.05	16.94	<.001	[10.67, 13.52]
Difference Score, γ_{01}	-0.31	0.13	69.92	-2.32	.023	[-0.57, -0.04]
Tx, γ_{02}	-2.53	0.98	68.72	-2.59	.012	[-4.48, -0.58]
Linear Growth						
Time, γ_{10}	1.15	0.10	46.03	10.98	<.001	[0.94, 1.36]
*Time*Difference Score,* γ_{11}	0.06	0.02	48.81	2.69	.010	[0.01, 0.1]
*Time*Tx*, γ_{12}	-0.14	0.15	47.41	-.92	.363	[-0.45, 0.17]
Goodness-of-Fit						
-2 LL	969.13					[10.65, 13.71]
AIC	989.13					[0.4, 0.96]

Note. Difference Score refers to receptive-expressive language discrepancy score computed at T1 using Mullen age equivalent scores. Time was parameterized as months since T1, thus, estimates of initial status are estimates of language scores at T1. -2 LL = -2 Log Likelihood; AIC = Akaike information criterion.

Appendix

Table S1.1. *Descriptive Statistics for T1 Variables by Number of Timepoints Completed*

Variable	**Completed Three Visits** *n* = 38	**Completed Two Visits** *n* = 21	**Completed One Visit** *n* = 11	
	N (%)	*N* (%)	*N* (%)	*p*
Sex at birth = female	9 (27.3%)	3 (14.3%)	2 (18.2%)	.73
≥ 1 autistic sibling	13 (36.1%)	5 (25.0%)	1 (9.1%)	.76
≥ 1 parent completed college	33 (89.2%)	15 (78.9%)	8 (72.7%)	.23
Income > $100k	21 (58.3%)	10 (52.6%)	3 (37.5%)	.77
	M (SD)	*M* (SD)	*M* (SD)	*p*
T1 Chronological age, months	18.13 (2.68)	17.9 (3.06)	18.18 (3.68)	.95
T1 Receptive Language AE	11.32 (5.49)	9.86 (5.63)	9.36 (2.66)	.42
T1 Expressive Language AE	10.92 (4.38)	10.57 (4.51)	7.45 (2.58)	.06
T1 NVMA (Visual Reception AE)	15.58 (3.92)	13.71 (3.96)	13.36 (3.41)	.11
T1 ADOS-2 Total	17.39 (4.73)	18.29 (4.89)	18.91 (4.57)	.59

Note. Family history of autism, parental educational attainment, and income were derived from a demographic questionnaire completed at T1. ADOS-2 = Autism Diagnostic Observation Schedule, Second Edition; AE = age equivalent score; NVMA = nonverbal mental age.

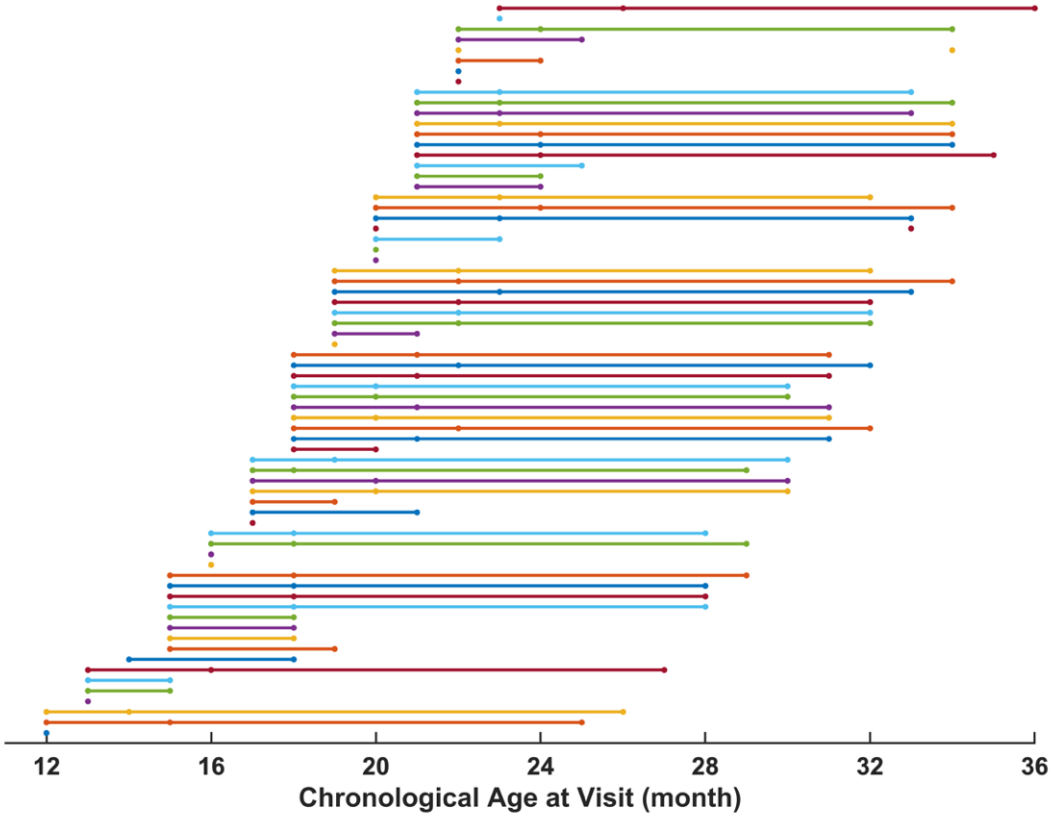

Figure S1.1. *Chronological age at study visit stratified by participant (N = 70).*

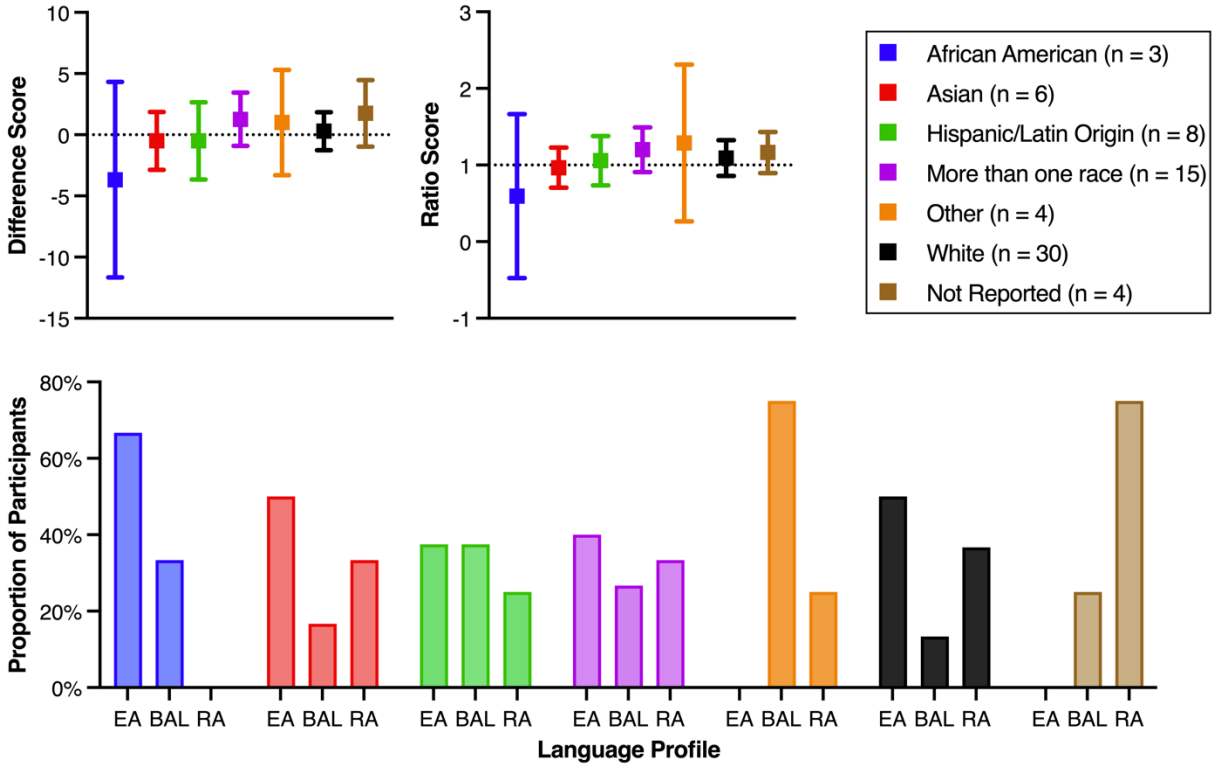

Figure S1.2. *Distribution of Difference Scores, Ratio Scores, and language profiles by race and ethnicity.*

References

Adamson, L. B., Bakeman, R., Deckner, D. F., & Romski, M. (2009). Joint engagement and the emergence of language in children with autism and down syndrome. *Journal of Autism and Developmental Disorders*, *39*(1), 84–96. https://doi.org/10.1007/s10803-008-0601-7

Adamson, L. B., Bakeman, R., Suma, K., & Robins, D. L. (2019). An expanded view of joint attention: skill, engagement, and language in typical development and autism. *Child Development*, *90*(1), e1–e18. https://doi.org/10.1111/cdev.12973

Algina, J., Keselman, H. J., & Penfield, R. D. (2005). An alternative to Cohen's standardized mean difference effect size: A robust parameter and confidence interval in the two independent groups case. *Psychological Methods*, *10*(3), 317–328. https://doi.org/10.1037/1082-989X.10.3.317

Anderson, D. K., Liang, J. W., & Lord, C. (2014). Predicting young adult outcome among more and less cognitively able individuals with autism spectrum disorders. *Journal of Child Psychology and Psychiatry*, *55*(5), 485–494. https://doi.org/10.1111/jcpp.12178

Anderson, D. K., Lord, C., Risi, S., DiLavore, P. S., Shulman, C., Thurm, A., … Pickles, A. (2007). Patterns of growth in verbal abilities among children with autism spectrum disorder. *Journal of Consulting and Clinical Psychology*, *75*(4), 594–604. https://doi.org/10.1037/0022-006X.75.4.594

Arutiunian, V., Lopukhina, A., Minnigulova, A., Shlyakhova, A., Davydova, E., Pereverzeva, D., … Dragoy, O. (2021). Expressive and receptive language in Russian primary-school-aged children with autism spectrum disorder. *Research in Developmental Disabilities*, *117*, 104042. https://doi.org/10.1016/j.ridd.2021.104042

Bacon, E. C., Moore, A., Lee, Q., Carter Barnes, C., Courchesne, E., & Pierce, K. (2020). Identifying prognostic markers in autism spectrum disorder using eye tracking. *Autism*, *24*(3), 658–669. https://doi.org/10.1177/1362361319878578

Bacon, E. C., Osuna, S., Courchesne, E., & Pierce, K. (2018). Naturalistic language sampling to characterize the language abilities of 3-year-olds with autism spectrum disorder. *Autism*. https://doi.org/10.1177/1362361318766241

Bal, V. H., Kim, S.-H., Cheong, D., & Lord, C. (2015). Daily living skills in individuals with autism spectrum disorder from 2 to 21 years of age. *Autism*, *19*(7), 774–784. https://doi.org/10.1177/1362361315575840

Bao, S., Sweatt, K. T., Lechago, S. A., & Antal, S. (2017). The effects of receptive and expressive instructional sequences on varied conditional discriminations. *Journal of Applied Behavior Analysis*, *50*(4), 775–788. https://doi.org/10.1002/jaba.404

Batki, A., Baron-Cohen, S., Wheelwright, S., Connellan, J., & Ahluwalia, J. (2000). Is there an innate gaze module? Evidence from human neonates. *Infant Behavior and Development*, *23*(2), 223–229. https://doi.org/10.1016/S0163-6383(01)00037-6

Bauer, D. J., Goldfield, B. A., & Reznick, J. S. (2002). Alternative approaches to analyzing individual differences in the rate of early vocabulary development. *Applied Psycholinguistics*, *23*(3), 313–335. https://doi.org/10.1017/S0142716402003016

Bedford, R., Elsabbagh, M., Gliga, T., Pickles, A., Senju, A., Charman, T., & Johnson, M. H. (2012). Precursors to social and communication difficulties in infants at-risk for autism: Gaze following and attentional engagement. *Journal of Autism and Developmental Disorders*, *42*(10), 2208–2218. https://doi.org/10.1007/s10803-012-1450-y

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

Belteki, Z., Lumbreras, R., Fico, K., Haman, E., & Junge, C. (2022). The vocabulary of infants with an elevated likelihood and diagnosis of autism spectrum disorder: A systematic review and meta-analysis of infant language studies using the CDI and MSEL.

International Journal of Environmental Research and Public Health, *19*(3), 1469. https://doi.org/10.3390/ijerph19031469

Bono, M. A., Daley, T., & Sigman, M. (2004). Relations among joint attention, amount of intervention and language gain in autism. *Journal of Autism and Developmental Disorders*, *34*(5), 495–505. https://doi.org/10.1007/s10803-004-2545-x

Bopp, K. D., & Mirenda, P. (2011). Prelinguistic predictors of language development in children with autism spectrum disorders over four-five years. *Journal of Child Language*, *38*(3), 485–503. https://doi.org/10.1017/S0305000910000140

Bopp, K. D., Mirenda, P., & Zumbo, B. D. (2009). Behavior predictors of language development over 2 years in children with autism spectrum disorders. *Journal of Speech, Language, and Hearing Research*, *52*(5), 1106–1120. https://doi.org/10.1044/1092-4388(2009/07-0262)

Bornstein, M. H., & Hendricks, C. (2012). Basic language comprehension and production in >100,000 young children from sixteen developing nations. *Journal of Child Language*, *39*(4), 899–918. https://doi.org/10.1017/S0305000911000407

Bottema-Beutel, K. (2016). Associations between joint attention and language in autism spectrum disorder and typical development: A systematic review and meta-regression analysis. *Autism Research*, *9*(10), 1021–1035. https://doi.org/10.1002/aur.1624

Bottema-Beutel, K., Lloyd, B., Watson, L., & Yoder, P. (2018). Bidirectional influences of caregiver utterances and supported joint engagement in children with and without autism spectrum disorder. *Autism Research*, *11*(5), 755–765. https://doi.org/10.1002/aur.1928

Bottema-Beutel, K., Woynaroski, T., Louick, R., Stringer Keefe, E., Watson, L. R., Yoder, P. J., … Bottema-Beutel, K. (2019). Longitudinal associations across vocabulary modalities in children with autism and typical development. *Autism*, *23*(2), 424–435. https://doi.org/10.1177/1362361317745856

Bricker, D., Pretti-Frontczak, K., Johnson, J., & Straka, E. (2002). *Assessment, Evaluation, and Programming System for Infants and Children, Second Edition* (2nd ed.). Baltimore: Paul H. Brookes Publishing.

Brignell, A., Williams, K., Jachno, K., Prior, M., Reilly, S., & Morgan, A. T. (2018). Patterns and predictors of language development from 4 to 7 years in verbal children with and without autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *48*(10), 3282–3295. https://doi.org/10.1007/s10803-018-3565-2

Bruyneel, E., Demurie, E., Warreyn, P., & Roeyers, H. (2019). The mediating role of joint attention in the relationship between motor skills and receptive and expressive language in siblings at risk for autism spectrum disorder. *Infant Behavior and Development*, *57*, 101377. https://doi.org/10.1016/j.infbeh.2019.101377

Bussu, G., Jones, E. J. H., Charman, T., Johnson, M. H., Buitelaar, J. K., Baron-Cohen, S., … Volein, A. (2018). Prediction of autism at 3 years from behavioural and developmental measures in high-risk infants: A Longitudinal cross-domain classifier analysis. *Journal of Autism and Developmental Disorders*, *48*(7), 2418–2433. https://doi.org/10.1007/s10803-018-3509-x

Chang, Y.-C., Shire, S. Y., Shih, W., Gelfand, C., & Kasari, C. (2016). Preschool deployment of evidence-based social communication intervention: JASPER in the Classroom. *Journal of Autism and Developmental Disorders*, *46*(6), 2211–2223. https://doi.org/10.1007/s10803-016-2752-2

Charman, T., Baron-Cohen, S., Swettenham, J., Baird, G., Drew, A., & Cox, A. (2003). Predicting language outcome in infants with autism and pervasive developmental disorder. *International Journal of Language and Communication Disorders*, *38*(3), 265–285. https://doi.org/10.1080/136820310000104830

Chawarska, K., MacAri, S., & Shic, F. (2012). Context modulates attention to social scenes in toddlers with autism. *Journal of Child Psychology and Psychiatry*, *53*(8), 903–913. https://doi.org/10.1111/j.1469-7610.2012.02538.x

Contaldo, A., Colombi, C., Pierotti, C., Masoni, P., & Muratori, F. (2020). Outcomes and moderators of Early Start Denver Model intervention in young children with autism spectrum disorder delivered in a mixed individual and group setting. *Autism: The International Journal of Research and Practice*, *24*(3), 718–729. https://doi.org/10.1177/1362361319888344

Crank, J. E., Sandbank, M., Dunham, K., Crowley, S., Bottema-Beutel, K., Feldman, J., & Woynaroski, T. G. (2021). Understanding the effects of naturalistic developmental behavioral interventions: A Project AIM meta-analysis. *Autism Research*, *14*(4), 817–834. https://doi.org/10.1002/aur.2471

Davidson, M. M., & Ellis Weismer, S. (2014). Characterization and prediction of early reading abilities in children on the autism spectrum. *Journal of Autism and Developmental Disorders*, *44*(4), 828–845. https://doi.org/10.1007/s10803-013-1936-2

Davidson, M. M., & Ellis Weismer, S. (2017). A discrepancy in comprehension and production in early language development in ASD: Is it clinically relevant? *Journal of Autism and Developmental Disorders*, *47*(7), 2163–2175. https://doi.org/10.1007/s10803-017-3135-z

Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., … Varley, J. (2010). Randomized, controlled trial of an intervention for toddlers with autism: The Early Start Denver Model. *PEDIATRICS*, *125*(1), e17–e23. https://doi.org/10.1542/peds.2009-0958

Edmunds, S. R., Ibañez, L. V., Warren, Z., Messinger, D. S., & Stone, W. L. (2017). Longitudinal prediction of language emergence in infants at high and low risk for autism spectrum disorder. *Development and Psychopathology*, *29*(1), 319–329. https://doi.org/10.1017/S0954579416000146

Ellis Weismer, S., Lord, C., Esler, A., Weismer, S. E., Lord, C., & Esler, A. (2010). Early language patterns of toddlers on the autism spectrum compared to toddlers with developmental delay. *Journal of Autism and Developmental Disorders*, *40*(10), 1259–1273. https://doi.org/10.1007/s10803-010-0983-1

Elsabbagh, M., Mercure, E., Hudry, K., Chandler, S., Pasco, G., Charman, T., … Johnson, M. H. (2012). Infant neural sensitivity to dynamic eye gaze is associated with later emerging autism. *Current Biology*, *22*(4), 338–342. https://doi.org/10.1016/j.cub.2011.12.056

Estes, A., Zwaigenbaum, L., Gu, H., St. John, T., Paterson, S., Elison, J. T., … Piven, J. (2015). Behavioral, cognitive, and adaptive development in infants with autism spectrum disorder in the first 2 years of life. *Journal of Neurodevelopmental Disorders*, *7*(1), 24–24. https://doi.org/10.1186/s11689-015-9117-6

Farroni, T., Csibra, G., Simion, F., & Johnson, M. H. (2002). Eye contact detection in humans from birth. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(14), 9602–9606. https://doi.org/10.1073/pnas.152159999

Fein, D., Pennington, B., Markowitz, P., Braverman, M., & Waterhouse, L. (1986). Toward a neuropsychological model of infantile autism: Are the social deficits primary? *Journal of the American Academy of Child Psychiatry*, *25*(2), 198–212. https://doi.org/10.1016/S0002-7138(09)60227-2

Filliter, J. H., Longard, J., Lawrence, M. A., Zwaigenbaum, L., Brian, J., Garon, N., … Bryson, S. E. (2015). Positive affect in infant siblings of children diagnosed with autism spectrum disorder. *Journal of Abnormal Child Psychology*, *43*(3), 567–575. https://doi.org/10.1007/s10802-014-9921-6

Frazier, T. W., Klingemier, E. W., Anderson, C. J., Gengoux, G. W., Youngstrom, E. A., & Hardan, A. Y. (2021). A longitudinal study of language trajectories and treatment outcomes of early intensive behavioral intervention for autism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-021-04900-5

Frost, K. M., Pomales-Ramos, A., & Ingersoll, B. (2022). Brief Report: Response to joint attention and object imitation as predictors of expressive and receptive language growth rate in young children on the autism spectrum. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-022-05567-2

Fuller, E. A., & Kaiser, A. P. (2020). The effects of early intervention on social communication outcomes for children with autism spectrum disorder: A meta-analysis. *Journal of Autism and Developmental Disorders*, *50*(5), 1683–1700. https://doi.org/10.1007/s10803-019-03927-z

Fusaroli, R., Weed, E., Fein, D., & Naigles, L. (2019). Hearing me hearing you: Reciprocal effects between child and parent language in autism and typical development. *Cognition*, *183*(September 2018), 1–18.

Gangi, D. N., Boterberg, S., Schwichtenberg, A. J., Solis, E., Young, G. S., Iosif, A.-M., & Ozonoff, S. (2021). Declining gaze to faces in infants developing autism spectrum disorder: Evidence from two independent cohorts. *Child Development*, *92*(3), e285–e295. https://doi.org/10.1111/cdev.13471

Gillespie-Lynch, K., Khalulyan, A., Del Rosario, M., McCarthy, B., Gomez, L., Sigman, M., & Hutman, T. (2015). Is early joint attention associated with school-age pragmatic language? *Autism*, *19*(2), 168–177. https://doi.org/10.1177/1362361313515094

Gillespie-Lynch, K., Sepeta, L., Wang, Y., Marshall, S., Gomez, L., Sigman, M., & Hutman, T. (2012). Early childhood predictors of the social competence of adults with autism. *Journal of Autism and Developmental Disorders*, *42*(2), 161–174. https://doi.org/10.1007/s10803-011-1222-0

Goldin-Meadow, S., Seligman, M. E. P., & Gelman, R. (1976). Language in the two-year old. *Cognition*, *4*(2), 189–202. https://doi.org/10.1016/0010-0277(76)90004-4

Green, J., Charman, T., McConachie, H., Aldred, C., Slonims, V., Howlin, P., … PACT Consortium. (2010). Parent-mediated communication-focused treatment in children with

autism (PACT): A randomised controlled trial. *Lancet (London, England)*, *375*(9732), 2152–2160. https://doi.org/10.1016/S0140-6736(10)60587-9

Grigorenko, E. L., Klin, A., Pauls, D. L., Senft, R., Hooper, C., & Volkmar, F. (2002). A descriptive study of hyperlexia in a clinically referred sample of children with developmental delays. *Journal of Autism and Developmental Disorders*, *32*(1), 3–12. https://doi.org/10.1023/A:1017995805511

Hardan, A. Y., Gengoux, G. W., Berquist, K. L., Libove, R. A., Ardel, C. M., Phillips, J., … Minjarez, M. B. (2015). A randomized controlled trial of Pivotal Response Treatment Group for parents of children with autism. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *56*(8), 884–892. https://doi.org/10.1111/jcpp.12354

Harrop, C., Libsack, E., Bernier, R., Dapretto, M., Jack, A., McPartland, J. C., … the, G. C. (2021). Do biological sex and early developmental milestones predict the age of first concerns and eventual diagnosis in autism spectrum disorder? *Autism Research*, *14*(1), 156–168. https://doi.org/10.1002/aur.2446

Hatch, B., Iosif, A.-M., Chuang, A., de la Paz, L., Ozonoff, S., & Miller, M. (2021). Longitudinal differences in response to name among infants developing ASD and risk for ADHD. *Journal of Autism and Developmental Disorders*, *51*(3), 827–836. https://doi.org/10.1007/s10803-020-04369-8

Howlin, P. (2003). Outcome in high-functioning adults with autism with and without early language delays: Implications for the differentiation between autism and asperger syndrome. *Journal of Autism and Developmental Disorders*, *33*(1), 3–13. https://doi.org/10.1023/A:1022270118899

Huberty, S., O'Reilly, C., Carter Leno, V., Steiman, M., Webb, S., & Elsabbagh, M. (2023). Neural mechanisms of language development in infancy. *Infancy*, *Advance online publication.* https://doi.org/10.1111/infa.12540

Hudry, K., Chandler, S., Bedford, R., Pasco, G., Gliga, T., Elsabbagh, M., … Charman, T. (2014). Early language profiles in infants at high-risk for autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *44*(1), 154–167. https://doi.org/10.1007/s10803-013-1861-4

Hudry, K., Leadbitter, K., Temple, K., Slonims, V., McConachie, H., Aldred, C., … Charman, T. (2010). Preschoolers with autism show greater impairment in receptive compared with expressive language abilities. *International Journal of Language and Communication Disorders*, *45*(6), 681–690. https://doi.org/10.3109/13682820903461493

Iverson, J. M., Northrup, J. B., Leezenbaum, N. B., Parladé, M. V., Koterba, E. A., & West, K. L. (2018). Early gesture and vocabulary development in infant siblings of children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *48*(1), 55–71. https://doi.org/10.1007/s10803-017-3297-8

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience*, *6*(10), 766–774. https://doi.org/10.1038/nrn1766

Jones, W., & Klin, A. (2013). Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism. *Nature*, *504*(7480), 427–431. https://doi.org/10.1038/nature12715

Kasari, C., Gulsrud, A. C., Wong, C., Kwon, S., & Locke, J. (2010). Randomized controlled caregiver mediated joint engagement intervention for toddlers with autism. *Journal of Autism and Developmental Disorders*, *40*(9), 1045–1056. https://doi.org/10.1007/s10803-010-0955-5

Kasari, C., Gulsrud, A., Freeman, S., Paparella, T., & Hellemann, G. (2012). Longitudinal follow-up of children with autism receiving targeted interventions on joint attention and play. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(5), 487–495. https://doi.org/10.1016/j.jaac.2012.02.019

Kasari, C., Gulsrud, A., Shire, S., & Strawbridge, C. (2022). *The JASPER Model for Children with Autism: Promoting Joint Attention, Symbolic Play, Engagement, and Regulation*. New York: Guilford Press.

Kasari, C., Paparella, T., Freeman, S., & Jahromi, L. B. (2008). Language outcome in autism: Randomized comparison of joint attention and play interventions. *Journal of Consulting and Clinical Psychology*, *76*(1), 125–137. https://doi.org/10.1037/0022-006X.76.1.125

Kenworthy, L., Wallace, G. L., Powell, K., Anselmo, C., Martin, A., & Black, D. O. (2012). Early language milestones predict later language, but not autism symptoms in higher functioning children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *6*(3), 1194–1202. https://doi.org/10.1016/j.rasd.2012.03.009

Kim, S. H., Bal, V. H., & Lord, C. (2018). Longitudinal follow-up of academic achievement in children with autism from age 2 to 18. *Journal of Child Psychology and Psychiatry*, *59*(3), 258–267. https://doi.org/10.1111/jcpp.12808

Kjelgaard, M. M., & Tager-Flusberg, H. (2001). An investigation of language impairment in autism: Implications for genetic subgroups. *Language and Cognitive Processes*, *16*(2–3), 287–308. https://doi.org/10.1080/01690960042000058

Kover, S. T., Edmunds, S. R., & Ellis Weismer, S. (2016). Brief Report: ages of language milestones as predictors of developmental trajectories in young children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *46*(7), 2501–2507. https://doi.org/10.1007/s10803-016-2756-y

Kover, S. T., McDuffie, A. S., Hagerman, R. J., & Abbeduto, L. (2013). Receptive vocabulary in boys with autism spectrum disorder: Cross-sectional developmental trajectories. *Journal of Autism and Developmental Disorders*, *43*(11), 2696–2709. https://doi.org/10.1007/s10803-013-1823-x

Kuhl, P. K. (2011). Social mechanisms in early language acquisition: Understanding integrated brain systems supporting language. *The Oxford Handbook of Social Neuroscience.*, 649–667.

Landa, R. J., Gross, A. L., Stuart, E. A., & Faherty, A. (2013). Developmental trajectories in children with and without autism spectrum disorders: The first 3 years. *Child Development*, *84*(2), 429–442. https://doi.org/10.1111/j.1467-8624.2012.01870.x

Landa, R. J., Holman, K. C., & Garrett-Mayer, E. (2007). Social and communication development in toddlers with early and later diagnosis of autism spectrum disorders. *Archives of General Psychiatry*. https://doi.org/10.1001/archpsyc.64.7.853

Lebarton, E. S., & Iverson, J. M. (2013). Fine motor skill predicts expressive language in infant siblings of children with autism. *Developmental Science*, *16*(6), 815–827. https://doi.org/10.1111/desc.12069

Leonard, H. C., Bedford, R., Pickles, A., Hill, E. L., & BASIS Team, the. (2015). Predicting the rate of language development from early motor skills in at-risk infants who develop autism spectrum disorder. *Research in Autism Spectrum Disorders*, *13–14*, 15–24. https://doi.org/10.1016/j.rasd.2014.12.012

Levin, A. R., Varcin, K. J., O'Leary, H. M., Tager-Flusberg, H., & Nelson, C. A. (2017). EEG power at 3 months in infants at high familial risk for autism. *Journal of Neurodevelopmental Disorders*, *9*(1), 34. https://doi.org/10.1186/s11689-017-9214-9

Lombardo, M. V., Busuoli, E. M., Schreibman, L., Stahmer, A. C., Pramparo, T., Landi, I., … Pierce, K. (2021). Pre-treatment clinical and gene expression patterns predict developmental change in early intervention in autism. *Molecular Psychiatry*, *26*(12), 7641–7651. https://doi.org/10.1038/s41380-021-01239-2

Longard, J., Brian, J., Zwaigenbaum, L., Duku, E., Moore, C., Smith, I. M., … Bryson, S. (2017). Early expressive and receptive language trajectories in high-risk infant siblings of

children with autism spectrum disorder. *Autism & Developmental Language Impairments*, *2*. https://doi.org/10.1177/2396941517737418

Lord, C., Risi, S., DiLavore, P. S., Shulman, C., Thurm, A., & Pickles, A. (2006). Autism from 2 to 9 years of age. *Archives of General Psychiatry*, *63*(6), 694–701. https://doi.org/10.1001/archpsyc.63.6.694

Lord, C., Rutter, M., DiLavore, P. S., Risi, S., Gotham, K., & Bishop, S. (2012). *Autism Diagnostic Observation Schedule, Second Edition (ADOS-2)*. Torrance, CA: Western Psychological Services.

Luyster, R. J., Kadlec, M. B., Carter, A., Tager-Flusberg, H., Ae, R. J. L., Beth, M., … Tager-Flusberg, H. (2008). Language assessment and development in toddlers with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *38*(8), 1426–1438. https://doi.org/10.1007/s10803-007-0510-1

Mair, P., & Wilcox, R. (2020). Robust statistical methods in R using the WRS2 package. *Behavior Research Methods*, *52*(2), 464–488. https://doi.org/10.3758/s13428-019-01246-w

Malesa, E., Foss-Feig, J., Yoder, P., Warren, Z., Walden, T., & Stone, W. L. (2013). Predicting language and social outcomes at age 5 for later-born siblings of children with autism spectrum disorders. *Autism: The International Journal of Research and Practice*, *17*(5), 558–570. https://doi.org/10.1177/1362361312444628

Maljaars, J., Noens, I., Scholte, E., & Berckelaer-Onnes, I. V. (2012). Language in low-functioning children with autistic disorder: Differences between receptive and expressive skills and concurrent predictors of language. *Journal of Autism and Developmental Disorders*, *42*(10), 2181–2191. https://doi.org/10.1007/s10803-012-1476-1

Mayo, J., Chlebowski, C., Fein, D. A., & Eigsti, I. M. (2013). Age of first words predicts cognitive ability and adaptive skills in children with ASD. *Journal of Autism and Developmental Disorders*, *43*(2), 253–264. https://doi.org/10.1007/s10803-012-1558-0

McDaniel, J., Yoder, P., Woynaroski, T., & Watson, L. R. (2018). Predicting receptive–expressive vocabulary discrepancies in preschool children with autism spectrum disorder. *Journal of Speech, Language, and Hearing Research*, *61*(6), 1426–1439. https://doi.org/10.1044/2018_JSLHR-L-17-0101

Mitchell, S., Brian, J., Zwaigenbaum, L., Roberts, W., Szatmari, P., Smith, I., & Bryson, S. (2006). Early language and communication development of infants later diagnosed with autism spectrum disorder. *Journal of Developmental & Behavioral Pediatrics*, *27*, S69–S78. https://doi.org/10.1097/00004703-200604002-00004

Mullen, E. M. (1995). Manual for the Mullen Scales of Early Learning. *Circle Pines, MN: American Guidance.*

Mundy, P., Delgado, C., Block, J., Venezia, M., Hogan, A., & Seibert, J. (2003). *The Early Social Communication Scales*. University of Miami.

Mundy, P., Sigman, M., & Kasari, C. (1990). A longitudinal study of joint attention and language development in autistic children. *Journal of Autism and Developmental Disorders*, *20*(1), 115–128. https://doi.org/10.1007/BF02206861

Munson, Jeffrey, Dawson, G., Sterling, L., Beauchaine, T., Zhou, A., … Abbott, R. (2008). Evidence for latent classes of IQ in young children with Autism Spectrum Disorder. *American Journal on Mental Retardation*, *113*(5), 439–452. https://doi.org/10.1352/2008.113

Nevill, R., Hedley, D., Uljarević, M., Sahin, E., Zadek, J., Butter, E., … Butter, E. (2019). Language profiles in young children with autism spectrum disorder: A community sample using multiple assessment instruments. *Autism*, *23*(1), 141–153. https://doi.org/10.1177/1362361317726245

Norrelgen, F., Fernell, E., Eriksson, M., Hedvall, Å., Persson, C., Sjölin, M., … Norrelgen, F. (2015). Children with autism spectrum disorders who do not develop phrase speech in

the preschool years. *Autism*, *19*(8), 934–943. https://doi.org/10.1177/1362361314556782

Northrup, J. B., & Iverson, J. M. (2015). Vocal coordination during early parent-infant interactions predicts language outcome in infant siblings of children with autism spectrum disorder. *Infancy*, *20*(5), 523–547. https://doi.org/10.1111/infa.12090

Ohashi, J. K., Mirenda, P., Marinova-Todd, S., Hambly, C., Fombonne, E., Szatmari, P., … Thompson, A. (2012). Comparing early language development in monolingual- and bilingual- exposed young children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *6*(2), 890–897. https://doi.org/10.1016/j.rasd.2011.12.002

Ostrolenk, A., Forgeot d'Arc, B., Jelenic, P., Samson, F., & Mottron, L. (2017). Hyperlexia: Systematic review, neurocognitive modelling, and outcome. *Neuroscience & Biobehavioral Reviews*, *79*, 134–149. https://doi.org/10.1016/j.neubiorev.2017.04.029

Ozonoff, S., Iosif, A.-M., Baguio, F., Cook, I. C., Hill, M. M., Hutman, T., … Young, G. S. (2010). A prospective study of the emergence of early behavioral signs of autism. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*(3), 256-266.e2. https://doi.org/10.1016/j.jaac.2009.11.009

Ozonoff, S., Young, G. S., Belding, A., Hill, M., Hill, A., Hutman, T., … Iosif, A. M. (2014). The broader autism phenotype in infancy: When does it emerge? *Journal of the American Academy of Child and Adolescent Psychiatry*, *53*(4), 398–407. https://doi.org/10.1016/j.jaac.2013.12.020

Ozonoff, S., Young, G. S., Carter, A., Messinger, D., Yirmiya, N., Zwaigenbaum, L., … Stone, W. L. (2011). Recurrence risk for autism spectrum disorders: A baby siblings research consortium study. *Pediatrics*, *128*(3). https://doi.org/10.1542/peds.2010-2825

Ozonoff, S., Young, G. S., Landa, R. J., Brian, J., Bryson, S., Charman, T., … Iosif, A.-M. (2015). Diagnostic stability in young children at risk for autism spectrum disorder: A Baby

Siblings Research Consortium study. *Journal of Child Psychology and Psychiatry*, *56*(9), 988–998. https://doi.org/10.1111/jcpp.12421

Panganiban, J., & Kasari, C. (2022). Super responders: Predicting language gains from JASPER among limited language children with autism spectrum disorder. *Autism Research*, *15*(8), 1565–1575. https://doi.org/10.1002/aur.2727

Paterson, S. J., Wolff, J. J., Elison, J. T., Winder-Patel, B., Zwaigenbaum, L., Estes, A., … IBIS Network. (2019). The importance of temperament for understanding early manifestations of autism spectrum disorder in high-risk infants. *Journal of Autism and Developmental Disorders*, *49*(7), 2849–2863. https://doi.org/10.1007/s10803-019-04003-2

Paul, R., Fuerst, Y., Ramsay, G., Chawarska, K., & Klin, A. (2011). Out of the mouths of babes: Vocal production in infant siblings of children with ASD. *Journal of Child Psychology and Psychiatry*, *52*(5), 588–598. https://doi.org/10.1111/j.1469-7610.2010.02332.x

Pegg, J. E., Werker, J. F., & McLeod, P. J. (1992). Preference for infant-directed over adult-directed speech: Evidence from 7-week-old infants. *Infant Behavior and Development*, *15*(3), 325–345. https://doi.org/10.1016/0163-6383(92)80003-D

Pickles, A., Anderson, D. K., & Lord, C. (2014). Heterogeneity and plasticity in the development of language: A 17-year follow-up of children referred early for possible autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *55*(12), 1354–1362. https://doi.org/10.1111/jcpp.12269

Pickles, A., Wright, N., Bedford, R., Steiman, M., Duku, E., Bennett, T., … Team, P. in A. S. (2022). Predictors of language regression and its association with subsequent communication development in children with autism. *Journal of Child Psychology and Psychiatry*, *63*(11), 1243–1251. https://doi.org/10.1111/jcpp.13565

Pierce, K., Wen, T. H., Zahiri, J., Andreason, C., Courchesne, E., Barnes, C. C., … Cheng, A. (2023). Level of attention to motherese speech as an early marker of autism spectrum disorder.

JAMA Network Open, *6*(2), e2255125. https://doi.org/10.1001/jamanetworkopen.2022.55125

Plate, S., Yankowitz, L., Resorla, L., Swanson, M. R., Meera, S. S., Estes, A., … Network, I. (2021). Infant vocalizing and phenotypic outcomes in autism: Evidence from the first 2 years. *Child Development*, *n/a*(n/a). https://doi.org/10.1111/cdev.13697

Prescott, K. E., & Ellis Weismer, S. (2022). Children with ASD and communication regression: Examining pre-loss skills and later language outcomes through the preschool years. *Journal of Autism and Developmental Disorders*, *52*(5), 1956–1970. https://doi.org/10.1007/s10803-021-05098-2

R Core Team. (2021). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.R-project.org/

Raudenbush, S. W., & Bryk, A. (2005). *Hierarchical Linear Models: Applications and Data Analysis Methods* (2nd ed.). Thousand Oaks, CA: SAGE Publications.

Reinhartsen, D. B., Tapia, A. L., Watson, L., Crais, E., Bradley, C., Fairchild, J., … Daniels, J. (2019). Expressive dominant versus receptive dominant language patterns in young children: Findings from the Study to Explore Early Development. *Journal of Autism and Developmental Disorders*, *49*(6), 2447–2460. https://doi.org/10.1007/s10803-019-03999-x

Rogers, S. J., Yoder, P., Estes, A., Warren, Z., McEachin, J., Munson, J., … Whelan, F. (2021). A multisite randomized controlled trial comparing the effects of intervention intensity and intervention style on outcomes for young children with autism. *Journal of the American Academy of Child & Adolescent Psychiatry*, *60*(6), 710–722. https://doi.org/10.1016/j.jaac.2020.06.013

Rozga, A., Hutman, T., Young, G. S., Rogers, S. J., Ozonoff, S., Dapretto, M., & Sigman, M. (2011). Behavioral profiles of affected and unaffected siblings of children with autism: Contribution of measures of mother–infant interaction and nonverbal communication. *Journal of*

Autism and Developmental Disorders, *41*(3), 287–301. https://doi.org/10.1007/s10803-010-1051-6

Sandbank, M., Bottema, -Beutel Kristen, Crowley, S., Cassidy, M., Feldman, J. I., Canihuante, M., & Woynaroski, T. (2020). Intervention effects on language in children with autism: A Project AIM meta-analysis. *Journal of Speech, Language, and Hearing Research*, *63*(5), 1537–1560. https://doi.org/10.1044/2020_JSLHR-19-00167

Schreibman, L., Dawson, G., Stahmer, A. C., Landa, R., Rogers, S. J., McGee, G. G., … Halladay, A. (2015). naturalistic developmental behavioral interventions: Empirically Validated treatments for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *45*(8), 2411–2428. https://doi.org/10.1007/s10803-015-2407-8

Seery, A., Vogel-Farley, V., Tager-Flusberg, H., & Nelson, C. A. (2013). Atypical lateralization of ERP response to native and non-native speech in infants at risk for autism spectrum disorder. *Developmental Cognitive Neuroscience*, *5*, 10–24. https://doi.org/10.1016/j.dcn.2012.11.007

Seol, K. I., Song, S. H., Kim, K. L., Oh, S. T., Kim, Y. T., Im, W. Y., … Cheon, K.-A. (2014). A comparison of receptive-expressive language profiles between toddlers with autism spectrum disorder and developmental language delay. *Yonsei Medical Journal*, *55*(6), 1721–1728. https://doi.org/10.3349/ymj.2014.55.6.1721

Singer, J., & Willet, J. (2003). *Applied Longitudinal Data Analysis*. New York, NY: Oxford University Press.

Smith, V., Mirenda, P., & Zaidman-Zait, A. (2007). Predictors of expressive vocabulary growth in children with autism. *Journal of Speech, Language, and Hearing Research*, *50*(1), 149–160. https://doi.org/10.1044/1092-4388(2007/013)

Sterrett, K., Magaña, M. T., Gulsrud, A., Paparella, T., & Kasari, C. (2022). Predictors of attrition in a randomized trial of a social communication intervention for infant-toddlers at risk for

autism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-022-05616-w

Stone, W., & Yoder, P. (2001). Predicting spoken language in children with autism. *Autism*, *5*(4), 341–361.

Swanson, M. R. (2020). The role of caregiver speech in supporting language development in infants and toddlers with autism spectrum disorder. *Development and Psychopathology*, *32*(4), 1230–1239. https://doi.org/10.1017/S0954579420000838

Swanson, M. R., Shen, M. D., Wolff, J. J., Elison, J. T., Emerson, R. W., Styner, M. A., … Gu, H. (2017). Subcortical brain and behavior phenotypes differentiate infants with autism versus language delay. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *2*(8), 664–672. https://doi.org/10.1016/j.bpsc.2017.07.007

Swineford, L. B., Guthrie, W., & Thurm, A. (2015). Convergent and divergent validity of the mullen scales of early learning in young children with and without autism spectrum disorder. *Psychological Assessment*, *27*(4), 1364–1378. https://doi.org/10.1037/pas0000116

Talbott, M. R., Nelson, C. A., & Tager-Flusberg, H. (2015). Maternal vocal feedback to 9-month-old infant siblings of children with ASD. *Autism Research*, *9*(4), 460–470. https://doi.org/10.1002/aur.1521

Thorup, E., Nyström, P., Gredebäck, G., Bölte, S., Falck-Ytter, T., & the EASE Team. (2018). Reduced alternating gaze during social interaction in infancy is associated with elevated symptoms of autism in toddlerhood. *Journal of Abnormal Child Psychology*, *46*(7), 1547–1561. https://doi.org/10.1007/s10802-017-0388-0

Thurm, A., Lord, C., Lee, L.-C. C., & Newschaffer, C. (2007). Predictors of language acquisition in preschool children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *37*(9), 1721–1734. https://doi.org/10.1007/s10803-006-0300-1

Thurm, A., Manwaring, S. S., Swineford, L., & Farmer, C. (2015). Longitudinal study of symptom severity and language in minimally verbal children with autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *56*(1), 97–104. https://doi.org/10.1111/jcpp.12285

Tiura, M., Kim, J., Detmers, D., & Baldi, H. (2017). Predictors of longitudinal ABA treatment outcomes for children with autism: A growth curve analysis. *Research in Developmental Disabilities*, *70*, 185–197. https://doi.org/10.1016/j.ridd.2017.09.008

Toth, K., Geraldine, A. E., Ae, D., Meltzoff, A. N., Jessica, A. E., Ae, G., & Fein, D. (2007). Early Social, Imitation, Play, and Language Abilities of Young Non-Autistic Siblings of Children with Autism. https://doi.org/10.1007/s10803-006-0336-2

Toth, K., Munson, J., Meltzoff, A. N., Dawson, G., N. Meltzoff, A., & Dawson, G. (2006). Early predictors of communication development in young children with autism spectrum disorder: Joint attention, imitation, and toy play. *Journal of Autism and Developmental Disorders*, *36*(8), 993–1005. https://doi.org/10.1007/s10803-006-0137-7

Volden, J., Smith, I. M., Szatmari, P., Bryson, S., Fombonne, E., Mirenda, P., … Thompson, A. (2011). Using the Preschool Language Scale, Fourth Edition to characterize language in preschoolers with autism spectrum disorders. *American Journal of Speech-Language Pathology*, *20*(3), 200–208. https://doi.org/10.1044/1058-0360(2011/10-0035)

Watters, R. G., Wheeler, L. J., & Watters, W. E. (1981). The relative efficiency of two orders for training autistic children in the expressive and receptive use of manual signs. *Journal of Communication Disorders*, *14*(4), 273–285. https://doi.org/10.1016/0021-9924(81)90012-5

Westerveld, M. F., Paynter, J., Trembath, D., Webster, A. A., Hodge, A. M., & Roberts, J. (2017). The emergent literacy skills of preschool children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *47*(2), 424–438. https://doi.org/10.1007/s10803-016-2964-5

Wickstrom, J., Farmer, C., Green Snyder, L., Mitz, A. R., Sanders, S. J., Bishop, S., & Thurm, A. (2021). Patterns of delay in early gross motor and expressive language milestone attainment in probands with genetic conditions versus idiopathic ASD from SFARI registries. *Journal of Child Psychology and Psychiatry*, *62*(11), 1297–1307. https://doi.org/10.1111/jcpp.13492

Wilcox, R. R. (2023). *A Robust Guide to Statistical Methods*. Switzerland: Springer Nature.

Woynaroski, T., Yoder, P., & Watson, L. R. (2016). Atypical cross-modal profiles and longitudinal associations between vocabulary scores in initially minimally verbal children with ASD. *Autism Research*, *9*(2), 301–310. https://doi.org/10.1002/aur.1516

Wynn, J. W., & Smith, T. (2003). Generalization between receptive and expressive language in young children with autism. *Behavioral Interventions*, *18*(4), 245–266. https://doi.org/10.1002/bin.142

Yankowitz, L. D., Petrulla, V., Plate, S., Tunc, B., Guthrie, W., Meera, S. S., … Parish-Morris, J. (2022). Infants later diagnosed with autism have lower canonical babbling ratios in the first year of life. *Molecular Autism*, *13*(1), 1–16. https://doi.org/10.1186/s13229-022-00503-8

STUDY 2

Neural Mechanisms Supporting Language Development in Infants and Toddlers with Autism Symptoms

Abstract

Increasing evidence suggests that early differences in functional brain development precede the emergence of autism behavioral features and other autism-associated developmental differences in early toddlerhood. As such, there is intense interest in identifying brain-based markers that can, in isolation or conjunction with other clinical markers, facilitate early identification of infants and toddlers at the highest risk of experiencing early language delays who may benefit from targeted early intervention.

Motivated by this gap, Study 2 builds on findings from Study 1 by testing whether patterns of spontaneous oscillatory power measured at baseline (T1) are associated with (1) concurrent receptive-expressive language phenotypes and (2) longitudinal growth in receptive and expressive language abilities among *N* = 70 infants and toddlers aged 12- to 23-months with autism symptoms. Data-driven analyses revealed significant associations between spontaneous theta (3-6 Hz) power and concurrent receptive-expressive language phenotypes, and robust, positive associations between spontaneous alpha power (6-9 Hz) measured at baseline (T1) and receptive and expressive language growth. These findings are particularly striking, given that Studies 1 and 2 found little evidence for associations between baseline (T1) *behavioral* predictors of receptive-expressive phenotypes and language growth. This study is a critical step toward understanding neural mechanisms driving typical and atypical language development in emerging autism and developing early markers to identify children who may benefit the most from interventions targeting spoken communication.

Neural Mechanisms Supporting Language Development in Infants and Toddlers with Autism Symptoms

Language delays are highly prevalent among infants and toddlers with autism or children with an elevated familial likelihood of autism (EL; Belteki, Lumbreras, Fico, Haman, & Junge, 2022; Marrus et al., 2018). Disruptions to language development are apparent as early as 12 months among infants later diagnosed with autism (Bussu et al., 2019; Franchini et al., 2018; Ozonoff et al., 2010), and children with autism often lag behind non-autistic peers in the acquisition of key language milestones, like first words (Kover, Edmunds, & Ellis Weismer, 2016). These early social differences are highly consequential for longer-term developmental outcomes in autism, as language abilities in toddlerhood are a robust predictor of long-term functioning and behavioral outcomes (Bal, Kim, Cheong, & Lord, 2015; Gillespie-Lynch et al., 2012; Gotham, Pickles, & Lord, 2012).

As language differences are often apparent before the age at which an autism diagnosis is made, there is intense interest in identifying behavioral and biological factors that contribute to between- and within-individual heterogeneity in early language abilities. The emergence of spoken language over the first and second years of life coincides with dynamic changes in structural and functional networks that support information processing capacities essential for social communication and spoken language. Understanding these neural network changes in autism could provide valuable mechanistic insight into the neural origins of language differences in autism and help identify objective prognostic markers.

Electroencephalographic (EEG) Markers of Autism in Infancy

EEG is a well-established, noninvasive technique that has been extensively used in infant research and is both scalable and highly sensitive to early developmental changes in functional circuitry. Noninvasive electroencephalography (EEG) has been invaluable in shaping our understanding of typical and atypical neurodevelopment across the lifespan and neural underpinnings of various cognitive, social, and behavioral operations and capacities.

Spontaneous or "resting state" EEG captures brain dynamics in the absence of overt tasks or cognitive demands by measuring electrical activity produced by populations of neurons in the cortex. These brain rhythms, or neural oscillations, refer to rhythmic fluctuations in the excitability of populations of neurons. At the most basic level, neural oscillations arise from shifts in excitatory-inhibitory states within populations of neurons (Buzsáki, 2011). EEG measures these electrical fields generated by neural populations through electrodes placed directly on the scalp. Whereas other neuroimaging methods offer an indirect index of neural activity by measuring peripheral processes associated with neural events (e.g., hemodynamic response, as in fMRI), EEG measures neural activity more directly and offers superior temporal resolution to methods like fMRI. Whereas task-based EEG studies provide valuable insight into mechanisms underpinning the processing of linguistic stimuli, for example, spontaneous EEG provides important insight into the intrinsic functional architecture of the developing brain that subserves the emergence of increasingly complex cognitive, social, and behavioral capacities across the first years of life (Anderson & Perone, 2018). The desirable psychometric properties of specific EEG metrics derived resting state EEG, including excellent test-retest reliability in infants and children (Levin et al., 2020; van der Velde, Haartsen, & Kemner, 2019), make it particularly well-suited for studies aimed at understanding individual differences or developing reliable, reproducible prognostic or predictive biomarkers.

Across the first years of life, patterns of brain activity measured via EEG undergo dramatic reorganization, reflecting the maturation of underlying cortical structure and refinement of neural circuitry. This reorganization is characterized by a shift in the distribution of spectral power from lower frequencies (below 6 Hz) towards higher frequencies (Marshall, Bar-Haim, & Fox, 2002), a change that unfolds alongside the emergence of major social and communication milestones (Anderson & Perone, 2018; Saby & Marshall, 2012). Increasing evidence from studies using EEG suggests infants with familial or genetic risk of autism show alterations in brain development early in the first year of life, even though overt behavioral signs of autism are

not evident until after 12 months. These studies have provided critical insight into emerging functional brain differences in autism (that is, brain markers associated with autism as a categorical diagnosis) and insight into heterogeneity in cognitive and behavioral development *within* the diagnostic category of autism.

Oscillatory activity within specific frequency bands (e.g., alpha, theta) or across the frequency spectrum has been studied extensively in children and adults with autism. For instance, evidence suggests autism is associated with a pattern of excessive power concentrated in lower frequency bands (e.g., delta, theta bands), an overall reduction in absolute and relative alpha power (typically defined as 6-12 Hz in adults, or 6-9 Hz among infants), differences in the spatial distribution of spectral power (i.e., hemispheric asymmetry), and reduced long-range coherence patterns, possibly coupled with enhanced short-range coherence (Wang et al., 2013).

In infancy, alterations in spectral power and the rate of developmental change thereof are evident among EL infants, often regardless of whether they develop autism in toddlerhood. Tierney et al. (2012) examined developmental trajectories of frontal spectral power (absolute power in delta, theta, alpha, beta, and gamma bands) among EL infants from 6 to 24 months of age. They reported that EL infants displayed lower frontal power across all bands at six months and showed marked differences in trajectories of change in frontal power across the first two years relative to infants without a family history of autism (low familial likelihood of autism, LL). In a more extensive study of EL and LL infants, including 61 later diagnosed with autism, (Huberty et al., 2021) also found EL infants have significantly lower absolute power at three months across all frequency bands and significantly steeper increase in absolute power from 3 - 36 months relative to LL infants. However, initial spectral power and developmental change in power were not associated with autism diagnostic outcome specifically, suggesting the effect of autism itself did not lead to alterations in brain development above and beyond the effect of familial genetic liability for autism.

Similarly, Levin et al. (2017) examined associations between resting frontal power at three months and later diagnostic and developmental outcomes among EL and LL infants. Again, diagnostic effects on spectral power were not observed. However, Dickinson et al. (2020) observed significant correlations between patterns of functional connectivity at three months (specifically, lower frontal connectivity and higher right temporoparietal connectivity) and elevated autism symptom severity at 18 months among EL and LL infants, suggesting that dimensional outcomes (rather than categorical, diagnostic outcomes) may be more valuable in shedding light on brain-behavior associations. The presence of *increased* right temporoparietal connectivity among infants with elevated autism symptoms later in toddlerhood is noteworthy, particularly given the importance of this region for social cognition (Adolphs, 2008) and evidence for *hypoconnectivity* later in toddlerhood (Dickinson, DiStefano, Lin, et al., 2018). While seemingly paradoxical, these findings fit well with the "developmental delay *versus* deviance" phenomenon discussed at length in the context of cognitive and behavioral development in autism (e.g., Baron-Cohen, 1991; Bartak et al., 1975) and the ontogenetic adaptation hypothesis previously discussed. That is, brain development in autism may be characterized by both slower and faster developmental timescales, where some aspects of structural/functional development emerge later or more slowly in autism, and others unfold earlier or on a faster timescale. These altered timescales, in turn, influence what infants are prepared to "learn" from their environment, thereby shaping subsequent cognitive and behavioral development.

EEG Predictors of Early Language Development in Autism

Significant developmental changes in the distribution of spectral power (e.g., maturation-related increase in the contribution of higher-frequency oscillations to the infant/toddler EEG power spectrum) coincide with sensitive periods for language acquisition across the first three years of life. For instance, the dominance of slow-frequency activity during the first six months may serve an adaptive purpose for language acquisition, ensuring the infant brain is well-equipped to process the temporal and acoustical properties of language input during this period

(i.e., infant-directed speech; Goswami, 2019; Menn et al., 2022). In turn, the emergence of faster oscillations towards the end of the first year is thought to support more complex processing capacities necessary for acquiring language and developing "expertise" in one's native language (Menn, Mannel, & Meyer, 2023; Ortiz-Mantilla, Hämäläinen, Realpe-Bonilla, & Benasich, 2016). Alterations in electrophysiological development associated with genetic risk of autism (Wang et al., 2013) may play a role in shaping language development in autism.

Evidence from prospective studies of EL infant siblings suggests activity within the alpha (Huberty et al., 2023; Levin et al., 2017; Tran et al., 2021), theta (Wilkinson et al., 2020), and gamma (Romeo et al., 2021; Wilkinson et al., 2019; Wilkinson et al., 2020) frequency bands are linked with concurrent or later expressive language skills in infancy and toddlerhood. For instance, converging evidence across unique samples suggests that absolute power (Huberty et al., 2023; Levin et al., 2017) and functional connectivity (Tran et al., 2021) within the alpha band during the first six months of life are predictive of both concurrent (Huberty et al., 2023) and later expressive language skills in toddlerhood (Levin et al., 2017; Tran et al., 2021) among EL infants. The association between gamma (30-50 Hz) activity and language abilities varies as a function of chronological age and autism diagnostic status. In overlapping samples of EL and LL infants, Wilkinson et al. (2020) and Romeo et al. (2021) report that reduced gamma power at six months or 24 months, respectively, predict stronger 24-month expressive language skills among EL autistic infants but not among non-autistic infants. In contrast, reduced gamma power at six months is associated with *poorer* 24-month expressive language abilities among non-autistic infants, suggesting neural mechanisms underpinning expressive language development may be altered in autism even before symptoms or language delays become apparent.

The neural mechanisms supporting receptive language development in EL infants and children with autism are less clear, particularly given that many studies reporting significant associations between oscillatory power and expressive language abilities failed to detect similar associations with receptive language. However, evidence from task-based event-related

potential (ERP) paradigms suggests that neural mechanisms underpinning infants' processing of social stimuli (e.g., faces; Glauser et al., 2022) and familiar linguistic stimuli (e.g., Kuhl et al., 2013) may also be linked with receptive language development in autism specifically. Further, other EEG/ERP evidence suggests that more domain-general processes indexing cortical excitation/inhibition regulation (e.g., neural response to stimulus repetition) may play a role in receptive language development (Kolesnik et al., 2019). Specifically, autistic and non-autistic 8-month-olds who show higher levels of cortical "reactivity" to repeated tones (suggestive of a failure to suppress neural response to repeated stimuli) show slower rates of receptive language growth from 8 to 36 months of age. Together, these findings suggest that receptive language development may rely on alternative neural mechanisms in autism (e.g., Glauser et al., 2022), perhaps due to broader disruptions to excitatory/inhibitory regulation and experience-dependent brain development. These broader domain-general neurodevelopmental disruptions may, for example, disrupt autistic infants' ability to detect regularities (repetition) in continuous speech, leading to the recruitment of alternative neural mechanisms and alterations in language development. However, it remains unclear whether features of spontaneous EEG activity, which provides a window into the brain's intrinsic functional architecture, are also linked with receptive language development. It is worth emphasizing that few studies have examined neurobiological predictors of language *growth* throughout development or language change in response to intervention among young children with autism symptoms, instead predicting language outcomes at a fixed timepoint.

Brain-Behavior Phenotypes in Infants and Toddlers with Autism Symptoms

Studies using resting-state EEG to identify brain-behavior associations among infants and toddlers with or at elevated likelihood of autism often select and define a region of interest (ROI) *a priori*. For example, studies examining EEG correlates of cognitive and language abilities among infants with or at genetic risk of autism often focus on spectral power in a given frequency band (e.g., alpha, 6-9 Hz or gamma, 30-50 Hz) within the frontal region (typically

defined as averaged power values across specific electrodes; e.g., F3 and F4 or F3, Fz, and F4; Carter Leno et al., 2021; Dickinson et al., 2019; Huberty et al., 2021, 2023; Levin et al., 2017; Pierce, Reilly, & Nelson, 2021; Tierney et al., 2012; Tran et al., 2021). This approach is attractive in that it allows for hypothesis-driven analyses and mitigates massive Type I error inflation that would arise from conducting hypothesis tests for each channel (and the substantial loss of statistical power that comes with the implementation of traditional techniques for controlling error rate, such as Bonferroni correction). However, averaging across a select set of sensors comes at the cost of losing potentially valuable insight into the spatial distribution of brain-behavior associations or failing to detect significant, meaningful associations altogether. This possibility is particularly relevant when studying brain-behavior development in the first years of life, when the neural mechanisms subserving newly emerging social cognitive or behavioral capacities, like language, may initially rely on alternative neural mechanisms than those identified in older populations (Friederici, Brauer, & Lohmann, 2011; van der Velde, White, & Kemner, 2021), or recruit multiple regions or distributed networks. Moreover, there is evidence from studies using EEG-based metrics (e.g., Dickinson, DiStefano, Lin, et al., 2018; Glauser et al., 2022; Lauttia et al., 2019; Nyström, Jones, Darki, Bölte, & Falck-Ytter, 2021; Wilkinson et al., 2020; Wilkinson, Levin, Gabard-Durnam, Tager-Flusberg, & Nelson, 2019) as well as structural and functional neuroimaging (e.g., Nair et al., 2021; Swanson et al., 2017) that infants and children with or at elevated familial likelihood of autism display distinct brain-behavior "phenotypes" from those who are developing typically or have a typical genetic risk of autism, suggesting that selecting regions of interest based on extant data from neurotypical or other clinical populations may be inappropriate. For these reasons, statistical approaches that provide a means to maintain a nominal Type I error rate without substantially reducing the dimensionality of resting state data (and thereby potentially missing meaningful and unanticipated effects) are particularly desirable (Buzzell, Morales, Valadez, Hunnius, & Fox, 2023; Meyer, Lamers, Kayhan, Hunnius, & Oostenveld, 2021).

The Present Study

Despite the importance of early language skills in neurotypical development and autism, we know little about the neural and behavioral mechanisms that may explain the remarkable variability in language outcomes and language trajectories in autism. Moreover, studies addressing these gaps in *community-referred* samples of young children with autism symptoms are relatively rare, as are studies employing EEG methods to shed light on developmental heterogeneity among children exhibiting the emerging autism phenotype.

Study 2 addresses these gaps by examining EEG correlates of early receptive-expressive language phenotypes and trajectories of language growth in a community-referred sample of infants and toddlers showing early signs of autism. Using a data-driven cluster-based permutation testing approach, Study 2 aimed to identify patterns of spontaneous (resting-state) EEG activity most strongly associated with (1) concurrent receptive-expressive language phenotypes and (2) developmental change in receptive and expressive language abilities within a population of "pre-diagnostic" infants and toddlers with autism symptoms. Theta (3-6 Hz) and alpha (6-9 Hz) oscillations are thought to play a critical role in the emergence of social and cognitive capacities during the second year of life (Henderson et al., 2002; Mundy et al., 2000; Mundy, Fox, & Card, 2003; Paulus, Kühn-Popp, Licata, Sodian, & Meinhardt, 2013; Perone & Gartstein, 2019; Smith & Bell, 2010) and are linked with structural and functional integrity of the developing brain (Valdés-Hernández et al., 2010). Motivated by our lab's recent findings indicating links between alpha power and concurrent language abilities in this sample of infants and toddlers (Cohenour, Dickinson, Jeste, Gulsrud, & Kasari; *under review*), Study 2 focuses specifically on spontaneous oscillatory power in the theta and alpha frequency bands.

Study Aims

Aim 1: Using a data-driven analytic approach, identify patterns of spontaneous (resting state) EEG activity significantly associated with concurrent receptive-expressive language discrepancy/profiles at baseline (T1).

Hypothesis 1: Measures of receptive-expressive language discrepancy will be significantly associated with concurrent spontaneous EEG power.

Aim 2: Using a data-driven analytic approach, identify patterns of spontaneous (resting state) EEG activity significantly associated with individual differences in receptive and expressive language growth across 12 months.

Hypothesis 2: Individual differences in receptive and expressive language growth will be significantly associated with levels of spontaneous alpha power measured at T1.

Method

Participants

Study 2 includes the same longitudinal sample participants described in Study 1 (see ***Participants*** on p. 22). Briefly, 80 children were deemed eligible for participation in the larger intervention study by virtue of having elevated scores on the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2), autism concerns from a study clinician, and no known co-occurring neurological, genetic, physical, or sensory impairments. Of the 80 eligible children, N = 70 (87.5%) consented to EEG and provided usable data. Participant characteristics are summarized in **Table 1.1** (see p. 24).

Intervention

An independent statistical group was responsible for randomizing eligible participants to either the Baby JASPER group (experimental treatment) or Standard Baby group (active control) as part of the larger intervention study. These interventions are described in Study 1 (see ***Interventions*** on p. 24). Both interventions are manualized and equivalent in contact and intensity.

Behavioral Measures

Data from assessments and questionnaires administered at T1 (baseline), T2 (exit; approximately two months after T1 at the end of the active intervention period), and T3 (follow-up; approximately 12 months after T1) were used to map trajectories of receptive and

expressive language growth. Complete descriptions of behavioral measures are provided in Study 1 (see ***Behavioral Measures,*** p. 25).

As described in Study 1, receptive and expressive age equivalent (AE) scores from the Mullen Scales of Early Learning (Mullen; Mullen 1996) were used to characterize receptive and expressive language development across 12 months. Language was assessed at T1, T2, and T3.

EEG Acquisition

Continuous task-free (i.e., spontaneous) EEG data were acquired during the T1 visit for a minimum of two minutes while children were held on a caregiver's lap in a dimly lit and sound-attenuated room. An unseen research assistant blew bubbles if the child became fussy during the recording, consistent with spontaneous EEG recording protocols employed in studies of infant and pediatric populations (Levin et al., 2017). Recordings were continued beyond two minutes (120 seconds) if the child remained calm to increase the likelihood that all participants would have sufficient usable data after removing noisy segments and artifacts (recording duration range: 122.83 to 452.77 seconds). Data were recorded using a 128-channel Hydrocel Geodesic Sensor Net (Electrical Geodesics, Inc.; Eugene, Oregon) and Net Amps 300 (Electrical Geodesics, Inc.) amplifier. Data were sampled at 500 Hz and recorded using Net Station 4.4.5 software, filtered online with a bandpass of 0.1 to 100 Hz, and referenced to the vertex (Cz). Electrode impedances were kept below 100 KΩ.

EEG Processing

Data processing was performed offline using the EEGLAB toolbox (Delorme & Makeig, 2004) and in-house MATLAB scripts. EEG data were high-pass filtered to remove frequencies below 1 Hz and low-pass filtered to remove frequencies above 50 Hz using a finite impulse response filter. Continuous data were then visually inspected, and noisy channels and sections with excessive noise or nonstereotyped artifacts were removed. Following the manual removal of noisy channels, data were cleaned using artifact subspace reconstruction (ASR), a principal

component analysis-based statistical technique that uses artifact-free reference data to identify and remove high amplitude artifacts exceeding a predetermined threshold (Chang, Hsu, Pion-Tonachini, & Jung, 2018). ASR was implemented in EEGLAB with default parameters and a rejection threshold of *k*=8. Clean data were then interpolated to the international 10-20 system 25-channel montage (Jasper, 1958) using the EEGLAB *interp_mont* function and decomposed into maximally independent components (ICs) using independent components analysis (ICA; Onton, Westerfield, Townsend, & Makeig, 2006). ICA is a blind source separation method that decomposes EEG signals into their maximally independent components, allowing for the removal of stereotyped artifacts representing non-neural activity (e.g., electrooculogram, electromyogram, and line noise). After decomposing the data using ICA, the *iclabel* function was used to automatically classify ICs into distinct categories, thus aiding the detection and removal of ICs representing non-neural sources. Specifically, any ICs with a majority probability of arising from non-neural sources (i.e., ICs with <50% probability brain) were removed from the data. As EEG recordings acquired from infant and toddler populations are often limited in duration, combining ASR and ICA is an effective and efficient approach to remove artifacts from pediatric datasets while retaining the coinciding neural signal (e.g., Dickinson et al., 2021; Tran et al., 2021).

Data preprocessing procedures resulted in the removal of 20.97 channels on average (SD = 6.48). The minimum amount of artifact-free data available across participants was 99.57 seconds (mean = 179.44, SD = 64.75).

Oscillatory Power

EEG data were exported to FieldTrip (Oostenveld, Fries, Maris, & Schoffelen, 2010) for the computation of spectral power. Multi-tapered Fast Fourier Transformation was implemented using the FieldTrip function *ft_freqanalysis* (1,000 sample Hanning windows with 50% overlap), yielding power spectral density estimates with 0.5 Hz frequency resolution for each channel.

A permutation procedure was employed to ensure that an equivalent amount of data underwent power analysis for each participant, thus ensuring power estimates were not impacted by variability in file length across participants. A total of 30 two-second epochs (60 seconds) of resting-state data were randomly selected for each participant and underwent power analysis (Xie, Toll, & Nelson, 2022). This procedure was repeated 1,000 times for each participant, with the power spectra calculated as the average across the permutations. This rigorous approach guaranteed that the power calculations were derived from a consistent amount of data for each participant, with the continuity of data within epochs maintained throughout the process.

Absolute power was calculated by summing power estimates within each frequency band (i.e., theta, 3-6 Hz; alpha, 6-9 Hz) at 0.5 Hz frequency resolution. Absolute power spectra values were converted into relative power by dividing them by the sum of the total spectrum (1-50 Hz), thus reflecting the proportion of total spectral power accounted for by each frequency bin. Relative power, which essentially corrects for total power, was used for analyses given differences in non-neural anatomical factors (e.g., skull thickness) are known to influence absolute power values (Benninger, Matthis, & Scheffner, 1984), and relative power values are more sensitive to developmental changes in frequency composition across early development (Clarke, Barry, McCarthy, & Selikowitz, 2001; Marshall et al., 2002).

Given the established associations between social-cognitive development in infancy and toddlerhood and oscillatory activity in the theta (3-6 Hz) and alpha (6-9 Hz) bands (Anderson & Perone, 2018), and our recent work identifying concurrent associations between alpha activity and language ability (Cohenour et al., *under review*), analyses focused on spontaneous power within these frequency bands.

Analysis Strategy

Overview of Cluster-Based Permutation Testing of Task-Free EEG Data

Cluster-based permutation testing is a nonparametric approach that leverages the inherent clustered structure of high-dimensional EEG data to simultaneously maintain a nominal Type I error rate without a dramatic loss of statistical power while preserving dimensionality (for instance, spatial dimensionality) of the EEG data (Maris & Oostenveld, 2007). These approaches to analyzing neural data have a long history of use in neuroimaging (e.g., Bullmore, 1999) and adult EEG, though they have been used less frequently in infant and developmental EEG studies until more recently (e.g., Çetinçelik, Rowland, & Snijders, 2023; Garcés et al., 2022; Maguire & Schneider, 2019; Marriott Haresign et al., 2023; Phillips et al., 2023; Shephard et al., 2019; Wass et al., 2018).

Cluster-based permutation tests are built around the assumption that true neural effects captured via EEG are clustered along a given dimension (e.g., temporal, spatial, spectral; the specific dimension depends on the research question and data structure at hand). For instance, it is expected that *spatial* effects would manifest as similar patterns of activity from multiple adjacent sensors, given that signals transmitted to neighboring sensors likely share a common cortical source due to the manner in which electrical fields "travel" through tissue to sensors on the scalp (i.e., volume conduction; Xie, Toll, & Nelson, 2022).

The simultaneous control of Type I Error and maintenance of statistical power afforded through nonparametric cluster-based tests is realized by implementing a two-step approach. At the first stage (the "cluster formation" stage), clusters in the dimension of interest (e.g., spectral, temporal, and/or spatial) are identified, guided by pre-specified parameters defined by the researcher, including the channel-level threshold for cluster formation (e.g., channel-level t statistics exceeding $|t| = 1.96$). Adjacent electrodes that surpass this threshold are then grouped into a cluster. If a cluster or clusters are identified in the data, they are then quantified using a cluster statistic (T), the most commonly used of which is computed as the sum of t-values for the cluster's constituent electrodes (i.e., *maxsum;* Oostenveld, Fries, Maris, & Schoffelen, 2010).

At the second "inference" stage, the statistical significance of the cluster is evaluated via Monte Carlo nonparametric permutation testing (1,000 permutations) under the null hypothesis of statistical independence (i.e., exchangeability). Specifically, the null hypothesis states that the observed cluster statistic is no larger than what would be observed by chance with randomly shuffled data. At this stage, the cluster formation procedure is re-implemented on the data 1,000 times, and the largest cluster statistic obtained in each permutation is stored, resulting in a permutation distribution of cluster statistics from the surrogate data. Estimated critical values (corresponding with alpha = .025 to account for two-sided testing) are then generated from the chance distribution and compared against the observed cluster statistic identified initially; if the observed cluster statistic exceeds the Monte Carlo-estimated critical value, the null hypothesis of statistical independence is rejected, and the cluster is considered to be statistically significant. By conducting hypothesis testing at the cluster level rather than the individual channel level, the familywise error rate can be successfully maintained at a nominal level, as has been demonstrated in simulation studies (Pernet, Latinus, Nichols, & Rousselet, 2015). Details of this analytical approach and its use in developmental EEG specifically are discussed at length in Meyer et al. (2021).

It is important to note that this approach to hypothesis testing necessarily alters the interpretation of statistically significant or non-significant effects. For instance, if cluster-based permutation testing is used to test the hypothesis that alpha power (averaged across the 0.5 Hz frequency bins) is associated with a behavioral variable, it would be appropriate to interpret a significant cluster as providing robust evidence for a significant brain-behavior association. Moreover, the spatial distribution of the cluster (i.e., the locations of the electrodes identified in the significant cluster) provides insight as to where the brain-behavior effect is strongest. A significant cluster should not be interpreted as indicating that all of the individual channels that comprise the cluster are statistically significant on their own, as significance testing only occurred at the cluster level.

Aim 1: Neural Correlates of *Receptive-Expressive Language Phenotypes*

Measures of receptive-expressive phenotypes included Difference Scores (receptive language AE minus expressive language AE), Ratio Scores (receptive language AE ÷ expressive language AE), and language profiles (expressive advantage, receptive advantage, and balanced) as measured at T1. These measures of receptive-expressive language phenotype are described at length in Study 1.

Cluster-based permutation testing was implemented in FieldTrip (Oostenveld et al., 2010) to test the association between spontaneous power in alpha and theta bands and the variables representing receptive-expressive language phenotypes computed in **Study 1.** For continuous measures of receptive-expressive language phenotypes (Difference and Ratio Scores), the *ft_statfun_correlationT* function within FieldTrip was implemented to identify groups of spatially adjacent channels in which the association between spectral power and the behavioral variable of interest exceeded a pre-specified threshold (critical value). Specifically, correlation coefficients (Spearman's r_s) were generated for each channel-level association and transformed to *t*-statistics. Neighboring channels exceeding the pre-specified threshold ($|t| = 1.995$) were grouped to form clusters. An analogous procedure was carried out using the *ft_statfun_indepsamplesF* to test whether relative theta or alpha power differed as a function of language profile. Adjacent channels with *F*-statistics exceeding the pre-defined threshold ($F = 3.314$) were formed into clusters.

Clusters identified at the cluster formation stage were then quantified with a cluster statistic computed using *maxsum* parameter in FieldTrip, which is calculated as the sum of the sample-level (channel-level) *t* statistics generated during cluster formation for each individual channel within a cluster. If a candidate cluster is identified at the first stage, the Monte-Carlo nonparametric permutation testing procedure was then implemented to evaluate the statistical significance of the cluster using the *ft_statistics_montecarlo* function. Critical values at the *cluster* level were derived from the chance distributions of surrogate cluster statistics and

compared against the observed cluster statistic; if the observed statistic exceeded the estimated critical value, the null hypothesis of statistical independence was rejected, and the observed cluster was considered statistically significant. Note that a critical value equivalent to alpha = .025 was used for analyses using correlational analyses to form clusters in order to account for two-tailed tests.

Aim 2: Neural Predictors of Receptive and Expressive Language Growth

In Study 1, unconditional linear growth models were constructed to describe trajectories of language growth across 12 months in this sample of infants and toddlers. Unconditional linear growth model specifications and descriptions are provided in the **Appendix**. Estimates of fixed effects, random effects, and goodness-of-fit indices for receptive language and expressive language unconditional growth models reported in Study 1 are reproduced in **Table 2.1**.

To test whether spontaneous EEG power measured at T1 is associated with individual differences in receptive and expressive language growth, model-based (i.e., empirical Bayes) estimates of individual growth parameters were extracted from receptive and expressive unconditional linear growth models. This approach has been used to examine associations between the rate of fine motor growth and later language outcomes among infants with an elevated familial likelihood of autism (Choi, Leech, Tager-Flusberg, & Nelson, 2018), associations between the pace of vocabulary growth in toddlerhood and vocabulary skills during preschool (Rowe, Raudenbush, & Goldin-Meadow, 2012), associations between individual differences in symptom trajectories and variation in structural or functional brain connectivity across adolescence (e.g., Chahal et al., 2019) and associations between pre-treatment functional connectivity and change in depressive symptoms from pre- to post-treatment (Crowther et al., 2015). These individual growth parameters ($\tilde{\pi}_{0\mathrm{i}}$, and $\tilde{\pi}_{1\mathrm{i}}$, describing child *i's* predicted initial status and predicted rate of change) are computed by combining information from the fixed effects coefficients and the random effects coefficients (which describe how child *i's* growth parameters deviate from their own estimated population average

growth trajectory). Model-based estimation of individual growth parameters is the preferred approach for extracting individual trajectories from growth models because it offers greater precision than other approaches (e.g., ordinary least squares regression; Singer & Willett, 2003). This is discussed in greater detail in the Appendix.

Table 2.1. *Unconditional Linear Growth Models for Receptive and Expressive language*

	Receptive Language					**Expressive Language**				
Fixed Effects	Est.	SE	*t*	*df*	*p*	Est.	SE	*t*	*df*	*p*
Intercept, γ_{00}	11.14	0.62	69.36	17.86	<.001	10.62	0.52	69.40	20.43	<.001
Linear Slope (Time), γ_{10}	1.17	0.08	42.65	14.67	<.001	1.10	0.08	48.86	13.35	<.001
Variance Components	Est.	SE	*z*	*p*		Est.	SE	*z*	*p*	
Level-1, σ_e^2	12.16	2.36	5.16	<.001		7.81	1.49	5.26	<.001	
Level-2, Intercept, σ_0^2	18.69	4.89	3.82	<.001		13.38	3.37	3.97	<.001	
Level-2, Slope, σ_1^2	0.14	0.07	2.05	.020		0.21	0.06	3.25	.001	
Correlation, ρ_{01}	0.35	0.29	1.20	.115		0.27	0.22	1.23	.220	
Goodness-of-Fit										
-2 Log Likelihood	1032.71					986.93				
AIC	1044.71					998.93				

Note. Results of hierarchical linear growth modeling for language age equivalent scores, with estimates of fixed effects, random effects, and goodness-of-fit indices AIC = Akaike information criterion.

Because the primary aim was to assess associations between EEG metrics at baseline and subsequent growth in language skills, analyses focused on individual estimates of linear slope for receptive and expressive language models. These individual estimates of linear growth were treated as dependent variables in cluster-based permutation analyses.

To test associations between T1 spontaneous alpha and theta power and language growth, the *ft_statfun_correlationT* function (Pearson's *r*) within FieldTrip was used to identify groups of spatially adjacent channels in which the association between spectral power and linear growth exceeded the pre-specified threshold (|*t*| = 1.995) were grouped to form clusters.

Results of cluster-based permutation analyses are displayed graphically using topographical plots (where cluster extent is visualized using symbols representing individual

electrodes, and cluster intensity is visualized using color) and scatterplots representing associations between spectral power and language variables.

When clusters are identified in the data, their corresponding cluster statistic, *T,* Monte-Carlo-estimated *p*-value, and effect size, *r*, are reported. Note that there is no established best practice for reporting cluster-level effect sizes following cluster-based permutation analyses (Meyer et al., 2021). However, one recommended approach is to calculate an effect size using the average of the cluster. Using an analogous approach to that recommended in Meyer et al. (2021), reported cluster-level effect sizes, *r*, reflect the strength of the association between the behavioral variable of interest and spectral power across the cluster (i.e., the averaged power values for channels comprising the significant cluster). The magnitude of these effect sizes may be interpreted similarly to conventional *r*-based effect sizes. Note that the findings reported here are significant after enforcing cluster-based controls for multiple comparisons at the sample (channel) level and adjustment for two-sided significance testing at the cluster level.

Results

Aim 1: Neural Correlates of *Receptive-Expressive Language Phenotypes*

Preliminary Analyses

Though I had hypothesized that neural correlates of receptive-expressive abilities would be evident within the traditionally defined "infant" theta (3-6 Hz) and alpha (6-9 Hz) frequency bands, I leveraged the flexibility of cluster-based permutation testing to examine whether there were potential effects outside of these canonical frequency ranges that would be worth exploring and testing in my main analyses. This decision was motivated both by the exploratory nature of this work as well as the inconsistent definitions of "alpha" and "theta" frequency ranges in infant and toddler-age populations. For these preliminary, exploratory analyses, I conducted cluster-based permutation testing for the entire 1 to 12 Hz frequency spectrum (binned with 0.50 Hz resolution), relaxing the cluster formation threshold to a value

corresponding to p = .10, given the primary objective was to explore patterns qualitatively prior to carrying out formal permutation-based hypothesis testing.

For Difference Scores and Ratio Scores, there was evidence for a potential effect within the 3 - 4 Hz frequency range and 3 - 4.5 Hz frequency range, respectively, consistent with the proposed theta frequency band. This was similar to the exploratory analyses of Language Profiles: these preliminary analyses revealed evidence for a potential effect of language profile within the 3 - 3.5 Hz frequency range. In light of these exploratory analyses, the proposed analysis plan was unchanged, such that cluster-based permutation analyses were carried out with both theta (3-6 Hz) and alpha (6-9 Hz) bands. Rather than identifying clusters within each 0.5 Hz bin in the alpha and theta ranges, power values were averaged across the frequency ranges, as is common practice and appropriate for these specific hypotheses.

Relative Power and Receptive-Expressive Language Discrepancy

Receptive-Expressive Difference Scores

There was a significant, positive association between relative theta power and Difference Scores, as identified in a left frontocentral cluster (T = 9.54, p = .032, r = .302). No clusters were identified within the alpha frequency band.

Receptive-Expressive Ratio Scores

Consistent with analyses of Difference Scores, There was a significant, positive association between theta power and Ratio Scores, as identified in a similar left front-central cluster (T = 11.40, p = .028; r = .296). No clusters were identified within the alpha frequency band. See Figure 2.1.

Relative Power and Receptive-Expressive Language Profiles

No clusters within the theta or alpha frequency band surpassed the pre-specified threshold for cluster formation (F = 3.13). For exploratory purposes, I opted to conduct two separate exploratory tests to determine whether mean relative alpha or theta power differed

significantly between RA and EA profiles, as well as between Balanced and EA profiles. This was achieved using the *ft_statfun_indepsamplesT* function in FieldTrip.

Expressive Advantage and Receptive Advantage Group Differences

For the analyses comparing RA and EA groups, the sample-level threshold for cluster formation was $|t| = 2.01$ ($df = 51$). A positive cluster was identified within the left frontocentral region, suggesting that mean theta power was higher among those with an RA profile than those with an EA profile, though the cluster did not surpass the threshold for statistical significance following permutation testing ($T = 6.29$, $p = .095$).

Expressive Advantage and Balanced Group Differences

For analyses comparing Balanced and EA profiles, the sample-level threshold for cluster formation was $|t| = 2.02$ ($df = 39$). No clusters were identified in either the alpha or theta frequency band at the cluster formation stage.

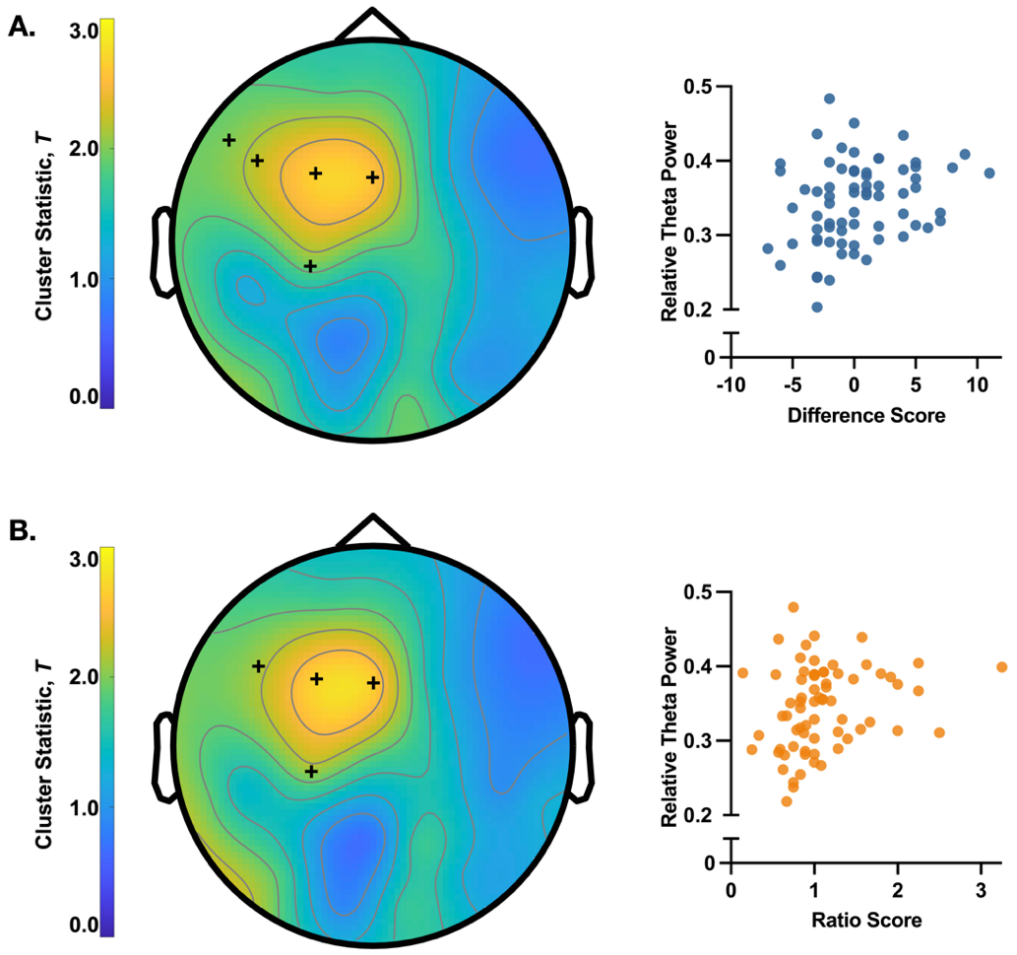

Figure 2.1. Cluster-based permutation analyses revealed significant associations between spontaneous relative theta (3-6 Hz) power and receptive-expressive language discrepancy, such that an increasing receptive language advantage is associated with higher levels of theta power. Scatterplots, right, illustrate the association between receptive-expressive language metrics and relative theta power summed across cluster channels. **A.** Relative theta power was positively associated with Difference Scores (p = .032), as seen in a cluster located in the left frontocentral region. **B**. Relative theta power was positively associated with Ratio Scores (p = .028) as evidenced in a left frontocentral cluster.

Aim 1 Summary

Data-driven analyses examining associations between spectral power and continuous measures of receptive-expressive language revealed significant associations between levels of spontaneous theta power and the degree of receptive-expressive language discrepancy, such that those with stronger receptive language skills relative to their expressive language skills tended to exhibit higher levels of theta power. Although categorical language profiles were derived from Ratio Scores, no clusters were identified in omnibus tests of Language Profiles.

Given the relatively small and unbalanced group sizes, the present sample may be underpowered to detect more subtle significant group differences that may be present between language profile groups.

Aim 2: Neural Correlates of Receptive and Expressive Language Growth

Preliminary Analyses

As with analyses of T1 receptive-expressive language phenotypes, preliminary exploratory analyses were undertaken to determine whether there were potential effects that fell outside the canonical frequency bands specified in my hypotheses. I conducted cluster-based permutation testing for the entire 1 to 12 Hz frequency spectrum (binned with 0.50 Hz resolution), relaxing the cluster formation threshold to a value corresponding to $p = .10$.

For individual receptive language growth parameters, there was some evidence for a potential effect within the 8 - 9 Hz frequency range. Similarly, for individual expressive language growth parameters, there was some evidence for a potential effect in the 7 - 8.5 Hz range. In both cases, potential effects fell within the "infant alpha" range of 6-9 Hz. The proposed analysis plan was unchanged, such that cluster-based permutation analyses were carried out with both theta (3-6 Hz) and alpha (6-9 Hz) bands. Power values were averaged across each frequency band prior to analyses.

Neural Correlates of Receptive Language Growth

Analyses revealed significant positive associations between relative alpha power at T1 and individual differences in the rate of receptive language growth, as evidenced in two significant clusters. Cluster 1 ($T = 7.27$, $p = 0.027$, $r = .32$) included left parietal-occipital regions whereas Cluster 2 ($T = 6.63$, $p = .035$, $r = .28$) included frontal regions. No clusters were identified within the theta band.

Neural Correlates of Expressive Language Growth

The rate of expressive language growth was significantly positively associated with relative alpha power. Two clusters were identified, including one spanning multiple cortical

regions within the left hemisphere (Cluster 1 T = 25.70, p = .011, r = .33) and a second, smaller cluster localized to the right temporoparietal region (Cluster 2 T = 8.78, p = .036, r = .38). As with analyses of receptive language growth, there was no evidence for any association between spontaneous theta power at baseline and rate of expressive language growth. See Figure 2.2.

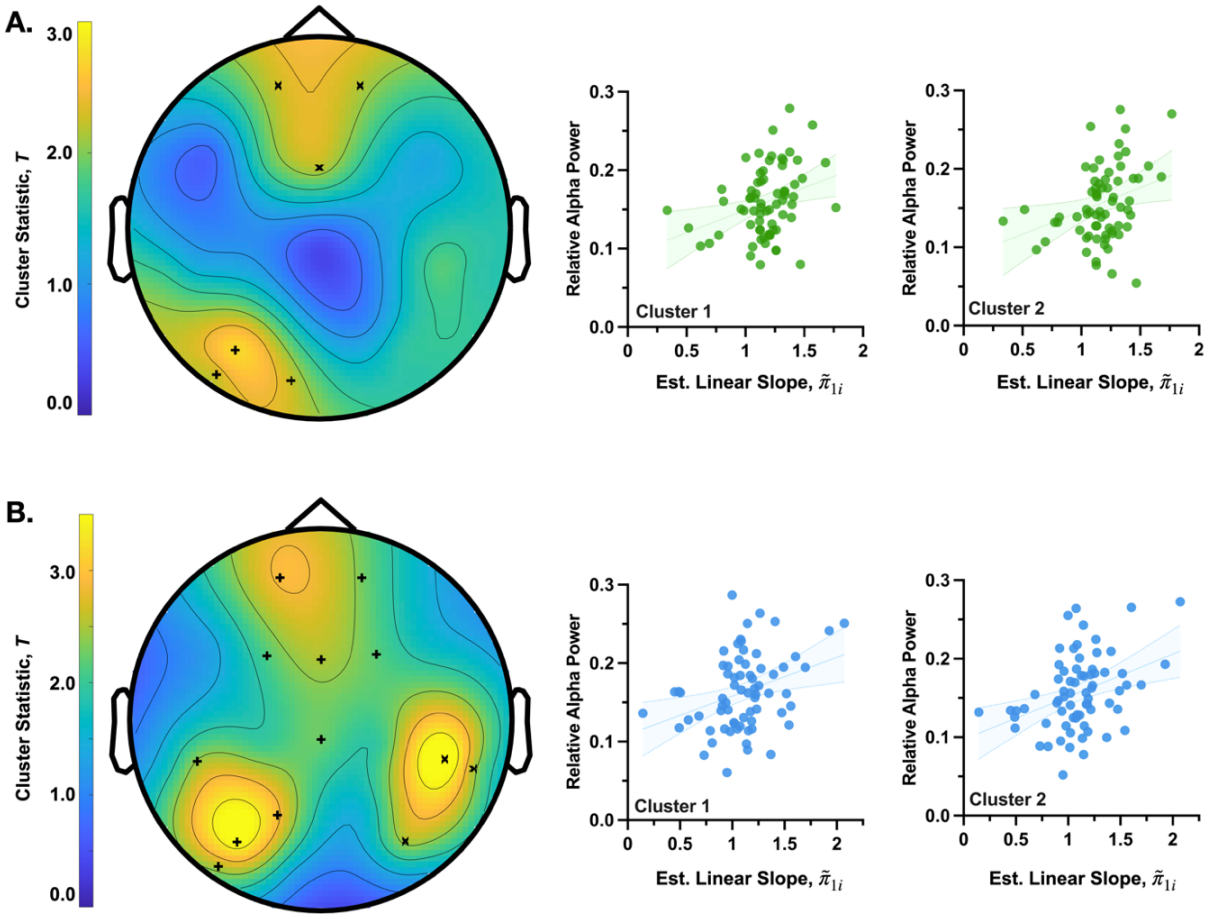

Figure 2.2. Results of cluster-based permutation analyses examining associations between T1 spectral power and receptive language growth (**A**) and expressive language growth (**B**). Children with higher levels of spontaneous relative alpha power at T1 showed significantly faster rate of growth across the 12-month measurement period relative to those with lower levels of relative alpha power at enrollment. Scatter plots depict the association between individual-level estimates of linear growth in language abilities (i.e., empirical Bayes estimates of growth parameters, $\tilde{\pi}_{1i}$) and relative alpha power summed across cluster-specific channels. **A. Receptive Language.** Levels of relative alpha power at T1 were significantly, positively associated with participant-level estimates of linear growth in receptive language AE scores (i.e., linear slope, $\tilde{\pi}_{1i}$) derived from hierarchical linear growth models. Cluster 1 (shown with + symbols; p = .027) was localized to left parieto-occipital regions whereas Cluster 2 (shown with x symbols, p = .035) involved frontal regions. **B. Expressive Language.** Levels of relative alpha power at T1 were significantly, positively associated with participant-level estimates of linear growth expressive language AE scores (i.e., linear slope, $\tilde{\pi}_{1i}$) derived from hierarchical linear growth models. Cluster 1 (shown with + symbols; p = .011) involved multiple cortical regions, whereas Cluster 2 (shown with x symbols, p = .036) included the right temporoparietal area.

Sensitivity Analysis: Excluding Children with Only One Timepoint

Receptive and expressive language unconditional growth models were re-fit using data from the subgroup of children who contributed data at two or more timepoints. This subset of the larger dataset included $n = 59$ children and a total of $n = 156$ measurement occasions. Model-based Bayes estimates of individual growth parameters extracted from these unconditional growth models were used as dependent variables in cluster-based permutation analyses, as in the primary analyses. The results were unchanged: relative alpha power was significantly associated with individual differences in the estimated rate of receptive language growth (Cluster $T = 6.84$, $p = .036$, $r = .30$) and expressive language growth (Cluster $T = 32.89$, $p = .008$, $r = .36$). The spatial distribution of significant effects was similar to that observed in the full sample, such that the strongest effects for receptive language were observed in left parieto-occipital regions, whereas effects for expressive language were more distributed across the scalp. Note that for sensitivity analyses of expressive language, a single large cluster was identified, the spatial distribution of which matched that of the two clusters identified in the primary expressive language analyses. As with primary analyses using data from all children, relative theta power was not significantly associated with individual receptive or expressive language growth parameters.

Discussion

This study leveraged cross-sectional and longitudinal behavioral and electrophysiological data collected from infants and toddlers showing early signs of autism enrolled in an early intervention study to examine whether measures of functional brain activity were predictive of concurrent receptive-expressive language phenotypes and longitudinal growth in receptive and expressive language abilities over 12 months. The present study is among the first to detail the EEG correlates of receptive-expressive phenotypes during the second year of life and provides novel insight into heterogeneity in language development among *community-referred* infants and toddlers with autism symptoms. It is worth highlighting

that although there is a growing body of evidence for infant and toddler EEG correlates of later language outcomes, these studies primarily include prospectively monitored infants with an elevated familial likelihood of autism (i.e., heightened genetic risk of autism due to the presence of an autistic sibling). While such studies have provided unprecedented insight into autism emergence and early-emerging differences in structural and functional brain development, the generalizability of these findings is somewhat limited, given EL infants likely represent a genotypically (e.g., Leppa et al., 2016) and phenotypically (Cohenour, Gulsrud, & Kasari, 2023) distinct subgroup from the broader autism population. Thus, extending this line of inquiry to populations of infants and toddlers identified in community settings (who likely better present the phenotypic, genetic, and sociodemographic diversity of the broader autism population) is, in and of itself, an important step towards translatable, clinically-practicable research on brain-behavioral development in autism.

This study is a first step towards identifying features of functional brain development that contribute to variability in early language skills among young children with autism symptoms and elucidating neural mechanisms that contribute to heterogeneity within the emerging autism phenotype. Addressing this gap in our understanding of the neural and behavioral mechanisms that shape social development during the "pre-diagnostic" period in the second year of life provides a foundation for the rigorous testing of prognostic and predictive markers that can help explain heterogeneity in development broadly, as well as heterogeneity response to very early interventions. Such markers could facilitate the identification of symptomatic infants and toddlers at the highest risk of experiencing co-occurring language difficulties who may benefit from targeted language intervention. Moreover, understanding the behavioral, environmental, and neural mechanisms that shape language development in the context of emerging autism could provide insight into treatment mechanisms or specific targets most likely to deliver the greatest benefit to child language outcomes.

Spontaneous Theta Power is Associated with Receptive-Expressive Language Phenotypes

Despite finding little evidence for associations between receptive-expressive language phenotypes and child-level demographic and behavioral variables (Study 1), there was evidence for a significant association between spontaneous theta power and receptive-expressive language metrics, such that higher relative theta power was associated with an increasing receptive language advantage (that is, on average, those who have stronger receptive language skills than expressive language skills tend to have higher levels of theta power than those who have similar or weaker receptive skills relative to their expressive skills). Interestingly, our lab has recently reported in this same sample that relative theta power was *not* significantly associated with concurrent receptive or expressive language skills when examined separately. In contrast, alpha power was robustly linked with concurrent language skills (Cohenour et al., *under review*). This suggests that the present results are not driven by mere differences in language level overall but rather something specific to the receptive-expressive discrepancy.

The relationship between levels of theta power and cognitive or broader developmental outcomes is complex and, at times, seemingly paradoxical. Theta oscillations dominate the neonatal EEG power spectrum and remain the dominant rhythm for much of the first year of life before declining in favor of higher-frequency oscillations (e.g., alpha; Saby & Marshall, 2012). Thus, increased levels of relative theta power in later infancy and early childhood are thought to reflect a global delay in brain maturation (McLaughlin et al., 2010). Indeed, elevated levels of spontaneous theta power have been reported among children who have experienced severe early psychosocial deprivation (Marshall, Fox, & BEIP Core Group, 2004; McLaughlin et al., 2010), infants from households experiencing socioeconomic disadvantage and high levels of maternal stress (e.g., Troller-Renfree et al., 2023), infants and children diagnosed with or at elevated familial risk of attention deficit hyperactivity disorder (ADHD; Shephard et al., 2019; Snyder & Hall, 2006), as well as children diagnosed with developmental dyslexia (Cainelli,

Vedovelli, Carretti, & Bisiacchi, 2023) compared to typically-developing controls. Moreover, higher levels of spontaneous theta power have been linked with poorer executive functioning skills during early childhood (Law et al., 2023), poorer long-term cognitive outcomes (e.g., Tan et al., 2023), and elevated levels of anxiety symptoms and ADHD symptomatology among children with and without early psychosocial risk (McLaughlin et al., 2010). Interestingly, declines in resting-state theta power across middle childhood (perhaps reflecting normative neuromaturational changes in the distribution of spectral power) are predictive of expressive vocabulary, but not receptive vocabulary, at age 11 years among neurotypical children (Meng et al., 2022).

In contrast, *task-related* increases in theta power have been linked with superior cognitive and behavioral performance and increased verbal and nonverbal cognitive functioning (Braithwaite, Jones, Johnson, & Holmboe, 2020; Jones et al., 2020). In infancy and early childhood, increases in theta power are observed during periods of sustained or anticipatory attention (Xie, Mallin, & Richards, 2019), social attention (Haartsen, Charman, Pasco, Johnson, & Jones, 2022; E.J.H. Jones, Venema, Lowy, Earl, & Webb, 2015), object exploration (Begus, Southgate, & Gliga, 2015; Orekhova, Stroganova, Posikera, & Elam, 2006), novelty detection (e.g., Köster, Langeloh, Michel, & Hoehl, 2021), and processing of speech (Begus, Gliga, & Southgate, 2016; Bosseler et al., 2013; Orekhova et al., 2006). Modulation of theta activity is thought to reflect a broader, adaptive attention-gating mechanism, enabling children to deploy attentional resources to elements of the environment that are most likely to provide opportunities for learning (Begus & Bonawitz, 2020).

The present findings suggest that children with lower levels of theta power, particularly in the left frontocentral region, are more likely to have comparatively delayed expressive language skills relative to their receptive skill level. Again, relative theta power itself was not related to receptive or expressive skill level overall in the present sample; rather, theta power was specifically linked with the magnitude of receptive-expressive discrepancy. These findings have

a few possible interpretations in light of the extant literature on resting and task-related theta activity in infancy and early childhood. First, while excessive theta power is typically considered a marker of neuromaturational delay (e.g., McLaughlin et al., 2010), in autism, this may reflect a beneficial *adaptation* to underlying genetic vulnerabilities or a leveraging of strengths common among children with autism. For instance, increased availability of theta oscillations may enable children to leverage areas of cognitive strength (e.g., local information processing and broader enhancements to perceptual functioning; Guy, Mottron, Berthiaume, & Bertone, 2019), which, in turn, provides an extra boost to receptive language by facilitating improved processing of linguistic input. The interpretation is consistent with the ontogenetic adaptation hypothesis for adaptive, alternative developmental trajectories in autism.

Spontaneous Relative Alpha Power Predicts Rate of Language Growth

Data-driven analyses of individual language growth parameters revealed a consistent pattern: higher alpha power was associated with more rapid receptive and expressive language growth in the present sample of infants and toddlers showing early behavioral signs of autism. Associations were observed in localized clusters on the scalp, potentially indicating a spatially distinct neural signature of early language development in emerging autism. These findings, coupled with observed theta-related effects for receptive-expressive phenotypes, emphasize the potential of theta- and alpha-based EEG metrics as neural indicators of risk for, or resilience against, more profound spoken language difficulties, and highlight the potential interconnected neural processes that set the stage for receptive and expressive language growth.

Developmental change in alpha oscillations across the first three years of life coincides with the emergence of increasingly complex social and communication capacities (Anderson & Perone, 2018). Given that these rhythms facilitate efficient communication across distributed regions (Chapeton et al., 2019), maturation-related increases in alpha power may provide the neural infrastructure needed for language acquisition. The present results are consistent with studies of EL infants later diagnosed with ASD reporting longitudinal associations between early

alpha-band activity and expressive language outcomes in later infancy and toddlerhood (Huberty et al., 2023; Levin et al., 2017; Tran et al., 2021). The widespread spatial distribution of the clusters linked with expressive language growth (compared with those linked with receptive language growth) is similar to the pattern identified in our analyses of concurrent expressive language ability (Cohenour et al., *under review*). Given spoken language production is later emerging (Bornstein & Hendricks, 2012; Fenson et al., 1994) and relies on the coordination of complex cognitive and motor systems, this more widespread effect may reflect a later specialization of brain networks for expressive language. Notably, the regions where this effect was strongest (see **Figure 2.2 B**) are primarily localized to left and right temporoparietal regions – regions that have long been implicated in language functioning and social cognition (Adolphs, 2008; Friederici et al., 2011; Paterson, Heim, Thomas Friedman, Choudhury, & Benasich, 2006). These regions appear to play a role in language trajectories among children with autism, too. Using functional magnetic resonance imaging (fMRI) in a community sample of children with and without autism, Lombardo and colleagues (2015) found evidence for hypoactivation in bilateral temporal cortices during speech processing among children with autism who exhibited "poorer" language outcomes (i.e., with Mullen receptive and expressive language T-scores < 40) relative to autistic children and neurotypical children without language delays.

In contrast with the growing evidence for links between alpha-band activity and expressive language skills in autism (e.g., Cohenour, Dickinson, Jeste, Gulsrud, & Kasari, *under review*; Huberty et al., 2023), evidence for neural mechanisms associated with receptive language is sparse. For example, studies have reported significant associations between alpha activity and concurrent expressive language skills but no such effects for receptive language skills (Huberty et al., 2023). Task-based studies of auditory processing among EL infants and toddlers report associations between EEG-based measures of cortical reactivity (an index of excitatory/inhibitory function) and receptive language growth across infancy and early childhood, such that children who fail to suppress neural responses to repeated non-linguistic auditory

stimuli show slower receptive language growth (Kolesnik et al., 2019). Here, we report novel findings concerning neural correlates of receptive language in that we observed significant associations between levels of spontaneous relative alpha power and receptive language growth. These effects were most apparent in frontal regions and left parietal regions. Networks involving frontal regions have been implicated in language functioning across the lifespan (Friederici et al., 2011; Friederici & Gierhan, 2013). Evidence from neuroimaging and lesion studies suggests that parietal regions may play a crucial role in specific aspects of language functioning, including phonological processing and semantic processing (see Coslett & Schwartz, 2018). Phonological processing involves the perception and encoding of linguistic units, thereby facilitating the segmentation of continuous speech into meaningful phonetic units (Kuhl, Conboy, Padden, Nelson, & Pruitt, 2005; Kuhl & Meltzoff, 1982), whereas semantic processing of language refers to the ability to make meaning of words and linguistic input (Friedrich & Friederici, 2008).Thus, at the most fundamental level, these information-processing capacities are prerequisites for language comprehension.

Notably, consistent with the results of our recent study examining neural correlates of concurrent language abilities in this sample of infants, there were no significant associations between levels of spontaneous relative theta power and language growth identified. I hypothesize that this may reflect the increasing importance of faster (i.e., alpha) oscillations during language learning across the second and third years of life and a diminishing importance of slower oscillations (e.g., delta, theta), which are thought to facilitate the processing of prosodic cues embedded in speech (Giraud & Poeppel, 2012) in early infancy.

Limitations and Strengths

The present study has several methodological strengths, a primary of which is the inclusion of a diverse, pre-diagnostic community-referred sample of symptomatic infants and toddlers. Studying brain-behavior development during this window could provide crucial insight into the neural and behavioral dynamics that shape the autism phenotype in infancy and early

toddlerhood. Moreover, given the symptomatic, pre-diagnostic stage captured in the present sample coincides with a window of heightened neuroplasticity when interventions may yield the largest "pay-off" for child outcomes (Klin, Klaiman, & Jones, 2015; Klin et al., 2020), identifying candidate biomarkers that can facilitate identification of children at highest risk of poorer language outcomes may be valuable.

The limitations associated with the behavioral analyses of receptive-expressive language phenotypes and language trajectories, including the limitations associated have been outlined in Study 1. With respect to the EEG component of this work, there are several limitations and promising areas for future work.

The present study was a focused investigation of links between language and spontaneous oscillatory power within hypothesis-driven, *a priori-defined* frequency bands: theta (3-6 Hz) and alpha (6-9 Hz). Associations between expressive language and spontaneous power in other frequency bands, including gamma (30 – 50 Hz), have been reported among EL infants (Romeo et al., 2021; Wilkinson et al., 2019). Alpha and theta EEG metrics offer desirable psychometric properties (Anaya, Ostlund, LoBue, Buss, & Pérez-Edgar, 2021; Levin et al., 2020; van der Velde et al., 2019), as well as higher signal-to-noise ratio and less sensitivity to non-neural noise as compared with gamma metrics (McEvoy, Hasenstab, Senturk, Sanders, & Jeste, 2015; van der Velde et al., 2019). These properties are particularly desirable for developing objective, reliable biomarkers that can be used at scale in the community. Similarly, spontaneous spectral power is one of many metrics for assaying functional brain development. Other EEG metrics, including functional connectivity (Dickinson et al., 2021; Dickinson, DiStefano, Senturk, et al., 2018; Peters et al., 2013; Tran et al., 2021) and functional network properties (Keown et al., 2017; Lewis et al., 2014), are atypical in autism and linked with concurrent or later cognitive, social, and language functioning. These alternative EEG measures merit further exploration in the context of language phenotypes in emerging autism.

This study draws data from a larger randomized controlled intervention study of an experimental social communication-focused early intervention and a domain-general early intervention. The objective of this dissertation was not to examine treatment effects but rather to characterize language abilities in the context of emerging autism to ultimately identify prognostic biomarkers for language outcomes in autism. However, testing whether pre-intervention receptive-expressive language phenotypes or pre-intervention EEG-based metrics of functional brain development moderate the effects of intervention on both language outcomes would be of great value in not only parsing heterogeneity in intervention response (particularly given as many as half of autistic children fail to make meaningful gains in language even in the presence of high-quality intervention; Panganiban & Kasari, 2022) but also in the identification of predictive markers that can facilitate the identification of children most likely to respond favorably to a given intervention approach (FDA-NIH Biomarker Working Group, 2020). These questions will be addressed in future studies.

Conclusions

The present study is among the first to examine neural correlates of receptive-expressive language phenotypes in emerging autism, providing new insight into mechanisms that may underpin language heterogeneity among children with autism symptoms. I report that children with receptive-expressive language phenotypes characterized by relative receptive language disadvantage exhibit lower levels of relative theta power as compared with children who present with more advanced receptive language skills relative to their expressive skill level. Our longitudinal findings suggest that higher levels of spontaneous alpha power may serve as a neural marker of resilience in autism, whereas lower levels of alpha power may signal underlying vulnerability for stalled language growth and poorer language outcomes. These findings provide a basis for future research expanding this line of inquiry to the intervention context (e.g., identifying brain-based predictive markers or markers of intervention response)

and, ultimately, to the development of scalable, clinically practicable tools to optimize care for children with or at high clinical risk of autism.

Appendix

Unconditional Growth Model Specifications

Level-1: $$Y_{it} = \pi_{0i} + \pi_{1i}TIME_{ti} + e_{ti}$$

Level-2: $$\pi_{0i} = \gamma_{00} + u_{0i}$$
$$\pi_{1i} = \gamma_{10} + u_{1i}$$

In the level-1 equation, π_{0i} represents child i's predicted language score at T1, and π_{1i} presents child *i*'s predicted rate of linear growth in language abilities. The term e_{ti} represents unobserved level-1 residuals for child *i* at *t* measurement occasion. We assume the level-1 residuals are normally distributed with a mean of 0 and variance σ_e^2.

In the level-2 equations, π_{0i} and π_{1i} are the individual intercept and linear slope growth parameters of the true trajectory for child *i.* The γ_{00} and γ_{10} terms are fixed effects coefficients that may be interpreted in a similar manner to regular regression coefficients. The level-2 residuals, u_{0i} and u_{1i}, represent unexplained variation in individual growth parameters (i.e., random effects); here, these values represent the deviation between child *i*'s true initial status and true linear slope, respectively, from their estimated average trajectory. To account for possible associations between initial status and rate of change, level-2 residuals are allowed to be correlated, resulting in a 2x2 variance-covariance matrix. We assume that level-2 residuals are bivariate normally distributed with a mean of 0, unknown variances (σ_0^2 and σ_1^2 for intercept and slope parameters, respectively) and unknown covariance σ_{01}.

Model-Based (Empirical Bayes) Estimates of Individual Growth Parameters

To evaluate the extent to which spectral power at T1 was associated with individual differences in rate of language growth, model-based estimates of individual growth parameters were extracted from receptive and expressive language growth models. Individual estimates of

linear slope parameters, $\tilde{\pi}_{1i}$, are obtained by combining information about child i's true population linear growth trajectory ($\hat{\pi}_{1i}$) with their level-2 residuals u_{1i}.

References

Adolphs, R. (2008). The social brain: Neural basis of social knowledge. *Annual Review of Psychology*, *60*(1), 693–716. https://doi.org/10.1146/annurev.psych.60.110707.163514

Anaya, B., Ostlund, B., LoBue, V., Buss, K., & Pérez-Edgar, K. (2021). Psychometric properties of infant electroencephalography: Developmental stability, reliability, and construct validity of frontal alpha asymmetry and delta–beta coupling. *Developmental Psychobiology*, *63*(6), e22178. https://doi.org/10.1002/dev.22178

Anderson, A., & Perone, S. (2018). Developmental change in the resting state electroencephalogram: Insights into cognition and the brain. *Brain and Cognition*, *126*, 40–52. https://doi.org/10.1016/j.bandc.2018.08.001

Bal, V. H., Kim, S.-H., Cheong, D., & Lord, C. (2015). Daily living skills in individuals with autism spectrum disorder from 2 to 21 years of age. *Autism*, *19*(7), 774–784. https://doi.org/10.1177/1362361315575840

Baron-Cohen, S. (1991). The development of a theory of mind in autism: Deviance and delay? *Psychiatric Clinics*, *14*(1), 33–51. https://doi.org/10.1016/S0193-953X(18)30323-X

Bartak, L., Rutter, M., & Cox, A. (1975). A comparative study of infantile autism and specific developmental receptive language disorder. *The British Journal of Psychiatry*, *126*(2), 127–145. Cambridge Core. https://doi.org/10.1192/bjp.126.2.127

Begus, K., & Bonawitz, E. (2020). The rhythm of learning: Theta oscillations as an index of active learning in infancy. *Developmental Cognitive Neuroscience*, *45*, 100810. https://doi.org/10.1016/j.dcn.2020.100810

Begus, K., Gliga, T., & Southgate, V. (2016). Infants' preferences for native speakers are associated with an expectation of information. *Proceedings of the National Academy of Sciences*, *113*(44), 12397–12402. https://doi.org/10.1073/pnas.1603261113

Begus, K., Southgate, V., & Gliga, T. (2015). Neural mechanisms of infant learning: Differences in frontal theta activity during object exploration modulate subsequent object recognition. *Biology Letters*, *11*(5), 20150041. https://doi.org/10.1098/rsbl.2015.0041

Belteki, Z., Lumbreras, R., Fico, K., Haman, E., & Junge, C. (2022). The vocabulary of infants with an elevated likelihood and diagnosis of autism spectrum disorder: A systematic review and meta-analysis of infant language studies using the CDI and MSEL. *International Journal of Environmental Research and Public Health*, *19*(3), 1469. https://doi.org/10.3390/ijerph19031469

Benninger, C., Matthis, P., & Scheffner, D. (1984). EEG development of healthy boys and girls. Results of a longitudinal study. *Electroencephalography and Clinical Neurophysiology*, *57*(1), 1–12. https://doi.org/10.1016/0013-4694(84)90002-6

Bosseler, A., Taulu, S., Pihko, E., Mäkelä, J., Imada, T., Ahonen, A., & Kuhl, P. (2013). Theta brain rhythms index perceptual narrowing in infant speech perception. *Frontiers in Psychology*, *4*.

Braithwaite, E. K., Jones, E. J. H., Johnson, M. H., & Holmboe, K. (2020). Dynamic modulation of frontal theta power predicts cognitive ability in infancy. *Developmental Cognitive Neuroscience*, *45*, 100818. https://doi.org/10.1016/j.dcn.2020.100818

Bullmore, E. T., Suckling, J., Overmeyer, S., Rabe-Hesketh, S., Taylor, E., & Brammer, M. J. (1999). Global, voxel, and cluster tests, by theory and permutation, for a difference between two groups of structural MR images of the brain. *IEEE Transactions on Medical Imaging*, *18*(1), 32–42. https://doi.org/10.1109/42.750253

Bussu, G., Jones, E. J. H., Charman, T., Johnson, M. H., Buitelaar, J. K., Baron-Cohen, S., … Volein, A. (2018). Prediction of autism at 3 years from behavioural and developmental measures in high-risk infants: A longitudinal cross-domain classifier analysis. *Journal of Autism and Developmental Disorders*, *48*(7), 2418–2433. https://doi.org/10.1007/s10803-018-3509-x

Buzsáki, G. (2011). *Rhythms of the Brain*. Oxford University Press.

Buzzell, G. A., Morales, S., Valadez, E. A., Hunnius, S., & Fox, N. A. (2023). Maximizing the potential of EEG as a developmental neuroscience tool. *Developmental Cognitive Neuroscience*, *60*, 101201. https://doi.org/10.1016/j.dcn.2023.101201

Cainelli, E., Vedovelli, L., Carretti, B., & Bisiacchi, P. (2023). EEG correlates of developmental dyslexia: A systematic review. *Annals of Dyslexia*, *73*(2), 184–213. https://doi.org/10.1007/s11881-022-00273-1

Carter Leno, V., Pickles, A., van Noordt, S., Huberty, S., Desjardins, J., Webb, S. J., … BASIS Team. (2021). 12-Month peak alpha frequency is a correlate but not a longitudinal predictor of non-verbal cognitive abilities in infants at low and high risk for autism spectrum disorder. *Developmental Cognitive Neuroscience*, *48*, 100938. https://doi.org/10.1016/j.dcn.2021.100938

Çetinçelik, M., Rowland, C. F., & Snijders, T. M. (2023). Ten-month-old infants' neural tracking of naturalistic speech is not facilitated by the speaker's eye gaze. *Developmental Cognitive Neuroscience*, *64*, 101297. https://doi.org/10.1016/j.dcn.2023.101297

Chahal, R., Weissman, D. G., Marek, S., Rhoads, S. A., Hipwell, A. E., Forbes, E. E., … Guyer, A. E. (2020). Girls' brain structural connectivity in late adolescence relates to history of depression symptoms. *Journal of Child Psychology and Psychiatry*, *61*(11), 1224–1233. https://doi.org/10.1111/jcpp.13184

Chang, C.-Y., Hsu, S.-H., Pion-Tonachini, L., & Jung, T.-P. (2018). Evaluation of Artifact Subspace Reconstruction for Automatic EEG Artifact Removal. *2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 1242–1245. https://doi.org/10.1109/EMBC.2018.8512547

Chapeton, J. I., Haque, R., Wittig, J. H., Inati, S. K., & Zaghloul, K. A. (2019). Large-scale communication in the human brain is rhythmically modulated through alpha coherence. *Current Biology*, *29*(17), 2801-2811.e5. https://doi.org/10.1016/j.cub.2019.07.014

Choi, B., Leech, K. A., Tager-Flusberg, H., & Nelson, C. A. (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*(1), 14–14. https://doi.org/10.1016/j.ejca.2011.06.019

Clarke, A. R., Barry, R. J., McCarthy, R., & Selikowitz, M. (2001). Age and sex effects in the EEG: Development of the normal child. *Clinical Neurophysiology*, *112*(5), 806–814. https://doi.org/10.1016/S1388-2457(01)00488-6

Cohenour, T. L., Gulsrud, A., & Kasari, C. (2023). Heterogeneity of autism symptoms in community-referred infants and toddlers at elevated or low familial likelihood of autism. *Autism Research*, *16*(9), 1739–1749. https://doi.org/10.1002/aur.2973

Coslett, H. B., & Schwartz, M. F. (2018). Chapter 18—The parietal lobe and language. In G. Vallar & H. B. Coslett (Eds.), *Handbook of Clinical Neurology* (Vol. 151, pp. 365–375). Elsevier. https://doi.org/10.1016/B978-0-444-63622-5.00018-8

Crowther, A., Smoski, M. J., Minkel, J., Moore, T., Gibbs, D., Petty, C., … Dichter, G. S. (2015). Resting-state connectivity predictors of response to psychotherapy in major depressive disorder. *Neuropsychopharmacology*, *40*(7), 1659–1673. https://doi.org/10.1038/npp.2015.12

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Dickinson, A., Daniel, M., Marin, A., Gaonkar, B., Dapretto, M., McDonald, N. M., & Jeste, S. (2021). Multivariate neural connectivity patterns in early infancy predict later autism symptoms. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(1), 59–69. https://doi.org/10.1016/j.bpsc.2020.06.003

Dickinson, A., DiStefano, C., Senturk, D., & Jeste, S. S. (2018). Peak alpha frequency is a neural marker of cognitive function across the autism spectrum. *European Journal of Neuroscience*, *47*(6), 643–651. https://doi.org/10.1111/ejn.13645

Dickinson, A., Varcin, K. J., Sahin, M., Nelson III, C. A., & Jeste, S. S. (2019). Early patterns of functional brain development associated with autism spectrum disorder in tuberous sclerosis complex. *Autism Research*, *12*(12), 1758–1773. https://doi.org/10.1002/aur.2193

Franchini, M., Duku, · E, Armstrong, · V, Brian, · J, Bryson, · S E, Garon, · N, … Smith, I. M. (2018). Variability in verbal and nonverbal communication in infants at risk for autism spectrum disorder: Predictors and outcomes. *Journal of Autism and Developmental Disorders*, *48*(10), 3417–3431. https://doi.org/10.1007/s10803-018-3607-9

Friederici, A. D., Brauer, J., & Lohmann, G. (2011). Maturation of the language network: From inter- to intrahemispheric connectivities. *PloS One*, *6*(6), e20726. https://doi.org/10.1371/journal.pone.0020726

Friederici, A. D., & Gierhan, S. M. (2013). The language network. *Current Opinion in Neurobiology*, *23*(2), 250–254. https://doi.org/10.1016/j.conb.2012.10.002

Friedrich, M., & Friederici, A. D. (2008). Neurophysiological correlates of online word learning in 14-month-old infants. *NeuroReport*, *19*(18), 1757. https://doi.org/10.1097/WNR.0b013e328318f014

Garcés, P., Baumeister, S., Mason, L., Chatham, C. H., Holiga, S., Dukart, J., … The EU-AIMS LEAP group authorship. (2022). Resting state EEG power spectrum and functional connectivity in autism: A cross-sectional analysis. *Molecular Autism*, *13*(1), 22. https://doi.org/10.1186/s13229-022-00500-x

Gillespie-Lynch, K., Sepeta, L., Wang, Y., Marshall, S., Gomez, L., Sigman, M., & Hutman, T. (2012). Early childhood predictors of the social competence of adults with autism. *Journal of Autism and Developmental Disorders*, *42*(2), 161–174. https://doi.org/10.1007/s10803-011-1222-0

Giraud, A.-L., & Poeppel, D. (2012). Cortical oscillations and speech processing: Emerging computational principles and operations. *Nature Neuroscience*, *15*(4), 511–517. https://doi.org/10.1038/nn.3063

Glauser, J., Wilkinson, C. L., Gabard-Durnam, L. J., Choi, B., Tager-Flusberg, H., & Nelson, C. A. (2022). Neural correlates of face processing associated with development of social communication in 12-month infants with familial risk of autism spectrum disorder. *Journal of Neurodevelopmental Disorders*, *14*(1), 6. https://doi.org/10.1186/s11689-021-09413-x

Goswami, U. (2019). Speech rhythm and language acquisition: An amplitude modulation phase hierarchy perspective. *Annals of the New York Academy of Sciences*, *1453*(1), 67–78. https://doi.org/10.1111/nyas.14137

Gotham, K., Pickles, A., & Lord, C. (2012). Trajectories of autism severity in children using standardized ADOS scores. *PEDIATRICS*, *130*(5), e1278–e1284. https://doi.org/10.1542/peds.2011-3668

Guy, J., Mottron, L., Berthiaume, C., & Bertone, A. (2019). A developmental perspective of global and local visual perception in autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *49*(7), 2706–2720. https://doi.org/10.1007/s10803-016-2834-1

Haartsen, R., Charman, T., Pasco, G., Johnson, M. H., & Jones, E. J. H. (2022). Modulation of EEG theta by naturalistic social content is not altered in infants with family history of autism. *Scientific Reports*, *12*(1), 20758. https://doi.org/10.1038/s41598-022-24870-7

Henderson, L. M., Yoder, P. J., Yale, M. E., & McDuffie, A. (2002). Getting the point: Electrophysiological correlates of protodeclarative pointing. *International Journal of Developmental Neuroscience*, *20*(3), 449–458. https://doi.org/10.1016/S0736-5748(02)00038-2

Huberty, S., Carter Leno, V., van Noordt, S. J. R., Bedford, R., Pickles, A., Desjardins, J. A., … Elsabbagh, M. (2021). Association between spectral electroencephalography power and

autism risk and diagnosis in early development. *Autism Research*, *14*(7), 1390–1403. https://doi.org/10.1002/aur.2518

Huberty, S., O'Reilly, C., Carter Leno, V., Steiman, M., Webb, S., & Elsabbagh, M. (2023). Neural mechanisms of language development in infancy. *Infancy*, *Advance online publication.* https://doi.org/10.1111/infa.12540

Jasper, H. (1958). Ten-Twenty Electrode System of the International Federation. *Electroencephalography and Clinical Neurophysiology*.

Jones, E. J. H., Goodwin, A., Orekhova, E., Charman, T., Dawson, G., Webb, S. J., & Johnson, M. H. (2020). Infant EEG theta modulation predicts childhood intelligence. *Scientific Reports*, *10*(1), 11232. https://doi.org/10.1038/s41598-020-67687-y

Jones, Emily J. H., Venema, K., Lowy, R., Earl, R. K., & Webb, S. J. (2015). Developmental changes in infant brain activity during naturalistic social experiences. *Developmental Psychobiology*, *57*(7), 842–853. https://doi.org/10.1002/dev.21336

Keown, C. L., Datko, M. C., Chen, C. P., Maximo, J. O., Jahedi, A., & Müller, R.-A. (2017). Network organization is globally atypical in autism: A graph theory study of intrinsic functional connectivity. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *2*(1), 66–75. https://doi.org/10.1016/j.bpsc.2016.07.008

Klin, A., Micheletti, M., Klaiman, C., Shultz, S., Constantino, J. N., & Jones, W. (2020). Affording autism an early brain development re-definition. *Development and Psychopathology*, *32*(4), 1175–1189. https://doi.org/10.1017/S0954579420000802

Klin, A., Shultz, S., & Jones, W. (2015). Social visual engagement in infants and toddlers with autism: Early developmental transitions and a model of pathogenesis. *Neuroscience and Biobehavioral Reviews*, *50*, 189–203. https://doi.org/10.1016/j.neubiorev.2014.10.006

Kolesnik, A., Begum Ali, J., Gliga, T., Guiraud, J., Charman, T., Johnson, M. H., … The BASIS Team. (2019). Increased cortical reactivity to repeated tones at 8 months in infants with later ASD. *Translational Psychiatry*, *9*(1), 46. https://doi.org/10.1038/s41398-019-0393-x

Köster, M., Langeloh, M., Michel, C., & Hoehl, S. (2021). Young infants process prediction errors at the theta rhythm. *NeuroImage*, *236*, 118074. https://doi.org/10.1016/j.neuroimage.2021.118074

Kover, S. T., Edmunds, S. R., & Ellis Weismer, S. (2016). Brief Report: ages of language milestones as predictors of developmental trajectories in young children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *46*(7), 2501–2507. https://doi.org/10.1007/s10803-016-2756-y

Kuhl, P. K., Coffey-Corina, S., Padden, D., Munson, J., Estes, A., & Dawson, G. (2013). Brain responses to words in 2-year-olds with autism predict developmental outcomes at age 6. *PloS One*, *8*(5), e64967. https://doi.org/10.1371/journal.pone.0064967

Kuhl, P. K., Conboy, B. T., Padden, D., Nelson, T., & Pruitt, J. (2005). Early speech perception and later language development: Implications for the "critical period." *Language Learning and Development*, *1*(3–4), 237–264. https://doi.org/10.1080/15475441.2005.9671948

Kuhl, P. K., & Meltzoff, A. N. (1982). The bimodal perception of speech in infancy. *Science (New York, N.Y.)*.

Lauttia, J., Helminen, T. M., Leppänen, J. M., Yrttiaho, S., Eriksson, K., Hietanen, J. K., & Kylliäinen, A. (2019). Atypical pattern of frontal EEG asymmetry for direct gaze in young children with autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *49*(9), 3592–3601. https://doi.org/10.1007/s10803-019-04062-5

Law, E. C., Han, M. X., Lai, Z., Lim, S., Ong, Z. Y., Ng, V., … Nelson, C. A. (2023). Associations between infant screen use, electroencephalography markers, and cognitive outcomes. *JAMA Pediatrics*, *177*(3), 311–318. https://doi.org/10.1001/jamapediatrics.2022.5674

Leppa, V., Kravitz, S., Martin, C., Andrieux, J., Le Caignec, C., Martin-Coignard, D., … Geschwind, D. (2016). Rare inherited and de novo CNVs reveal complex contributions to ASD risk in multiplex families. *American Journal of Human Genetics*, *99*(3), 540–554. https://doi.org/10.1016/j.ajhg.2016.06.036

Levin, A. R., Naples, A. J., Scheffler, A. W., Webb, S. J., Shic, F., Sugar, C. A., … and the Autism Biomarkers Consortium for Clinical Trials. (2020). Day-to-Day test-retest reliability of eeg profiles in children with autism spectrum disorder and typical development. *Frontiers in Integrative Neuroscience*, *14*. Retrieved from https://www.frontiersin.org/articles/10.3389/fnint.2020.00021

Levin, A. R., Varcin, K. J., O'Leary, H. M., Tager-Flusberg, H., & Nelson, C. A. (2017). EEG power at 3 months in infants at high familial risk for autism. *Journal of Neurodevelopmental Disorders*, *9*(1), 34. https://doi.org/10.1186/s11689-017-9214-9

Lewis, J. D., Evans, A. C., Pruett, J. R., Botteron, K., Zwaigenbaum, L., Estes, A., … Piven, J. (2014). Network inefficiencies in autism spectrum disorder at 24 months. *Translational Psychiatry*, *4*(5), e388–e388. https://doi.org/10.1038/tp.2014.24

Lombardo, M. V., Pierce, K., Eyler, L., Barnes, C. C., Ahrens-Barbeau, C., Solso, S., … Courchesne, E. (2015). Different functional neural substrates for good and poor language outcome in autism. *Neuron*, *86*(2), 567–577. https://doi.org/10.1016/j.neuron.2015.03.023

Maguire, M. J., & Schneider, J. M. (2019). Socioeconomic status related differences in resting state EEG activity correspond to differences in vocabulary and working memory in grade school. *Brain and Cognition*, *137*, 103619. https://doi.org/10.1016/j.bandc.2019.103619

Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscience Methods*, *164*(1), 177–190. https://doi.org/10.1016/j.jneumeth.2007.03.024

Marriott Haresign, I., Phillips, E. a. M., Whitehorn, M., Lamagna, F., Eliano, M., Goupil, L., … Wass, S. V. (2023). Gaze onsets during naturalistic infant-caregiver interaction associate with 'sender' but not 'receiver' neural responses, and do not lead to changes in inter-brain synchrony. *Scientific Reports*, *13*(1), 3555. https://doi.org/10.1038/s41598-023-28988-0

Marrus, N., Hall, L. P., Paterson, S. J., Elison, J. T., Wolff, J. J., Swanson, M. R., … Gu, H. (2018). Language delay aggregates in toddler siblings of children with autism spectrum disorder. *Journal of Neurodevelopmental Disorders*, *10*(1), 29. https://doi.org/10.1186/s11689-018-9247-8

Marshall, P. J., Bar-Haim, Y., & Fox, N. A. (2002). Development of the EEG from 5 months to 4 years of age. *Clinical Neurophysiology*, *113*(8), 1199–1208. https://doi.org/10.1016/S1388-2457(02)00163-3

Marshall, P. J., Fox, N. A., & BEIP Core Group. (2004). a comparison of the electroencephalogram between institutionalized and community children in Romania. *Journal of Cognitive Neuroscience*, *16*(8), 1327–1338. https://doi.org/10.1162/0898929042304723

McEvoy, K., Hasenstab, K., Senturk, D., Sanders, A., & Jeste, S. S. (2015). Physiologic artifacts in resting state oscillations in young children: Methodological considerations for noisy data. *Brain Imaging and Behavior*, *9*(1), 104–114. https://doi.org/10.1007/s11682-014-9343-7

McLaughlin, K. A., Fox, N. A., Zeanah, C. H., Sheridan, M. A., Marshall, P., & Nelson, C. A. (2010). Delayed maturation in brain electrical activity partially explains the association between early environmental deprivation and symptoms of attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *68*(4), 329–336. https://doi.org/10.1016/j.biopsych.2010.04.005

Meng, X., Sun, C., Du, B., Liu, L., Zhang, Y., Dong, Q., … Nan, Y. (2022). The development of brain rhythms at rest and its impact on vocabulary acquisition. *Developmental Science*, *25*(2), e13157. https://doi.org/10.1111/desc.13157

Menn, K. H., Mannel, C., & Meyer, L. (2023). Does electrophysiological maturation shape language acquisition? *Perspectives on Psychological Science : A Journal of the Association for Psychological Science*, 17456916231151584. https://doi.org/10.1177/17456916231151584

Menn, K. H., Michel, C., Meyer, L., Hoehl, S., & Männel, C. (2022). Natural infant-directed speech facilitates neural tracking of prosody. *NeuroImage*, *251*, 118991. https://doi.org/10.1016/j.neuroimage.2022.118991

Meyer, M., Lamers, D., Kayhan, E., Hunnius, S., & Oostenveld, R. (2021). Enhancing reproducibility in developmental EEG research: BIDS, cluster-based permutation tests, and effect sizes. *Developmental Cognitive Neuroscience*, *52*, 101036. https://doi.org/10.1016/j.dcn.2021.101036

Mundy, P., Card, J., & Fox, N. (2000). EEG correlates of the development of infant joint attention skills. *Developmental Psychobiology*, *36*(4), 325–338.

Mundy, P., Fox, N., & Card, J. (2003). EEG coherence, joint attention and language development in the second year. *Developmental Science*, *6*(1), 48–54. https://doi.org/10.1111/1467-7687.00253

Nair, A., Jalal, R., Liu, J., Tsang, T., McDonald, N. M., Jackson, L., … Dapretto, M. (2021). Altered Thalamocortical Connectivity in 6-Week-Old Infants at High Familial Risk for Autism Spectrum Disorder. *Cerebral Cortex*, *31*(9), 4191–4205. https://doi.org/10.1093/cercor/bhab078

Nyström, P., Jones, E., Darki, F., Bölte, S., & Falck-Ytter, T. (2021). Atypical topographical organization of global form and motion processing in 5-month-old infants at risk for autism. *Journal of Autism and Developmental Disorders*, *51*(1), 364–370. https://doi.org/10.1007/s10803-020-04523-2

Onton, J., Westerfield, M., Townsend, J., & Makeig, S. (2006). Imaging human EEG dynamics using independent component analysis. *Neuroscience & Biobehavioral Reviews*, *30*(6), 808–822. https://doi.org/10.1016/j.neubiorev.2006.06.007

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2010). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological Data.

Computational Intelligence and Neuroscience, *2011*, 156869. https://doi.org/10.1155/2011/156869

Orekhova, E. V., Stroganova, T. A., Posikera, I. N., & Elam, M. (2006). EEG theta rhythm in infants and preschool children. *Clinical Neurophysiology*, *117*(5), 1047–1062. https://doi.org/10.1016/j.clinph.2005.12.027

Ortiz-Mantilla, S., Hämäläinen, J. A., Realpe-Bonilla, T., & Benasich, A. A. (2016). Oscillatory dynamics underlying perceptual narrowing of native phoneme mapping from 6 to 12 months of age. *Journal of Neuroscience*, *36*(48), 12095–12105. https://doi.org/10.1523/JNEUROSCI.1162-16.2016

Ozonoff, S., Iosif, A.-M., Baguio, F., Cook, I. C., Hill, M. M., Hutman, T., … Young, G. S. (2010). A prospective study of the emergence of early behavioral signs of autism. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*(3), 256-266.e2. https://doi.org/10.1016/j.jaac.2009.11.009

Paterson, S. J., Heim, S., Thomas Friedman, J., Choudhury, N., & Benasich, A. A. (2006). Development of structure and function in the infant brain: Implications for cognition, language and social behaviour. *Neuroscience & Biobehavioral Reviews*, *30*(8), 1087–1105. https://doi.org/10.1016/j.neubiorev.2006.05.001

Paulus, M., Kühn-Popp, N., Licata, M., Sodian, B., & Meinhardt, J. (2013). Neural correlates of prosocial behavior in infancy: Different neurophysiological mechanisms support the emergence of helping and comforting. *NeuroImage*, *66*, 522–530. https://doi.org/10.1016/j.neuroimage.2012.10.041

Pernet, C. R., Appelhoff, S., Gorgolewski, K. J., Flandin, G., Phillips, C., Delorme, A., & Oostenveld, R. (2019). EEG-BIDS, an extension to the brain imaging data structure for electroencephalography. *Scientific Data*, *6*(1), 103. https://doi.org/10.1038/s41597-019-0104-8

Perone, S., & Gartstein, M. A. (2019). Relations between dynamics of parent-infant interactions and baseline EEG functional connectivity. *Infant Behavior and Development*, *57*, 101344. https://doi.org/10.1016/j.infbeh.2019.101344

Peters, J. M., Taquet, M., Vega, C., Jeste, S. S., Fernández, I. S., Tan, J., … Warfield, S. K. (2013). Brain functional networks in syndromic and non-syndromic autism: A graph theoretical study of EEG connectivity. *BMC Medicine*, *11*(1), 54. https://doi.org/10.1186/1741-7015-11-54

Phillips, E. A. M., Goupil, L., Whitehorn, M., Bruce-Gardyne, E., Csolsim, F. A., Marriott-Haresign, I., & Wass, S. V. (2023). Proactive or reactive? Neural oscillatory insight into the leader–follower dynamics of early infant–caregiver interaction. *Proceedings of the National Academy of Sciences*, *120*(15), e2122481120. https://doi.org/10.1073/pnas.2122481120

Pierce, L. J., Reilly, E., & Nelson, C. A. (2021). Associations between maternal stress, early language behaviors, and infant electroencephalography during the first year of life. *Journal of Child Language*, *48*(4), 737–764. https://doi.org/10.1017/S0305000920000501

Romeo, R. R., Choi, B., Gabard-Durnam, L. J., Wilkinson, C. L., Levin, A. R., Rowe, M. L., … Nelson, C. A. (2021). Parental language input predicts neuroscillatory patterns associated with language development in toddlers at risk of autism. *Journal of Autism and Developmental Disorders*. https://doi.org/10.1007/s10803-021-05024-6

Rowe, M. L., Raudenbush, S. W., & Goldin-Meadow, S. (2012). The pace of vocabulary growth helps predict later vocabulary skill. *Child Development*, *83*(2), 508–525. https://doi.org/10.1111/j.1467-8624.2011.01710.x

Saby, J. N., & Marshall, P. J. (2012). The utility of EEG band power analysis in the study of infancy and early childhood. *Developmental Neuropsychology*, *37*(3), 253–273. https://doi.org/10.1080/87565641.2011.614663

Shephard, E., Fatori, D., Mauro, L. R., de Medeiros Filho, M. V., Hoexter, M. Q., Chiesa, A. M., … Polanczyk, G. V. (2019). Effects of maternal psychopathology and education level on neurocognitive development in infants of adolescent mothers living in poverty in Brazil. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *4*(10), 925–934. https://doi.org/10.1016/j.bpsc.2019.05.009

Singer, J., & Willet, J. (2003). *Applied Longitudinal Data Analysis*. New York, NY: Oxford University Press.

Smith, C. L., & Bell, M. A. (2010). Stability in infant frontal asymmetry as a predictor of toddlerhood internalizing and externalizing behaviors. *Developmental Psychobiology*, *52*(2), 158–167. https://doi.org/10.1002/dev.20427

Snyder, S. M., & Hall, J. R. (2006). A meta-analysis of quantitative EEG power associated with attention-deficit hyperactivity disorder. *Journal of Clinical Neurophysiology*, *23*(5), 441. https://doi.org/10.1097/01.wnp.0000221363.12503.78

Swanson, M. R., Shen, M. D., Wolff, J. J., Elison, J. T., Emerson, R. W., Styner, M. A., … Gu, H. (2017). Subcortical brain and behavior phenotypes differentiate infants with autism versus language delay. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *2*(8), 664–672. https://doi.org/10.1016/j.bpsc.2017.07.007

Tan, E., Tang, A., Debnath, R., Humphreys, K. L., Zeanah, C. H., Nelson, C. A., & Fox, N. A. (2023). Resting brain activity in early childhood predicts IQ at 18 years. *Developmental Cognitive Neuroscience*, *63*, 101287. https://doi.org/10.1016/j.dcn.2023.101287

Tierney, A. L., Gabard-Durnam, L., Vogel-Farley, V., Tager-Flusberg, H., & Nelson, C. A. (2012). Developmental trajectories of resting eeg power: An endophenotype of autism spectrum disorder. *PLoS ONE*, *7*(6). https://doi.org/10.1371/journal.pone.0039127

Tran, X. A., McDonald, N., Dickinson, A., Scheffler, A., Frohlich, J., Marin, A., … Spurling Jeste, S. (2021). Functional connectivity during language processing in 3-month-old infants at

familial risk for autism spectrum disorder. *European Journal of Neuroscience*, *53*(5), 1621–1637. https://doi.org/10.1111/ejn.15005

Troller-Renfree, S. V., Sperber, J. F., Hart, E. R., Costanzo, M. A., Gennetian, L. A., Meyer, J. S., … Noble, K. G. (2023). Associations between maternal stress and infant resting brain activity among families residing in poverty in the U.S. *Biological Psychology*, *184*, 108683. https://doi.org/10.1016/j.biopsycho.2023.108683

Valdés-Hernández, P. A., Ojeda-González, A., Martínez-Montes, E., Lage-Castellanos, A., Virués-Alba, T., Valdés-Urrutia, L., & Valdes-Sosa, P. A. (2010). White matter architecture rather than cortical surface area correlates with the EEG alpha rhythm. *NeuroImage*, *49*(3), 2328–2339. https://doi.org/10.1016/j.neuroimage.2009.10.030

van der Velde, B., Haartsen, R., & Kemner, C. (2019). Test-retest reliability of EEG network characteristics in infants. *Brain and Behavior*, *9*(5), e01269. https://doi.org/10.1002/brb3.1269

van der Velde, B., White, T., & Kemner, C. (2021). The emergence of a theta social brain network during infancy. *NeuroImage*, *240*, 118298. https://doi.org/10.1016/j.neuroimage.2021.118298

Wang, J., Barstein, J., Ethridge, L. E., Mosconi, M. W., Takarae, Y., & Sweeney, J. A. (2013). Resting state EEG abnormalities in autism spectrum disorders. *Journal of Neurodevelopmental Disorders*, *5*(1), 1–14. https://doi.org/10.1186/1866-1955-5-24

Wass, S. V., Noreika, V., Georgieva, S., Clackson, K., Brightman, L., Nutbrown, R., … Leong, V. (2018). Parental neural responsivity to infants' visual attention: How mature brains influence immature brains during social interaction. *PLoS Biology*, *16*(12), e2006328. https://doi.org/10.1371/journal.pbio.2006328

Wilkinson, C. L., Gabard-Durnam, L. J., Kapur, K., Tager-Flusberg, H., Levin, A. R., & Nelson, C. A. (2020). Use of longitudinal EEG measures in estimating language development in

infants with and without familial risk for autism spectrum disorder. *Neurobiology of Language*, *1*(1), 33–53. https://doi.org/10.1162/nol_a_00002

Wilkinson, C. L., Levin, A. R., Gabard-Durnam, L. J., Tager-Flusberg, H., & Nelson, C. A. (2019). Reduced frontal gamma power at 24 months is associated with better expressive language in toddlers at risk for autism. *Autism Research*. https://doi.org/10.1002/aur.2131

Xie, W., Mallin, B. M., & Richards, J. E. (2019). Development of brain functional connectivity and its relation to infant sustained attention in the first year of life. *Developmental Science*, *22*(1), e12703. https://doi.org/10.1111/desc.12703

Xie, W., Toll, R. T., & Nelson, C. A. (2022). EEG functional connectivity analysis in the source space. *Developmental Cognitive Neuroscience*, *56*, 101119. https://doi.org/10.1016/j.dcn.2022.101119

GENERAL DISCUSSION

Recent years have brought significant advances in our understanding of communication and language development in autism and factors that may contribute to variability in language growth. There is a pressing need to identify markers – whether behavioral/clinical, demographic, neural, or a combination – that can shed light on early heterogeneity in communication and language development in autism and ultimately facilitate earlier identification of children with the highest risk for poor language outcomes. Towards this goal, this dissertation sought to explore behavioral and brain-based factors contributing to language heterogeneity in emerging autism by leveraging electroencephalography (EEG) and behavioral data collected from a sample of community-referred, racially, and ethnically diverse infants and toddlers with heightened clinical risk of autism.

Study 1 examined *within-child* variability in language abilities by characterizing early receptive-expressive language phenotypes – that is, the extent to which receptive language and expressive language skills are of a similar developmental level. Clinically, understanding the prevalence of atypical receptive-expressive profiles – and co-occurring clinical and behavioral characteristics of children who present with an atypical language profile – may have important implications for early identification (e.g., distinguishing children with non-autism language delay from children likely to develop autism), and intervention planning and targets. Consistent with hypotheses, results revealed an increased prevalence of children with language profiles characterized by more advantage expressive language skills than receptive language skills. Contrary to expectations, receptive-expressive language phenotypes were not significantly associated with concurrent demographic, cognitive, and behavioral characteristics. However, receptive-expressive language phenotype at baseline significantly predicted the rate of expressive language growth, such that those with weaker language comprehension skills relative to language production skills showed slower expressive language growth than children with more typical receptive-expressive language profiles.

Building on this work, **Study 2** aimed to shed light on intrinsic neural mechanisms that may drive individual differences in receptive-expressive language phenotypes and language trajectories. Specifically, data-driven analyses were used to test whether levels of spontaneous oscillatory power measured during task-free EEG were predictive of concurrent receptive-expressive phenotypes and subsequent language growth. Study 2 identified significant associations between levels of spontaneous theta power and concurrent receptive-expressive language phenotypes, and significant associations between levels of spontaneous alpha power at T1 and longitudinal growth of receptive and expressive language skills.

The presence of robust brain-behavior associations, particularly given the absence of robust behavioral associations with receptive-expressive phenotypes and language growth, is striking and lends itself to a specific hypothesis: *individual differences in language abilities may be driven by differences in the integrity of lower-level, domain-general neurocognitive mechanisms that brain-based measures, such as EEG, are sensitive to*. This hypothesis is consistent with evidence for very early disruptions to domain-general attentional mechanisms and alterations in structural and functional brain development that appear in infancy *before* autism symptoms are detectable (Bedford et al., 2012; Constantino et al., 2017; Elsabbagh et al., 2013, 2009; Elsabbagh & Johnson, 2016; Johnson, 2017; Johnson, Jones, & Gliga, 2015; Johnson et al., 2015; E. J. H. Jones, Gliga, Bedford, Charman, & Johnson, 2014; W. Jones & Klin, 2013). The ontogenetic adaptation framework suggests that disruptions to these early domain-general social cognitive mechanisms arise from “adaptive” co-opting of these capacities (which play a crucial role in social and communication development in neurotypical infancy) for non-social functions, for instance.

Receptive and Expressive Language Development

Consistent with evidence from studies of older children with an autism diagnosis (e.g., Ellis Weismer & Kover, 2015; Ellis Weismer et al., 2010; Hudry et al., 2010; Reinhartsen et al., 2019), 12- to 23-month-old infants and toddlers exhibiting early signs of autism show an

elevated rate of atypical language profiles, and particularly, profiles characterized by a higher expressive language skill level than receptive language skill level. Given that there is little evidence to suggest that children with autism exhibit what appears to be an autism-specific atypical receptive-expressive language profile prior to 12 months (Hudry et al., 2014; Swanson et al., 2017), the present findings suggest that autism-associated alterations in receptive-expressive development likely co-emerge with core autisms symptoms themselves.

Though this dissertation was not designed to investigate causal mechanisms, it is worth considering what may be driving the emergence of these atypical profiles – whether receptively-advantaged or expressively-advantaged – in the first place. That is, what might lead children to have intact language understanding but relative delays in language production, or vice versa? For children with a receptive advantage profile, it is possible that their relatively delayed expressive language skills reflect underlying neuromotor deficits rather than something social-cognitive in nature. EL infants show delays in the development of gross and fine motor skills across the first years of life (Bedford, Pickles, & Lord, 2016; Begum Ali, et al., 2020; Choi, Leech, Tager-Flusberg, & Nelson, 2018), and fine motor skills as early as six months of age have been shown to predict later expressive language outcomes in toddlerhood (Choi et al., 2018). Children with autism show an increased prevalence of oromotor anomalies relative to children with neurotypical development or non-autism developmental delays (e.g., Rogers, Hepburn, Stackhouse, & Wehner, 2003; West, 2019), and among children diagnosed with autism, early oromotor skills have been shown to predict concurrent and later expressive language abilities, including minimally verbal or verbally-fluent status (Belmonte et al., 2013; Gernsbacher, Sauer, Geye, Schweigert, & Hill Goldsmith, 2008; Thurm, Lord, Lee, & Newschaffer, 2007). However, a recent study found no associations between the size of receptive-expressive vocabulary discrepancy and imitative and non-imitative oral-motor function (capacities critical for speech production), though their sample included preschool-age children who were significantly older than those in the present sample (McDaniel, Yoder, Woynaroski, &

Watson, 2018). Notably, gross and fine motor scores derived from the Mullen were not significantly associated with receptive-expressive discrepancy metrics in the present sample. However, a more targeted assessment of oromotor functioning would provide greater clarity.

In contrast, the driving force behind *expressive* language advantage (or, put otherwise, relative delays in receptive language) may be more social-cognitive in nature, which would be consistent with the hypothesis that language differences are rooted in fundamental attentional differences. Recent evidence suggests that measures of social visual attention (i.e., attention to a speaker's face) are significantly associated with later receptive-expressive language phenotype, such that autistic preschool-age children who spent less time attending to a speaker had more atypical language profiles (i.e., a greater expressive advantage) eight months later (McDaniel et al., 2018). On average, infants later diagnosed with autism show altered patterns of social visual attention (Chawarska, Macari, & Shic, 2013; Chawarska, Ye, Shic, & Chen, 2016; Constantino et al., 2017; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Klin, Shultz, & Jones, 2015; Pierce et al., 2016, 2023), dampened responsivity to speech as measured behaviorally (e.g., response to name) and using physiological markers of attention and arousal, such as heart rate variability (Hatch et al., 2021; Perdue et al., 2017), and greater difficulties integrating audio-visual speech information (Guiraud et al., 2012) than neurotypical infants. The cumulative effect of these early perceptual/attentional differences may only become observable in behavior *after* the first year of life, when environmental demands and developmental tasks, like language learning and production, require the integration of these systems. For instance, across the second year of life, enhanced visual attention to the mouth and eyes of a speaker is thought to support language acquisition by giving children access to the most language-rich, socially salient aspects of their environment (Habayeb et al., 2021; Hillairet de Boisferon, Tift, Minar, & Lewkowicz, 2018; Lewkowicz & Hansen-Tift, 2012); if the attentional mechanisms that enable children to derive any benefit from enhanced attention to linguistic-relevant cues are altered, then language development itself may be disrupted. Thus, the expressive advantage

language profile, predominant in the present sample, may reflect early-emerging anomalies in lower-level attention mechanisms that are especially pronounced in this subgroup of children with autism symptoms.

Receptive-Expressive Phenotype Predicts Expressive Language Growth

The observed association between initial receptive-expressive language phenotype and expressive language growth (where children with balanced or receptive-advantage profiles showed faster expressive language growth over time) is largely consistent with models of typical language acquisition, which posit that language comprehension drives language production (Bornstein & Hendricks, 2012; Fenson et al., 1994). If the atypical attention hypothesis holds, then it may be that children with an expressive advantage profile have a dual disadvantage in spoken language acquisition: that is, they may experience a reduction in the ability to attend to or process language input (hindering language growth overall), and weaker receptive language foundation on which to build expressive language skills. Clinically, the association between initial language profile and subsequent language growth suggests that examining receptive-expressive phenotypes (in conjunction with domain-specific language performance) may provide unique information about language prognosis and perhaps even facilitate the identification of children at risk for slowed or plateaued expressive language growth (despite having relatively intact initial expressive language skills) who would otherwise be overlooked as candidates for early language intervention.

Spontaneous Theta Power is Linked with Within-Individual Variability in Language Abilities

Although cross-sectional analyses failed to detect concurrent associations between demographic and behavioral variables of interest and receptive-expressive phenotype, analyses of spontaneous EEG power revealed consistent, robust associations between receptive-expressive phenotype and relative theta power. Specifically, lower levels of spontaneous theta power were associated with a more atypical language profile (i.e., an expressive advantage). In

contrast, children with higher levels of theta power tended to have more balanced or receptive advantaged language profiles. While increased levels of relative theta power are often considered a marker of neuromaturational delay in early childhood, among infants and toddlers with autism, this may be a neural adaptation – and potentially an *advantageous* adaptation – to underlying areas of vulnerability and strength. In infancy and early childhood, increases in theta activity have been observed during sustained attention and processing of social stimuli, including spoken language (Begus, Southgate, & Gliga, 2015; Bosseler et al., 2013; Haartsen, Charman, Pasco, Johnson, & Jones, 2022; Jones, Venema, Lowy, Earl, & Webb, 2015; Orekhova, Stroganova, & Posikera, 1999). As such, it has been proposed that theta activity may underpin a (social) attention-gating system that allows infants and toddlers to deploy attentional resources to the most social information-rich elements of the environment (Begus et al., 2015). In keeping with the altered attentional mechanisms hypothesis for atypical expressive language advantage, higher levels of spontaneous theta power, as observed among children with a stronger receptive-than-expressive language presentation, may serve an adaptive function by providing additional "scaffolding" supporting social attention. This neural infrastructure may, in turn, provide more opportunities for language learning or enable children to derive greater benefit from these learning opportunities achieved via social interactions. While this interpretation would be consistent with the ontogenetic adaptation hypothesis, future work should explore whether similar brain-behavior associations are observed among chronological- or mental age-matched neurotypical children and children with non-autism developmental delays to tease apart the specificity of this effect to autism (versus language delay more broadly).

Spontaneous Alpha Power Predicts Rate of Language Growth

Analyses revealed that infants and toddlers with autism symptoms who exhibit higher levels of spontaneous alpha power show an accelerated rate of language growth. This suggests that increased alpha power provides the neural infrastructure that supports language learning,

either by directly supporting language-specific functions or by reinforcing a domain-general cognitive mechanism that benefits language acquisition. For example, our recent study examining concurrent associations between resting-state EEG power and joint attention revealed robust associations between relative alpha power and children's ability to efficiently and accurately respond to others' bids for joint attention, such that higher alpha power was predictive of stronger concurrent response to joint attention skills among infants and toddlers with autism symptoms (Cohenour et al., *under review*).

Towards Precision Medicine: Spontaneous Alpha Power as a Candidate Biomarker

While the aim of this dissertation was not to evaluate treatment effects, the observed association between levels of alpha power and language growth provides a theoretical and empirical foundation for future work focused on intervention-related markers. Just as there is marked phenotypic heterogeneity in autism, there is also vast heterogeneity in intervention response. For instance, while some children make remarkable gains in response to intervention, others struggle to develop fluent language even when provided early, intensive, evidence-based treatments (Eldevik et al., 2010; Panganiban & Kasari, 2022). Identifying statistically reliable, clinically validated, objective biomarkers that stratify individuals into meaningful subpopulations or shed light on biological mechanisms underlying ostensive behavioral changes in response to treatment could provide crucial insight that ultimately leads to more personalized, tailored approaches to intervention. EEG-based metrics are promising for use as brain-based biomarkers, given that EEG tends to be lower cost, more readily available in community healthcare settings, and better tolerated by young children than neuroimaging approaches like MRI (McPartland, 2016, 2017).

Given evidence that pre-intervention levels of spontaneous alpha power are predictive of concurrent joint attention and language abilities (Cohenour et al., under review) as well as the subsequent rate of language growth, testing whether pre-intervention levels of alpha power moderate the effect of early interventions on language or social communication outcomes could

provide mechanistic insight into the neural groundwork that sets the stage for learning and whether differences in these underlying neural mechanisms may contribute to individual differences in intervention response.

Conclusions

Children with autism spectrum disorder often exhibit delays in the acquisition of spoken language, and a substantial minority of children still struggle to develop fluent speech by the time they enter primary school. Early acquisition of spoken language is highly consequential for longer-term developmental and functional outcomes across the lifespan; thus, there is a pressing need to understand behavioral, environmental, and intrinsic neural mechanisms that shape language growth and drive individual differences in language abilities in autism. This dissertation provides insight into language heterogeneity in the second year of life among infants and toddlers exhibiting early signs of autism. The findings reported here emphasize that within- and between-individual differences in language abilities among children with a high clinical likelihood of autism likely co-emerge with autism symptoms, and early variability in receptive-expressive language phenotypes may play a role in shaping subsequent development of expressive language skills. Building on these findings, I also identified robust associations between EEG-based measures of functional brain development and individual differences in concurrent language abilities and trajectories of language growth. Early heterogeneity in language acquisition in autism may be driven by alterations in foundational information-processing mechanisms that support various social and communication functions. This dissertation provides preliminary evidence that EEG-based measures of functional brain activity may be sensitive to individual differences in the mechanisms that directly or indirectly support successful language acquisition in autism. Together, these findings lay a roadmap for a future program of research aimed at identifying multimodal (brain, behavioral) markers that can identify children who would benefit the most from targeted language interventions and markers that can

facilitate the optimization and personalization of early interventions supporting social and communication development.

References

Adamson, L. B., Bakeman, R., Deckner, D. F., & Romski, M. (2009). Joint engagement and the emergence of language in children with autism and down syndrome. *Journal of Autism and Developmental Disorders*, *39*(1), 84–96. https://doi.org/10.1007/s10803-008-0601-7

American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association. https://doi.org/10.1176/appi.books.9780890425596

Bal, V. H., Kim, S.-H., Cheong, D., & Lord, C. (2015). Daily living skills in individuals with autism spectrum disorder from 2 to 21 years of age. *Autism*, *19*(7), 774–784. https://doi.org/10.1177/1362361315575840

Barbaro, J., & Dissanayake, C. (2017). Diagnostic stability of autism spectrum disorder in toddlers prospectively identified in a community-based setting: Behavioural characteristics and predictors of change over time. *Autism*, *21*(7), 830–840. https://doi.org/10.1177/1362361316654084

Bedford, R., Elsabbagh, M., Gliga, T., Pickles, A., Senju, A., Charman, T., & Johnson, M. H. (2012). Precursors to social and communication difficulties in infants at-risk for autism: Gaze following and attentional engagement. *Journal of Autism and Developmental Disorders*, *42*(10), 2208–2218. https://doi.org/10.1007/s10803-012-1450-y

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

Begum Ali, J., Charman, T., Johnson, M. H., Jones, E. J. H., & and the BASIS/STAARS Team. (2020). Early motor differences in infants at elevated likelihood of autism spectrum disorder and/or attention deficit hyperactivity disorder. *Journal of Autism and Developmental Disorders*, *50*(12), 4367–4384. https://doi.org/10.1007/s10803-020-04489-1

Begus, K., Southgate, V., & Gliga, T. (2015). Neural mechanisms of infant learning: Differences in frontal theta activity during object exploration modulate subsequent object recognition. *Biology Letters*, *11*(5), 20150041. https://doi.org/10.1098/rsbl.2015.0041

Belmonte, M. K., Saxena-Chandhok, T., Cherian, R., Muneer, R., George, L., & Karanth, P. (2013). Oral motor deficits in speech-impaired children with autism. *Frontiers in Integrative Neuroscience*, *7*. https://doi.org/10.3389/fnint.2013.00047

Bennett, T., Szatmari, P., Bryson, S., Volden, J., Zwaigenbaum, L., Vaccarella, L., … Boyle, M. (2008). Differentiating autism and Asperger syndrome on the basis of language delay or impairment. *Journal of Autism and Developmental Disorders*, *38*(4), 616–625. https://doi.org/10.1007/s10803-007-0428-7

Bornstein, M. H., & Hendricks, C. (2012). Basic language comprehension and production in >100,000 young children from sixteen developing nations. *Journal of Child Language*, *39*(4), 899–918. https://doi.org/10.1017/S0305000911000407

Bosseler, A., Taulu, S., Pihko, E., Mäkelä, J., Imada, T., Ahonen, A., & Kuhl, P. (2013). Theta brain rhythms index perceptual narrowing in infant speech perception. *Frontiers in Psychology*, *4*. https://doi.org/10.3389/fpsyg.2013.00690

Chawarska, K., Macari, S., Powell, K., DiNicola, L., & Shic, F. (2016). Enhanced social attention in female infant siblings at risk for autism. *Journal of the American Academy of Child and Adolescent Psychiatry*, *55*(3), 188–195. https://doi.org/10.1016/j.jaac.2015.11.016

Chawarska, K., MacAri, S., & Shic, F. (2012). Context modulates attention to social scenes in toddlers with autism. *Journal of Child Psychology and Psychiatry*, *53*(8), 903–913. https://doi.org/10.1111/j.1469-7610.2012.02538.x

Chawarska, K., Macari, S., & Shic, F. (2013). Decreased spontaneous attention to social scenes in 6-month-old infants later diagnosed with autism spectrum disorders. *Biological Psychiatry*, *74*(3), 195–203. https://doi.org/10.1016/j.biopsych.2012.11.022

Choi, B., Leech, K. A., Tager-Flusberg, H., & Nelson, C. A. (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*(1), 14–14. https://doi.org/10.1016/j.ejca.2011.06.019

Constantino, J. N. (2019). Early behavioral indices of inherited liability to autism. *Pediatric Research*, *85*(2), 127–133. https://doi.org/10.1038/s41390-018-0217-3

Constantino, J. N., Kennon-McGill, S., Weichselbaum, C., Marrus, N., Haider, A., Glowinski, A. L., … Jones, W. (2017). Infant viewing of social scenes is under genetic control and is atypical in autism. *Nature*, *547*(7663), 340–344. https://doi.org/10.1038/nature22999

Crnic, K. A., Ragozin, A. S., Greenberg, M. T., Robinson, N. M., & Basham, R. B. (1983). Social interaction and developmental competence of preterm and full-term infants during the first year of life. *Child Development*, *54*(5), 1199–1199. https://doi.org/10.2307/1129675

Davidson, M. M., & Ellis Weismer, S. (2017). A Discrepancy in comprehension and production in early language development in ASD: Is it clinically relevant? *Journal of Autism and Developmental Disorders*, *47*(7), 2163–2175. https://doi.org/10.1007/s10803-017-3135-z

Dawson, G., Rieder, A. D., & Johnson, M. H. (2023). Prediction of autism in infants: Progress and challenges. *The Lancet. Neurology*, *22*(3), 244–254. https://doi.org/10.1016/S1474-4422(22)00407-0

Dickinson, A., Daniel, M., Marin, A., Gaonkar, B., Dapretto, M., McDonald, N. M., & Jeste, S. (2021). Multivariate neural connectivity patterns in early infancy predict later autism symptoms. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *6*(1), 59–69. https://doi.org/10.1016/j.bpsc.2020.06.003

Dickinson, A., Varcin, K. J., Sahin, M., Nelson III, C. A., & Jeste, S. S. (2019). Early patterns of functional brain development associated with autism spectrum disorder in tuberous sclerosis complex. *Autism Research*, *12*(12), 1758–1773. https://doi.org/10.1002/aur.2193

Eldevik, S., Hastings, R. P., Hughes, J. C., Jahr, E., Eikeseth, S., & Cross, S. (2010). Using participant data to extend the evidence base for intensive behavioral intervention for children with autism. *American Journal on Intellectual and Developmental Disabilities*, *115*(5), 381–405. https://doi.org/10.1352/1944-7558-115.5.381

Ellis Weismer, S., & Kover, S. T. (2015). Preschool language variation, growth, and predictors in children on the autism spectrum. *Journal of Child Psychology and Psychiatry*, *56*(12), 1327–1337. https://doi.org/10.1111/jcpp.12406

Ellis Weismer, S., Lord, C., Esler, A., Weismer, S. E., Lord, C., & Esler, A. (2010). Early language patterns of toddlers on the autism spectrum compared to toddlers with developmental delay. *Journal of Autism and Developmental Disorders*, *40*(10), 1259–1273. https://doi.org/10.1007/s10803-010-0983-1

Elsabbagh, M., Fernandes, J., Jane Webb, S., Dawson, G., Charman, T., & Johnson, M. H. (2013). disengagement of visual attention in infancy is associated with emerging autism in toddlerhood. *Biological Psychiatry*, *74*(3), 189–194. https://doi.org/10.1016/j.biopsych.2012.11.030

Elsabbagh, M., & Johnson, M. H. (2016). Autism and the social brain: The first-year puzzle. *Biological Psychiatry*, *80*(2), 94–99. https://doi.org/10.1016/j.biopsych.2016.02.019

Elsabbagh, M., Volein, A., Holmboe, K., Tucker, L., Csibra, G., Baron-Cohen, S., … Johnson, M. H. (2009). Visual orienting in the early broader autism phenotype: Disengagement and facilitation. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *50*(5), 637–642. https://doi.org/10.1111/j.1469-7610.2008.02051.x

FDA-NIH Biomarker Working Group. (2020). *BEST (Biomarkers, EndpointS, and other Tools) Resource*. Silver Spring.

Fenson, L., Dale, P. S., Reznick, J. S., Bates, E., Thal, D. J., Pethick, S. J., … Stiles, J. (1994). Variability in early communicative development. *Monographs of the Society for Research in Child Development*, *59*(5), i–185. https://doi.org/10.2307/1166093

Flanagan, H. E., Perry, A., & Freeman, N. L. (2012). Effectiveness of large-scale community-based Intensive Behavioral Intervention: A waitlist comparison study exploring outcomes and predictors. *Research in Autism Spectrum Disorders*, *6*(2), 673–682. https://doi.org/10.1016/j.rasd.2011.09.011

Gabard-Durnam, L. J., Wilkinson, C., Levin, A. R., Nelson, C. A., Kapur, K., & Tager-Flusberg, H. (2019). Longitudinal EEG power in the first postnatal year differentiates autism outcomes. *Nature Communications*, *10*(1), 4188–4188. https://doi.org/10.1038/s41467-019-12202-9

Gernsbacher, M. A., Sauer, E. A., Geye, H. M., Schweigert, E. K., & Hill Goldsmith, H. (2008). Infant and toddler oral- and manual-motor skills predict later speech fluency in autism. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *49*(1), 43–50. https://doi.org/10.1111/j.1469-7610.2007.01820.x

Gillespie-Lynch, K., Sepeta, L., Wang, Y., Marshall, S., Gomez, L., Sigman, M., & Hutman, T. (2012). Early childhood predictors of the social competence of adults with autism. *Journal of Autism and Developmental Disorders*, *42*(2), 161–174. https://doi.org/10.1007/s10803-011-1222-0

Giraud, A.-L., & Poeppel, D. (2012). Cortical oscillations and speech processing: Emerging computational principles and operations. *Nature Neuroscience*, *15*(4), 511–517. https://doi.org/10.1038/nn.3063

Granpeesheh, D., Dixon, D. R., Tarbox, J., Kaplan, A. M., & Wilke, A. E. (2009). The effects of age and treatment intensity on behavioral intervention outcomes for children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *3*(4), 1014–1022. https://doi.org/10.1016/j.rasd.2009.06.007

Grzadzinski, R., Amso, D., Landa, R., Watson, L., Guralnick, M., Zwaigenbaum, L., … Piven, J. (2021). Pre-symptomatic intervention for autism spectrum disorder (ASD): Defining a

research agenda. *Journal of Neurodevelopmental Disorders*, *13*(1), 49. https://doi.org/10.1186/s11689-021-09393-y

Guy, J., Mottron, L., Berthiaume, C., & Bertone, A. (2019). A developmental perspective of global and local visual perception in autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *49*(7), 2706–2720. https://doi.org/10.1007/s10803-016-2834-1

Haartsen, R., Charman, T., Pasco, G., Johnson, M. H., & Jones, E. J. H. (2022). Modulation of EEG theta by naturalistic social content is not altered in infants with family history of autism. *Scientific Reports*, *12*(1), 20758. https://doi.org/10.1038/s41598-022-24870-7

Habayeb, S., Tsang, T., Saulnier, C., Klaiman, C., Jones, W., Klin, A., & Edwards, L. A. (2021). Visual traces of language acquisition in toddlers with autism spectrum disorder during the second year of life. *Journal of Autism and Developmental Disorders*, *51*(7), 2519–2530. https://doi.org/10.1007/s10803-020-04730-x

Hatch, B., Iosif, A.-M., Chuang, A., de la Paz, L., Ozonoff, S., & Miller, M. (2021). Longitudinal differences in response to name among infants developing ASD and risk for ADHD. *Journal of Autism and Developmental Disorders*, *51*(3), 827–836. https://doi.org/10.1007/s10803-020-04369-8

Hazlett, H. C., Gu, H., Munsell, B. C., Kim, S. H., Styner, M., Wolff, J. J., … Piven, J. (2017). Early brain development in infants at high risk for autism spectrum disorder. *Nature*, *542*(7641), 348–351. https://doi.org/10.1038/nature21369

Herlihy, L., Knoch, K., Vibert, B., & Fein, D. (2015). Parents' first concerns about toddlers with autism spectrum disorder: Effect of sibling status. *Autism*, *19*(1), 20–28. https://doi.org/10.1177/1362361313509731

Hillairet de Boisferon, A., Tift, A. H., Minar, N. J., & Lewkowicz, D. J. (2018). The redeployment of attention to the mouth of a talking face during the second year of life. *Journal of Experimental Child Psychology*, *172*, 189–200. https://doi.org/10.1016/j.jecp.2018.03.009

Howlin, P., Mawhood, L., & Rutter, M. (2000). Autism and developmental receptive language disorder—a follow-up comparison in early adult life. II: Social, behavioural, and psychiatric outcomes. *Journal of Child Psychology and Psychiatry*, *41*(5), 561–578.

Howlin, P., Moss, P., Savage, S., & Rutter, M. (2013). Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *Journal of the American Academy of Child & Adolescent Psychiatry*, *52*(6), 572-581.e1. https://doi.org/10.1016/j.jaac.2013.02.017

Hudry, K., Chandler, S., Bedford, R., Pasco, G., Gliga, T., Elsabbagh, M., … Charman, T. (2014). Early language profiles in infants at high-risk for autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *44*(1), 154–167. https://doi.org/10.1007/s10803-013-1861-4

Hudry, K., Leadbitter, K., Temple, K., Slonims, V., McConachie, H., Aldred, C., … Charman, T. (2010). Preschoolers with autism show greater impairment in receptive compared with expressive language abilities. *International Journal of Language and Communication Disorders*, *45*(6), 681–690. https://doi.org/10.3109/13682820903461493

Jansson-Verkasalo, E., Ruusuvirta, T., Huotilainen, M., Alku, P., Kushnerenko, E., Suominen, K., … Hallman, M. (2010). Atypical perceptual narrowing in prematurely born infants is associated with compromised language acquisition at 2 years of age. *BMC Neuroscience*, *11*, 88. https://doi.org/10.1186/1471-2202-11-88

Johnson, M. H., Jones, E. J. H., & Gliga, T. (2015). Brain adaptation and alternative developmental trajectories. *Development and Psychopathology*, *27*(2), 425–442. https://doi.org/10.1017/S0954579415000073

Jones, E. J. H., Gliga, T., Bedford, R., Charman, T., & Johnson, M. H. (2014). Developmental pathways to autism: A review of prospective studies of infants at risk. *Neuroscience & Biobehavioral Reviews*, *39*, 1–33. https://doi.org/10.1016/j.neubiorev.2013.12.001

Jones, E. J. H., Venema, K., Lowy, R., Earl, R. K., & Webb, S. J. (2015). Developmental changes in infant brain activity during naturalistic social experiences. *Developmental Psychobiology*, *57*(7), 842–853. https://doi.org/10.1002/dev.21336

Jones, W., & Klin, A. (2013). Attention to eyes is present but in decline in 2–6-month-old infants later diagnosed with autism. *Nature*, *504*(7480), 427–431. https://doi.org/10.1038/nature12715

Karmiloff-Smith, A. (2009). Nativism versus neuroconstructivism: Rethinking the study of developmental disorders. *Developmental Psychology*, *45*(1), 56–63. https://doi.org/10.1037/a0014506

Karp, E. A., Ibañez, L. V., Warren, Z., & Stone, W. L. (2017). Brief Report: What drives parental concerns about their 18-month-olds at familial risk for autism spectrum disorder? *Journal of Autism and Developmental Disorders*, *47*(5), 1535–1541. https://doi.org/10.1007/s10803-017-3060-1

Kerr-Wilson, C. O., Mackay, D. F., Smith, G. C. S., & Pell, J. P. (2012). Meta-analysis of the association between preterm delivery and intelligence. *Journal of Public Health*, *34*(2), 209–216. https://doi.org/10.1093/pubmed/fdr024

Kim, S. H., Bal, V. H., & Lord, C. (2018). Longitudinal follow-up of academic achievement in children with autism from age 2 to 18. *Journal of Child Psychology and Psychiatry*, *59*(3), 258–267. https://doi.org/10.1111/jcpp.12808

Klin, A., Lin, D. J., Gorrindo, P., Ramsay, G., & Jones, W. (2009). Two-year-olds with autism orient to non-social contingencies rather than biological motion. *Nature*, *459*(7244), 257–261. https://doi.org/10.1038/nature07868

Klin, A., Micheletti, M., Klaiman, C., Shultz, S., Constantino, J. N., & Jones, W. (2020). Affording autism an early brain development re-definition. *Development and Psychopathology*, *32*(4), 1175–1189. https://doi.org/10.1017/S0954579420000802

Klin, A., Shultz, S., & Jones, W. (2015). Social visual engagement in infants and toddlers with autism: Early developmental transitions and a model of pathogenesis. *Neuroscience and Biobehavioral Reviews*, *50*, 189–203. https://doi.org/10.1016/j.neubiorev.2014.10.006

Kuhl, P. K. (2011). Social mechanisms in early language acquisition: Understanding integrated brain systems supporting language. *The Oxford Handbook of Social Neuroscience.*, 649–667.

Lewkowicz, D. J., & Hansen-Tift, A. M. (2012). Infants deploy selective attention to the mouth of a talking face when learning speech. *Proceedings of the National Academy of Sciences*, *109*(5), 1431–1436. https://doi.org/10.1073/pnas.1114783109

Luyster, R. J., Kadlec, M. B., Carter, A., Tager-Flusberg, H., Ae, R. J. L., Beth, M., … Tager-Flusberg, H. (2008). Language assessment and development in toddlers with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *38*(8), 1426–1438. https://doi.org/10.1007/s10803-007-0510-1

Maenner, M. J., Warren, Z., Williams, A. R., Amoakohene, E., Bakian, A. V., Bilder, D. A., … Shaw, K. A. (2023). Prevalence and characteristics of autism spectrum disorder among children aged 8 years—Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2020. *MMWR Surveillance Summaries*, *72*(2), 1–14. https://doi.org/10.15585/mmwr.ss7202a1

McDaniel, J., Yoder, P., Woynaroski, T., & Watson, L. R. (2018). Predicting receptive–expressive vocabulary discrepancies in preschool children with autism spectrum disorder. *Journal of Speech, Language, and Hearing Research*, *61*(6), 1426–1439. https://doi.org/10.1044/2018_JSLHR-L-17-0101

McMahon, C. R., Malesa, E. E., Yoder, P. J., & Stone, W. L. (2007). Parents of children with autism spectrum disorders have merited concerns about their later-born infants. *Research and Practice for Persons with Severe Disabilities*, *32*(2), 154–160. https://doi.org/10.2511/rpsd.32.2.154

McPartland, J. C. (2016). Considerations in biomarker development for neurodevelopmental disorders. *Current Opinion in Neurology*, *29*(2), 118–122. https://doi.org/10.1097/WCO.0000000000000300

McPartland, J. C. (2017). Developing clinically practicable biomarkers for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *47*(9), 2935–2937. https://doi.org/10.1007/s10803-017-3237-7

Orekhova, E. V., Elsabbagh, M., Jones, E. J., Dawson, G., Charman, T., Johnson, M. H., & The BASIS Team. (2014). EEG hyper-connectivity in high-risk infants is associated with later autism. *Journal of Neurodevelopmental Disorders*, *6*(1), 40. https://doi.org/10.1186/1866-1955-6-40

Orekhova, E. V., Stroganova, T. A., & Posikera, I. N. (1999). Theta synchronization during sustained anticipatory attention in infants over the second half of the first year of life. *International Journal of Psychophysiology*, *32*(2), 151–172. https://doi.org/10.1016/S0167-8760(99)00011-2

Ozonoff, S., Young, G. S., Landa, R. J., Brian, J., Bryson, S., Charman, T., … Iosif, A.-M. (2015). Diagnostic stability in young children at risk for autism spectrum disorder: A Baby Siblings Research Consortium study. *Journal of Child Psychology and Psychiatry*, *56*(9), 988–998. https://doi.org/10.1111/jcpp.12421

Panganiban, J., & Kasari, C. (2022). Super responders: Predicting language gains from JASPER among limited language children with autism spectrum disorder. *Autism Research*, *15*(8), 1565–1575. https://doi.org/10.1002/aur.2727

Peña, M., Pittaluga, E., & Mehler, J. (2010). Language acquisition in premature and full-term infants. *Proceedings of the National Academy of Sciences*, *107*(8), 3823–3828. https://doi.org/10.1073/pnas.0914326107

Peña, M., Werker, J., & Dehaene-Lambertz, G. (2012). Earlier speech exposure does not accelerate speech acquisition. *Journal of Neuroscience*, *32*(33), 11159–11163. https://doi.org/10.1523/JNEUROSCI.6516-11.2012

Perdue, K. L., Edwards, L. A., Tager-Flusberg, H., Nelson, C. A., Charles, ·, & Nelson, A. (2017). Differing developmental trajectories in heart rate responses to speech stimuli in infants at high and low risk for autism spectrum disorder. *Journal of Autism and Developmental Disorders*, *47*(8), 2434–2442. https://doi.org/10.1007/s10803-017-3167-4

Pierce, K., Marinero, S., Hazin, R., McKenna, B., Barnes, C. C., & Malige, A. (2016). Eye tracking reveals abnormal visual preference for geometric images as an early biomarker of an autism spectrum disorder subtype associated with increased symptom severity. *Biological Psychiatry*, *79*(8), 657–666. https://doi.org/10.1016/j.biopsych.2015.03.032

Pierce, K., Wen, T. H., Zahiri, J., Andreason, C., Courchesne, E., Barnes, C. C., … Cheng, A. (2023). Level of attention to motherese speech as an early marker of autism spectrum disorder. *JAMA Network Open*, *6*(2), e2255125. https://doi.org/10.1001/jamanetworkopen.2022.55125

Ramsey, R. K., Nichols, L., Ludwig, N. N., Fein, D., Adamson, L. B., & Robins, D. L. (2018). Brief Report: Sex differences in parental concerns for toddlers with autism risk. *Journal of Autism and Developmental Disorders*, *48*(12), 4063–4069. https://doi.org/10.1007/s10803-018-3583-0

Reinhartsen, D. B., Tapia, A. L., Watson, L., Crais, E., Bradley, C., Fairchild, J., … Daniels, J. (2019). Expressive dominant versus receptive dominant language patterns in young children: Findings from the Study to Explore Early Development. *Journal of Autism and Developmental Disorders*, *49*(6), 2447–2460. https://doi.org/10.1007/s10803-019-03999-x

Rogers, S. J., Estes, A., Lord, C., Vismara, L., Winter, J., Fitzpatrick, A., … Dawson, G. (2012). Effects of a brief Early Start Denver model (ESDM)-based parent intervention on

toddlers at risk for autism spectrum disorders: A randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *51*(10), 1052–1065. https://doi.org/10.1016/j.jaac.2012.08.003

Rogers, S. J., Hepburn, S. L., Stackhouse, T., & Wehner, E. (2003). Imitation performance in toddlers with autism and those with other developmental disorders. *Journal of Child Psychology and Psychiatry*, *5*, 763–781.

Ruzzo, E. K., Pérez-Cano, L., Jung, J.-Y., Wang, L.-K., Kashef-Haghighi, D., Hartl, C., … Wall, D. P. (2019). Inherited and de novo genetic risk for autism impacts shared networks. *Cell*, *178*(4), 850-866.e26. https://doi.org/10.1016/j.cell.2019.07.015

Sacrey, L. A., Zwaigenbaum, L., Bryson, S., Brian, J., Smith, I. M., Roberts, W., … Armstrong, V. (2015). Can parents' concerns predict autism spectrum disorder? A prospective study of high-risk siblings from 6 to 36 months of age. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*(6), 470–478. https://doi.org/10.1016/j.jaac.2015.03.014

Shen, M. D., Kim, S. H., McKinstry, R. C., Gu, H., Hazlett, H. C., Nordahl, C. W., … Gu, H. (2017). Increased extra-axial cerebrospinal fluid in high-risk infants who later develop autism. *Biological Psychiatry*, *82*(3), 186–193. https://doi.org/10.1016/j.biopsych.2017.02.1095

Swanson, M. R., Donovan, K., Paterson, S., Wolff, J. J., Parish-Morris, J., Meera, S. S., … IBIS Network. (2019). Early language exposure supports later language skills in infants with and without autism. *Autism Research*, *12*(12), 1784–1795. https://doi.org/10.1002/aur.2163

Swanson, M. R., Shen, M. D., Wolff, J. J., Elison, J. T., Emerson, R. W., Styner, M. A., … Gu, H. (2017). Subcortical brain and behavior phenotypes differentiate infants with autism versus language delay. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, *2*(8), 664–672. https://doi.org/10.1016/j.bpsc.2017.07.007

Szatmari, P., Bryson, S. E., Boyle, M. H., Streiner, D. L., & Duku, E. (2003). Predictors of outcome among high functioning children with autism and Asperger syndrome. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *44*(4), 520–528. https://doi.org/10.1111/1469-7610.00141

Talbott, M. R., Nelson, C. A., & Tager-Flusberg, H. (2015). Diary reports of concerns in mothers of infant siblings of children with autism across the first year of life. *Journal of Autism and Developmental Disorders*, *45*(7), 2187–2199. https://doi.org/10.1007/s10803-015-2383-z

Thurm, A., Lord, C., Lee, L.-C. C., & Newschaffer, C. (2007). Predictors of language acquisition in preschool children with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *37*(9), 1721–1734. https://doi.org/10.1007/s10803-006-0300-1

van Noort-van der Spek, I. L., Franken, M.-C. J. P., & Weisglas-Kuperus, N. (2012). Language functions in preterm-born children: A systematic review and meta-analysis. *Pediatrics*, *129*(4), 745–754. https://doi.org/10.1542/peds.2011-1728

Vivanti, G., Dissanayake, C., & The Victorian ASELCC Team. (2016). outcome for children receiving the Early Start Denver Model before and after 48 months. *Journal of Autism and Developmental Disorders*, *46*(7), 2441–2449. https://doi.org/10.1007/s10803-016-2777-6

West, K. L. (2019). Infant motor development in autism spectrum disorder: A synthesis and meta-analysis. *Child Development*, *90*(6), 2053–2070. https://doi.org/10.1111/cdev.13086

Wolff, Jason J., Gerig, G., Lewis, J. D., Soda, T., Styner, M. A., Vachet, C., … Piven, J. (2015). Altered corpus callosum morphology associated with autism over the first 2 years of life. *Brain*, *138*(7), 2046–2058. https://doi.org/10.1093/brain/awv118

Wolff, Jason JJ, Gu, H., Gerig, G., Elison, J. T., Styner, M., Gouttard, S., … Piven, J. (2012). Differences in white matter fiber tract development present from 6 to 24 months in infants with autism. *American Journal of Psychiatry*, *169*, 589–600. https://doi.org/10.1176/appi.ajp.2011.11091447

Zwaigenbaum, L., Brian, J., Smith, I. M., Sacrey, L.-A. R., Franchini, M., Bryson, S. E., … Roncadin, C. (2021). Symptom trajectories in the first 18 months and autism risk in a prospective high-risk cohort. *Journal of Child Psychology and Psychiatry*, *62*(12), 1435–1443. https://doi.org/10.1111/jcpp.13417